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**14th International Symposium
on Hodgkin Lymphoma**

ABSTRACT BOOK

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Topic: ABSTRACT

T001: CHOP/miniCHOP and Tiselimuzab in Elderly patients with classical Hodgkin Lymphoma (cHL). A report of the phase II CATER-HL trial (HD12) from the Australasian Lymphoma and Leukaemia Group (ALLG)

Tara Cochrane^{1,2}, Sze Ting Lee³, Robin Gasiorowski^{4,5}, Shane A. Gangatharan^{6,7}, Fernando Roncolato⁸, William Ep Renwick^{9,10}, Jock Simpson^{11,12}, Amanda Johnston¹³, Uwe Hahn^{14,15}, Philip Wong^{16,17}, Masa Lasica¹⁸, Ann Solterbeck¹⁹, Robert Traficante¹⁹, Sally Mapp^{20,21}, Bianca Devitt^{22,23}, Dhvani Pandya²⁴, Julia Carlson²⁴, Tracey Gerber²⁴, Mark Hertzberg²⁵, Eliza Hawkes^{26,27}, Colm Keane^{20,28}

¹Gold Coast University Hospital, Southport, Queensland, Australia, ²Griffith University, School of Medicine and Dentistry, Griffith Health, Nathan, Australia, ³Dept of Molecular Imaging and Therapy, Austin Health, Melbourne, Australia, ⁴Concord Hospital, Sydney, Australia, ⁵University of Sydney, Australia, ⁶Fiona Stanley Hospital, Murdoch, Australia, ⁷University of Western Australia, Crawley, Australia, ⁸St George Hospital, Sydney, Australia, ⁹Western Health, Footscray, Australia, ¹⁰University of Melbourne, Melbourne Australia, ¹¹Mid North Coast Cancer Institute, Port Macquarie, Australia, ¹²University of UNSW, Sydney, Australia, ¹³Westmead Hospital, Sydney, Australia, ¹⁴Royal Adelaide Hospital and The Queen Elizabeth Hospital, Adelaide Australia, ¹⁵SA Pathology, Adelaide, Australia, ¹⁶Toowoomba Hospital, Toowoomba, Australia, ¹⁷University of Queensland, Rural Clinical School, Brisbane, Australia, ¹⁸St Vincent's Hospital, Melbourne, Australia, ¹⁹Statistical Revelations Pty Ltd, Ocean Grove, Australia, ²⁰Princess Alexandra Hospital, Brisbane, Australia, ²¹University of Queensland, Faculty of Medicine, Brisbane, Australia, ²²Eastern Health, Oncology, Box Hill, Australia, ²³Monash University Eastern Health Clinical School, Melbourne, Australia, ²⁴Australasian Lymphoma and Leukaemia Group, Melbourne Australia, ²⁵Prince of Wales Hospital, Randwick, Australia, ²⁶Olivia Newton John Cancer Research Institute at Austin Health, Melbourne, Australia, ²⁷Monash University, School of Public Health and Preventive Medicine, Melbourne, Australia, ²⁸University of Queensland, Frazer Institute, Brisbane, Australia

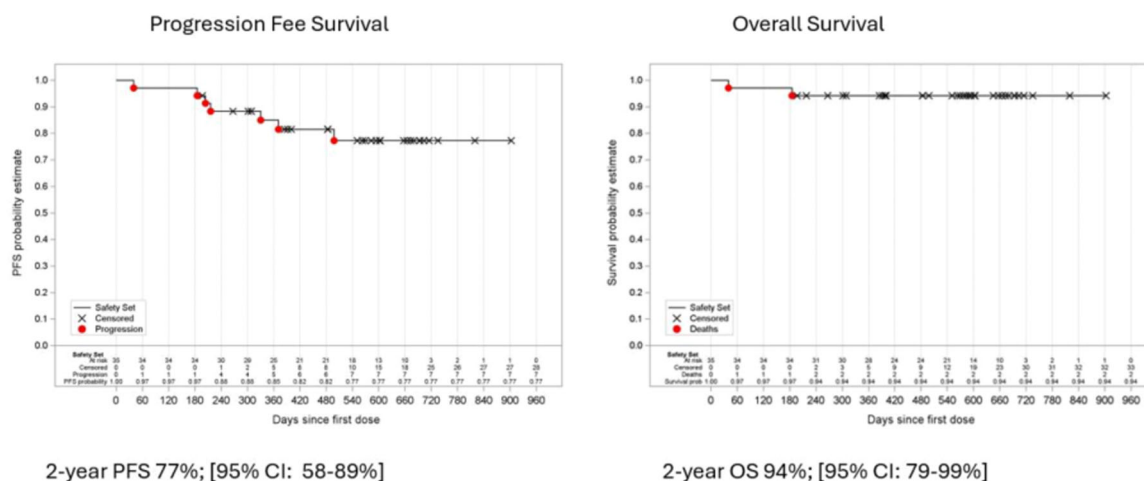


Figure 1: 2-year PFS and OS of the entire HD12 cohort.

Anti-PD-1 therapy with Adriamycin, vinblastine, dacarbazine (AVD) is effective in older patients (pts) with cHL with limited data in those ≥ 70 years. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) is active in older cHL pts but has not been combined with anti-PD-1.

Methods: CATER-HL (ALLG-HD12) is a single arm phase II study of anti-PD-1 agent, tiselimuzab (T), with CHOP or miniCHOP in older (≥ 61 years) pts with untreated cHL. Eligible pts were stage 2 unfavourable to stage 4, with no anthracycline/immunotherapy contraindications. T monotherapy (200 mg q3W) was given for 3 cycles, followed by T in combination with CHOP (or miniCHOP if aged >80 or frail) q3W for 4–6 cycles (T-CHOP[mini]). Radiotherapy (RT) or 4 extra doses of T was allowed for those with residual PET-CT avidity or if stage 2 (RT). Primary end points were complete remission (CR) and deliverability of T monotherapy (no grade 3/4 toxicity and no symptomatic progressive disease [PD]). Secondary end points were post-therapy overall response (ORR)/CR, PFS, OS and quality of life (QOL).

Results: 35 pts from 11 Australian sites were enrolled from May 2023–2025. Baseline characteristics: median age 74 years (range 63–90), ≥ 70 years 69%, male 66%, ECOG 0–1 86%, European ethnicity 77%, advanced stage 89%, EBER-ish positive 46%, median Charlson's co-morbidity score 4 (range 3–12). After T monotherapy the CR rate was 17% (ORR 69%); deliverability was 86%. 5 pts ceased T monotherapy prematurely: 2 from immune related adverse event (IRAE) of grade 4 hepatitis and 3 for other reasons. 30 pts commenced T-CHOP[mini]

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(CHOP:70%, miniCHOP:30%). After 2 cycles of T-CHOP[mini] the ORR was 87% (CR 50%). At the end of T-CHOP[mini], ORR was 87% (CR 67%). Median follow up is 562 days (range 24–902). Estimated 2-year PFS/OS is 77%/94% (Figure 1) and 81%/100% for the 30 pts who commenced T-CHOP(mini). Grade 3/4 treatment emergent AEs affected 51% of pts: infection 17%, hepatitis 11%, fever 9% peripheral neuropathy 6%, confusion 6%. IRAEs affected 37% pts: thyroid dysfunction 14%, hepatitis 14%, raised creatinine kinase 3%, pancreatitis 3%, pruritis 3%. 2 pts died from PD, there was no treatment related mortality. QOL scores improved by 10% after T monotherapy, and 7% post therapy.

Conclusion: T monotherapy is deliverable and demonstrated early metabolic response. Sequential treatment with T-CHOP[mini] is well tolerated with promising PFS and OS in this predominantly over 70 year old cohort.

T002: Simplified Geriatric Assessment (sGA) in Older Patients With Classical Hodgkin Lymphoma (cHL): The Prospective ELDHL Project of the Fondazione Italiana Linfomi (FIL)

Vittorio Ruggero Zilioli¹, Francesco Merli², Alessandra Tucci³, Stefano Luminari^{2,4}, Giuseppe Colloca⁵, Cristina Muzi¹, Benedetta Puccini⁶, Chiara Paganì³, Candida Vitale⁷, Francesca Gaia Rossi⁸, Erika Meli¹, Anna Guidetti⁹, Simone Maifredi³, Dario Marino¹⁰, Alberto Fabbri¹¹, Nilla Maschio¹², Manuel Gotti¹³, Andrea Bernardelli¹⁴, Salvatrice Mancuso¹⁵, Anna Mele¹⁶, Guido Gini¹⁷, Ilaria Del Giudice¹⁸, Sara Bigliardi¹⁹, Elisabetta Scarpa²⁰, Barbara Botto²¹, Gloria Margiotta-Casaluci²², Andrea Maria Soccodato²³, Monica Tani²⁴, Arcangelo Liso²⁵, Michał Kurlapski²⁶, Leonardo Flenghi²⁷, Anna Merli²⁸, Antonello Sica²⁹, Francesca Ricci³⁰, Francesca Perutelli⁷, Roberta Battistini³¹, Andrés José María Ferreri³², Daniele Laszlo³³, Francesco Gaudio³⁴, Manuela Zanni³⁵, Emanuele Cencini¹¹, Valentina Tabanelli³⁶, Luca Guerra³⁷, Claudio Agostinelli^{38,39}, Luigi Marcheselli⁴⁰, Caterina Mammi⁴¹, Michele Spina⁴², Annalisa Arcani⁴³

¹Division of Hematology, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, ²Hematology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy, ³Hematology Division, ASST Spedali Civili di Brescia, Brescia, Italy, ⁴Department CHIMOMO, University of Modena and Reggio Emilia, Modena, Italy, ⁵Oncological Frailty Unit. Department of Imaging and Radio-Oncology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy, ⁶Lymphoma Unit, Hematology Department, Careggi Hospital and University of Florence, Firenze, Italy, ⁷Department of Molecular Biotechnology and Health Sciences, University of Torino and University Division of Hematology, A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy, ⁸UO Ematologia, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico di Milano, Milano, Italy, ⁹Division of Hematology and Stem Cell Transplantation, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, University of Milano, Milano, Italy, ¹⁰Transplant Unit, Veneto Institute of Oncology IOV IRCCS, Padova, Italy, ¹¹Unit of Hematology, Azienda Ospedaliera Universitaria Senese and University of Siena, Siena, Italy, ¹²Onco Hematology Unit, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy, ¹³Division of Hematology Fondazione IRCCS Policlinico S. Matteo Pavia Italy, ¹⁴Hematology and Bone Marrow Transplant Unit, General Medicine Department, Azienda Ospedaliera Universitaria Integrata di Verona, Verona, Italy, ¹⁵Dipartimento di Promozione della Salute, Materno-Infantile, di Medicina Interna e Specialistica di Eccellenza "G. D'Alessandro", Università degli Studi di Palermo, Palermo, Italy, ¹⁶Department of Hematology and Bone Marrow Transplant, Hospital Card. G. Panico, Tricase, Italy, ¹⁷Clinic of Hematology AOU delle Marche- Polytechnic University of Marche, Ancona, Italy, ¹⁸Division of Hematology, Department of Translational and Precision Medicine, Sapienza University, Rome, Italy, ¹⁹Oncology Unit Azienda USL di Modena, Area Sud Sede di Sassuolo, Sassuolo Italy, ²⁰Hematology Unit, General Hospital Ca' Foncello, Treviso, Italy, ²¹Division of Hematology, Città della Salute e della Scienza Hospital and University, Torino, Italy, ²²Division of Hematology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy, ²³UOC Internal Medicine - Hematology Unit, Azienda Ospedaliera della Valtellina e della Valchiavenna, Sondrio, Italy, ²⁴Department of Hematology, Ospedale Santa Maria delle Croci, Ravenna, Italy, ²⁵Department of Medicine and Surgery, University of Perugia and Hematology/Oncology Unit, Terni Hospital, Terni, Italy, ²⁶Department of Hematology and Transplantation, University Clinical Centre, Medical University of Gdańsk, Gdańsk, Poland, ²⁷Hematology, Santa Maria della Misericordia Hospital, Perugia, Italy, ²⁸U.O. Ematologia Ospedale degli Infermi di Rimini, Rimini, Italy, ²⁹Department of Precision Medicine University of Campania "Luigi Vanvitelli", Naples, Via S. Pansini 5, 80131 Naples, Italy, ³⁰Department of Oncology and Hematology, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy, ³¹UOC Hematology and Stem Cell Transplantation, AO San Camillo Forlanini, Roma, Italy, ³²Università Vita-Salute San Raffaele, Milano - Programma Strategico Linfomi, IRCCS Ospedale San Raffaele, Milano, Italy, ³³Department of Medical Oncology, Humanitas Gavazzeni, Bergamo, Italy, ³⁴Bari Hematology and Stem Cell Transplantation Unit, AOU Consorziale Policlinico, Bari, Italy, ³⁵Hematology Unit, Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, ³⁶Division of Haematopathology, IEO, European Institute of Oncology IRCCS, Milano, Italy, ³⁷Department of Nuclear Medicine, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, ³⁸Haematopathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, ³⁹Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, Italy, ⁴⁰Fondazione Italiana Linfomi Onlus, Modena, Italy, ⁴¹Gruppo Amici dell'Ematologia GRADE Onlus Foundation, Reggio Emilia, Italy, ⁴²Division of Medical Oncology and Immune-Related Tumors, Centro di Riferimento Oncologico di Aviano IRCCS, Italy, ⁴³Hematology Unit, Ospedale Guglielmo da Saliceto, Piacenza, Italy

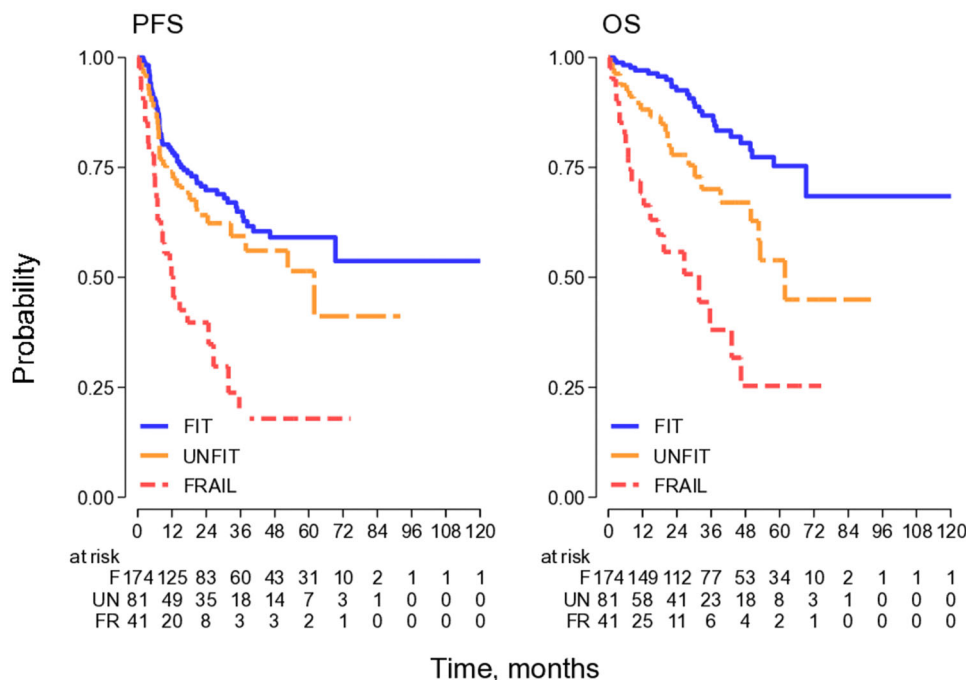


Figure 1: Progression Free Survival (PFS) and Overall Survival (OS) by simplified Geriatric Assessment (sGA).

Background: Older patients (pts) with cHL generally have a poor prognosis, due to both inferior disease control and increased treatment(tx)-related toxicity. Recently, novel first-line txs have improved pts outcomes through enhanced efficacy. In this context, accurate stratification of functional status is crucial to identify pts who may benefit from standard versus alternative txs. The FIL sGA is based on chronological age and on determination of Activities of Daily Living (ADL), Instrumental ADL and Cumulative Illness Rating Scale for Geriatrics (CIRS-G). It is an easy-to-use tool that has proven to effectively stratify pts in the setting of DLBCL.

Purpose: To prospectively validate the use of sGA at diagnosis for older pts with cHL.

Methods: We conducted the prospective ELDHL study including pts aged >64 years with cHL who underwent FIL-sGA before tx. Tx choice was left to the physician's discretion. The endpoints were Overall Survival (OS) and Progression Free Survival (PFS) with the aim of developing a potential new prognostic model.

Results: A total of 311 consecutive pts were analyzed (median age 74 years, range 65–91; 56% males). At baseline, 68% had advanced stage disease, 39% B symptoms, 34% extranodal sites, 10% bulky disease. According to sGA, pts were classified as fit (58%), unfit (27%) and frail (15%). Most pts received ABVD-like tx (95% of fit, 81% of unfit, and 50% of frail pts, respectively). In the whole cohort, Overall Response Rate (ORR) was 70.2%, with a Complete Response Rate (CRR) of 61.7%. At a median follow up of 39 months, 5-year PFS was 52% (95% CI, 44 to 58%), and 5-year OS 63% (95% CI, 55 to 71%). Outcomes significantly differed across sGA categories: ORR was 76%, 67% and 50% ($p = 0.010$), CRR 66%, 61% and 41% ($p = 0.021$), 5-year OS 75%, 54%, and 25% ($p < 0.001$), and 5-year PFS 59%, 51% and 18% ($p < 0.001$), in fit, unfit, and frail pts, respectively. After adjusting for Ann Arbor stage, in advanced stage cHL pts sGA stratification maintained its prognostic power in terms of both 5-year OS (70%, 47% and 11%; $p < 0.001$) and 5-year PFS (52%, 51% and 12%; $p < 0.001$), in fit, unfit and frail pts, respectively.

Conclusion: In older pts with cHL, the definition of fitness status by sGA allowed to stratify pts into three distinct categories (fit, unfit, and frail) associated with significantly different survival outcomes. The prognostic role of sGA was independent from other risk factors and particularly relevant for pts with advanced stage disease.

T003: Durable Remissions and Late Immune-Related Toxicities After Frontline Pembrolizumab + AVD in Classic Hodgkin Lymphoma

Ryan Lynch¹, Thomas Kuczmarski², Chaitra Ujjani¹, Christina Poh³, Edus Warren¹, Stephen Smith¹, Mazyar Shadman¹, Brian Till¹, Vikram Raghunathan¹, Yolanda Tseng¹, Hongyan Du¹, Heather Rasmussen¹, Jenna Voutsinas¹, Ajay Gopal¹

¹Fred Hutch Cancer Center, ²MaineHealth, ³City of Hope National Medical Center

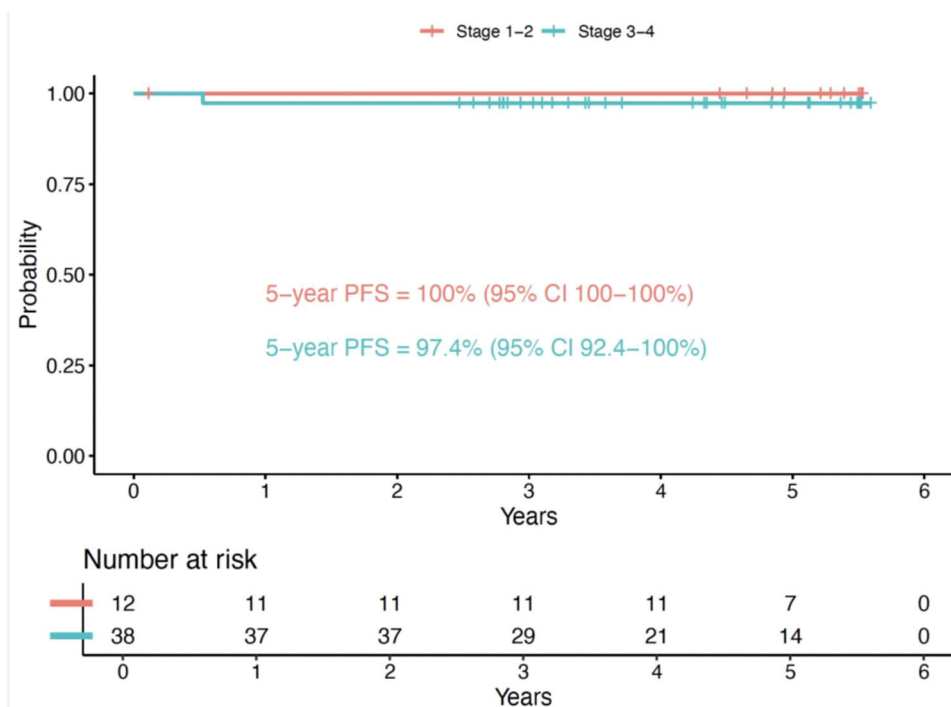


Figure 1: 5-year PFS stratified by early stage vs. advanced stage.

Introduction: We previously reported efficacy of frontline pembrolizumab + AVD in CHL (Lynch et al, Blood 2023; ASH 2024). With emergence of highly effective frontline regimens that omit checkpoint inhibitors, better characterization of immune-related adverse events (irAEs), including management required, is needed.

Methods: We analyzed additional long-term follow-up of patients with previously untreated CHL treated with pembrolizumab plus concurrent AVD, as previously described (NCT03331341). In addition to survival outcomes, we analyzed treatment-emergent irAEs during and after study therapy.

Results: At median follow-up of 4.8 years, 5-year progression-free survival (PFS) and overall survival (OS) were 98% (95% CI 94%–100%) and 100% (95% CI 100%–100%), respectively. Five-year PFS was 100% (95% CI 100%–100%) in early-stage and 97% (95% CI 92%–100%) in advanced-stage disease.

Forty-one patients (82%) experienced at least 1 irAE during APVD, most commonly ALT elevation (29, 58%), rash (19, 38%), AST elevation (16, 32%), and hypothyroidism (4, 8%). Six patients (12%) required oral corticosteroids for an irAE during treatment. One patient with Guillain-Barré syndrome required IVIG and prolonged hospitalization.

Ten patients (20%) experienced a new irAE at least 30 days after the last pembrolizumab dose and completion of study therapy. These emerged at median 67 days (range, 33–858). Two grade 4 late irAEs were observed (pneumonitis and adrenal insufficiency), both requiring prolonged hospitalization.

Other late irAEs included hypothyroidism (5, 10%) and single cases of anterior uveitis, arthritis, AST elevation, colitis, hyperthyroidism, psoriasis, and rash.

All irAEs during or after treatment resolved except adrenal insufficiency (1, 2%) and hypothyroidism (7, 14%), requiring indefinite corticosteroid and levothyroxine replacement, respectively.

Conclusion: APVD was highly active in untreated CHL, with durable remissions in nearly all treated patients. irAEs, including grade ≥ 3 events, occurred during and after study therapy. Although most were reversible, there were late irAEs including grade 4 events as well as endocrinopathies that will require lifelong supplementation. Discussion of risks and benefits relative to other effective frontline regimens is important when selecting therapy for untreated CHL.

P004: Low-dose nivolumab combined with AVD chemotherapy (Nivo40-AVD) for advanced classic Hodgkin lymphoma: interim results

Mobil Akhmedov¹, Pervin Zeynalova², Mariya Vernyuk¹, Sergey Semochkin¹, Liliya Khairullina¹, Irina Cherkashina¹, Alevtina Chervontseva¹, Vladimir Lunin¹, Alexander Fedenko¹, Andrey Kaprin¹

¹Hertsen Moscow Oncology Research Institute, ²Lapino Clinical Hospital

Background: Nivolumab plus AVD (N-AVD) is currently approved for newly diagnosed advanced-stage classical Hodgkin lymphoma (cHL). However, substantially lower nivolumab doses (0.1–0.33 mg/kg) have demonstrated clinical activity in relapsed/refractory settings. We evaluated the efficacy and safety of a low-dose nivolumab regimen (Nivo40-AVD) in untreated advanced cHL.

Methods: This is an interim analysis of an investigator-initiated phase II trial (NCT06984146). Eligible patients were ≥ 18 years with stage IIB disease with bulky mediastinal mass and/or extranodal involvement, or stage III–IV cHL, with adequate cardiac function and no history of autoimmune disease. Exclusion criteria were uncontrolled infection, decompensated organ failure unrelated to lymphoma, pregnancy, and inability to consent. Treatment consisted of six cycles of Nivo40-AVD (nivolumab 40 mg; doxorubicin 25 mg/m²; vinblastine 6 mg/m²; dacarbazine 375 mg/m² on days 1 and 15). PET/CT was performed after cycle 2 and at the end of treatment. Consolidative radiotherapy was permitted for partial response. The primary endpoint was 2-year progression-free survival (PFS); secondary endpoints included overall response rate (ORR), complete response (CR), overall survival (OS), and adverse events rate.

Results: At data cutoff, 35/54 patients were enrolled; 20 (57%) completed therapy and were evaluable. Median age was 36 years (range 19–73). Most patients had stage IV disease (55%), B-symptoms (80%), extranodal involvement (70%), and nodular sclerosis subtype (95%); 75% were female. EBV positivity was observed in 15%. Median nivolumab dose was 0.56 mg/kg (range 0.35–0.74). ORR was 100%, with CR in 90% of patients. At a median follow-up of 10 months, PFS was 100%. Grade 3–4 adverse events included neutropenia (65%) and transaminitis (10%).

Conclusions: Low-dose nivolumab combined with AVD is feasible and demonstrates promising efficacy as frontline therapy for advanced cHL. Follow-up is ongoing. Updated results will be presented at the meeting.

P005: Real-World Tolerability and Efficacy of BrECADD in Advanced-Stage Hodgkin Lymphoma: A Multicenter Brazilian Experience

Giovanna Peruzini¹, Matheus Garcia¹, Ruddy De Barros², Thiana De Moura³, Rafaella Samico⁴, Natalia Zing⁵, Raquel Brito⁶, Vanessa Bovolenta¹, Jayr Schimdt¹, Arthur Braga¹, Thais Fisher¹, Talita Silveira¹

¹AC Camargo Cancer Center, ²Centron, ³Hospital Clon, ⁴Hospital Câncer Muriaé, ⁵BP Hospital, ⁶UFUberaba

Background: Since the introduction of the ABVD and BEACOPP regimen, Hodgkin Lymphoma (HL) has achieved high cure rates. Since then, new therapeutic regimens have been investigated aiming to improve outcomes and reduce toxicity (mainly with intensive regimen), particularly in advanced-stage HL. In this context, the HD21 trial comparing BrECADD regimen (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone) with BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone), demonstrated lower toxicity, as well as improved 4-year progression-free survival (94.3% vs. 90.9%) and maintain overall survival (98.6% vs. 98.2%). The main treatment-related adverse events (AEs) include anemia, thrombocytopenia, neutropenia, and neuropathy, with dose reductions required due to AEs in 34% of patients treated with BEACOPP and 21% of those receiving BrECADD. These results suggest that the BrECADD combination may preserve or even improve therapeutic efficacy, while reducing the incidence of adverse events and, consequently, the need for dose modifications.

Aims: To describe the initial real-world data on the use of the BrECADD regimen for advanced-stage HL in Brazilian centers.

Methods: This is an observational, retrospective study conducted across six private Brazilian referral centers in Onco-Hematology. A total of 22 patients diagnosed and treated at these institutions between September 2023 and January 2026 were included.

Results: Among the 22 patients included, the first one was treated at sep/2023. Five had not yet completed the therapeutic protocol or realized final PET. The median age of the cohort was 36 years (range: 17–51 years), with 14 females and 8 males. Performance status was assessed using the Eastern Cooperative Oncology Group (ECOG) scale, with 100% of patients classified as ECOG 0 at treatment initiation. Regarding disease staging, most patients presented with advanced disease, with Ann Arbor stage IV observed in 68.2% (15 patients). The International Prognostic Score (IPS), 68.2% of patients had an IPS of 0–2, while 31.8% had an IPS $\geq$ 3. As preliminary results, 3/22 (13.63%) patients had iPET positive and realized 6 cycles of treatment. One of this patients had PET with Deauville 4 at the end of the treatment and was sent to radiotherapy (now is waiting for final evaluation). No one patient had refractory disease or relapse (this is a very premature real life cohort).

P006: BrECADD in Three Days: Condensing an Intensive First-Line Regimen in Classic Hodgkin Lymphoma

Christian Peter Jaworek^{1,2}, Maja Supprian^{1,2}, Paul J. Bröckelmann^{1,2,3}, Hishan Tharmaseelan^{1,2}, Justin Ferdinandus^{1,2}, Dennis Eichenauer^{1,2}, Anne Sophie Robertz^{1,2}, Janina Jablonski^{1,2}, Vincent Combüchen⁴, Jan-Oliver Staak¹, Karin Töpelt¹, Jan-Michel Heger¹, Jon Felix Rischewski¹, Jannik Stemler^{1,5}, Wolfram Klapper⁶, Bastian Von Tresckow⁷

¹University of Cologne, Faculty of Medicine and University Hospital of Cologne, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD), Cologne, Germany, ²German Hodgkin Study Group (GHSG), Cologne, Germany, ³MV Zentrum Hämatologie und Onkologie, Sachsenring 69, 50677 Cologne, Germany, ⁴University of Cologne, Faculty of Medicine and University Hospital Cologne, Institute of Transfusion Medicine, Cologne, Germany, ⁵Institute of Translational Research, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany, ⁶Department of Pathology, Hematopathology Section, University Hospital Schleswig-Holstein Campus, Kiel, Germany, ⁷Department of Hematology and Stem Cell Transplantation, West German Cancer Center, University Hospital Essen, University of Duisburg-Essen, Essen, Germany

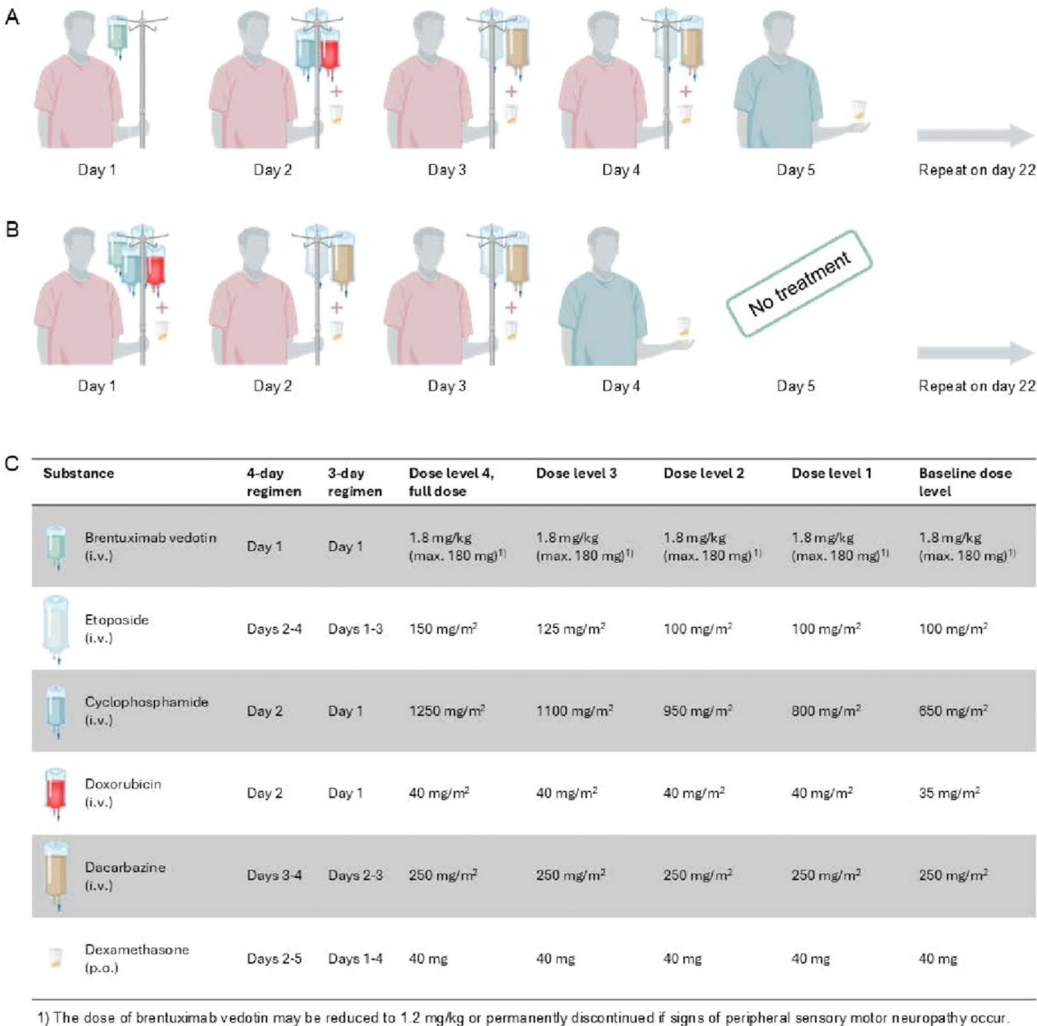


Figure 1: Comparison of 4-day versus 3-day BrECADD regimen. (A) Conventional 4-day BrECADD regimen, (B) Condensed 3-day BrECADD regimen, (C) Drug schedule and dosing for both regimens, including dose levels.

Intensive multi-agent treatment regimens have substantially improved outcomes in advanced-stage classic Hodgkin lymphoma (cHL). BrECADD is the first-line regimen that demonstrated the highest efficacy in cHL reported to date (Borchmann et al., Lancet 2024). The regimen combines brentuximab vedotin (BV) with etoposide, cyclophosphamide, doxorubicin, dacarbazine and dexamethasone given in 21-day intervals with cytotoxic agents during the first four days. Simplifying multi-day treatment schedules has the potential to reduce treatment burden and logistical demands in routine clinical practice. We thus developed a condensed BrECADD protocol with BV being administered alongside etoposide, cyclophosphamide, doxorubicin and dexamethasone on day 1 of each cycle, reducing i.v. administration days to only three (~25%). From January 2024 to February 2026, 22 patients were treated with the newly developed 3-day BrECADD protocol. Data was retrospectively collected from medical records for patients treated at the University Hospital in Cologne. Primary objective was to describe feasibility and safety. Secondary objectives included evaluation of treatment response, one-year-progression free survival (PFS) and one-year-overall survival (OS). A total of 96 treatment cycles were administered across the 22 patients. CTCAE Grade ≥ 3 adverse events occurred in 13 patients (59%), with hematological toxicities being most frequent. Five patients (23%) had grade ≥ 3 infections (3 viral, 2 bacterial), and 4 patients (18%) had febrile neutropenia without pathogen detection. After 2 treatment cycles of BrECADD, a complete remission (CR) was achieved in 18 patients (82%). Irradiation due to PET-positive residual disease was performed in 2 patients (9%). No treatment discontinuations occurred. With a median follow up of 19 months (min-max: 4–26), one-year PFS and OS were both 100%. Based on these encouraging results, the condensed 3-day protocol is considered feasible and beneficial for logistical considerations in clinical practice. We thus recommend the condensed 3-day protocol for future BrECADD use.

P007: Six Cycles of Pembrolizumab (PEM) Induction Followed by Abbreviated AVD: A Phase II Trial of Front-Line PET-adapted Therapy in Early Unfavorable and Advanced-Stage Classic Hodgkin Lymphoma (cHL)

Megan Melody¹, Hatice Savas², Joseph Schroers-Martin³, Reem Karmali², Yangruijie Ma², Caroline Mangan², Wajihah Zehra², Ryan Avery², Kenneth Carson², Fahad Faruqi², Habib Shaikh², Ruohui Chen², Renee Cheng², Leo Gordon², Ranjana Advani³, Jane Winter²

¹Tampa General Hospital Cancer Institute, Tampa, FL, ²Northwestern University Feinberg School of Medicine, Chicago, IL, ³Stanford Cancer Institute, Stanford, CA

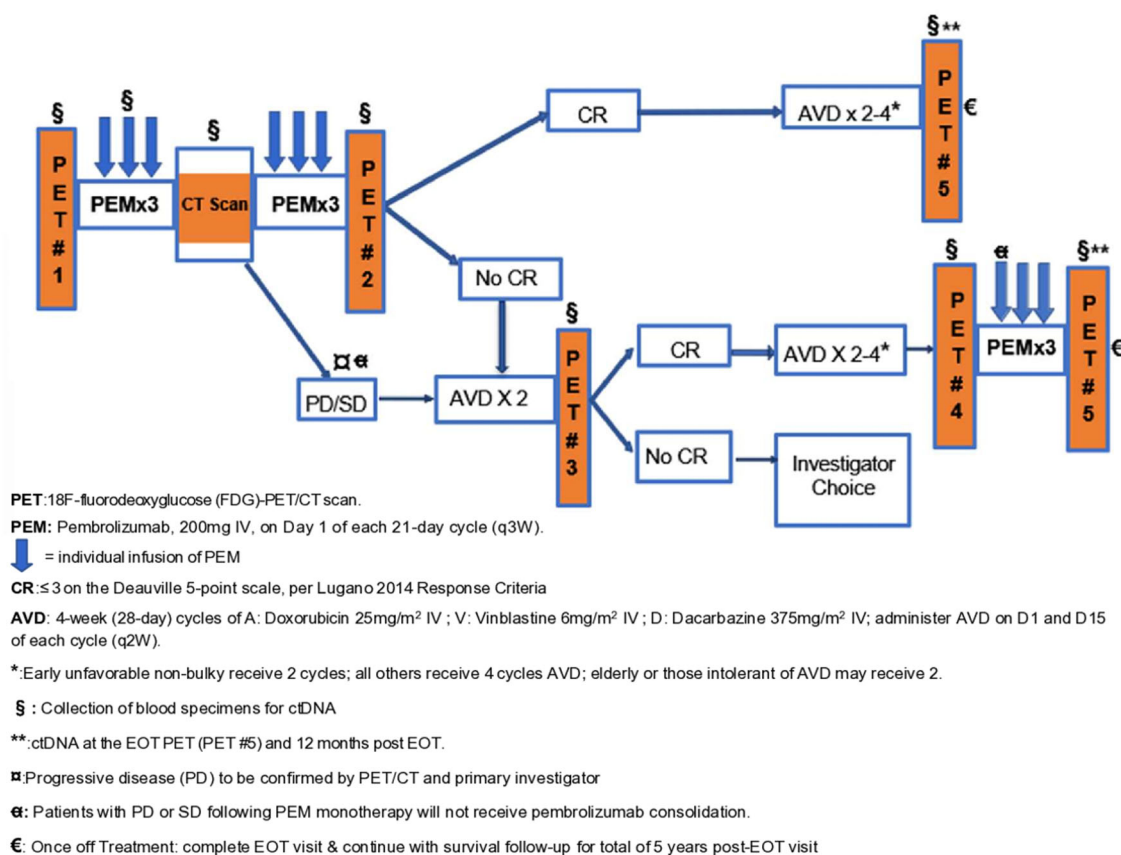


Figure 1: Study Schema.

Background: In NU16H08 (NCT03226249), 3 cycles of pembrolizumab (PEM) resulted in complete (37%) or near complete (25%) metabolic responses (CMR) in two thirds of untreated patients (pts) w/classic Hodgkin lymphoma (cHL) and 100% PFS/OS at 5 yrs when followed by 4–6 cycles of AVD (ASH 2024, abstr# 1664). Based on these findings, we hypothesized that PEM x 6 would yield a higher CMR rate than PEM x 3 and allow for a larger subset of pts to receive an abbreviated course of AVD while preserving efficacy.

Methods: Adult pts >18 yrs w/untreated stage III/IV cHL or stage I/II cHL w/at least 1 NCCN unfavorable risk factor received PEM X 6 followed by 2–6 AVD cycles (+/- PEM consolidation) based on response, stage, and bulk (see SCHEMA). The primary objective was CMR rate after PEM induction by PET scan, w/secondary objectives including efficacy of PEM followed by abbreviated AVD, safety, and PFS/OS. Exploratory objectives included clearance of circulating tumor DNA (ctDNA) as a predictor of response and association w/PET results.

Results: Thirty pts were enrolled: median age of 29 (25–33), 63% female, 50% stage III/IV, 50% w/early-stage unfavorable cHL (9 bulky, 5 B-symptoms, 7 ESR > 50). 26 pts completed all PEM x 6; 2 pts went off study after PEM x 1 (1w/grade 3 encephalitis, 1 w/grade 3 headache). Two pts transitioned to AVD after PEM x 3 (1 w/grade 3 pancreatitis, 1 w/progression of disease). PET scans following PEM x 6 (PET #2) were centrally reviewed: CMR (Deauville 1–3) in 27% (n = 8; 95% CI: 12%–46%), partial metabolic response (Deauville 4–5) in 60% (n = 18). Three pts (10%) had an overall reduction in disease burden w/PEM, but new PET+ sites (progressive disease). Two pts were PET+ (Deauville 4) after AVD x 2 and escalated to BrECADD; 1 pt completed 4 cycles and 1 pt received 2 and transitioned to proton irradiation due to toxicity. CMR was 100% for all pts at end of treatment (n = 28) who received AVD following PEM. At a median follow-up of 15.1 months (range 1.0–24.2), no pt has progressed or relapsed; median PFS has not been reached.

Conclusions: Induction with PEM x 6 was not more effective than PEM x 3 in producing CMR. Planned correlative analysis of ctDNA may provide a better assessment of disease status post-PEM, aiding in future de-escalation strategies. Upfront treatment with PEM was associated with significant toxicities, possibly reflecting the robust immune response in this young patient population.

P008: Real-world experience with first-line Nivolumab-AVD in advanced-stage Classical Hodgkin Lymphoma

Francisca Hernández Mohedo¹, Laura Curras Sanchez¹, Laura Jimenez Blanco¹, Ana Isabel Martinez Conejo¹, Maria Teresa Escudero Soler¹, Maria Luisa Rubio De La Rubia¹, Carlos Ramos Font¹, Jose Manuel Puerta Puerta¹

¹Hospital Universitario Virgen de las Nieves. Granada

Table 1. Baseline descriptive characteristics of the patients.

Age (years), median (range)	24 (18 - 58)
Sex Male/Female, n (%)	4/3 (52/43)
Histologica subtype, n (%)	
Nodular sclerosis	5 (71)
NOS type	2 (29)
Stage, n (%)	
II	1 (14)
III	2 (29)
IV	4 (52)
B symptoms, n (%)	6 (86)
Splenic disease, n (%)	3 (43)
Extranoda involvement, n (%)	7 (100)
Bulky disease, n (%)	5 (71)
Ann Arbor IV	5 (71)
Classic IPS, median (range)	4 (2 - 4)
Hemoglobin, median (range)	11 g/dL (8,4 - 14,8 g/dL)
Leukocytes, median (range)	10,5 x10 ³ /µl (3,3 - 5,8 x10 ³ /µl)
Lymphocytes, mediana (range)	1,14 x10 ³ /µl (0,23 - 3,46 x10 ³ /µl)
Albumin, median (range)	3,5 g/dL (2,2 - 4 g/dL)
TMTV at diagnosis, median (range)	309 (26 - 845)
TLG at diagnosis, median (range)	1013 (243 - 2620)

TLG: total lesion glycolysis; TMTV: Total metabolic tumor volume.

Table 2. Response to tretament.

TMTV on iPET = 0	4 (52)
TMTV on iPET > 0	3 (43)
TMTV on PET-EOT = 0	6 (86)
TMTV on PET-EOT > 0	1 (14)
Response on iPET, n (%)	
PET negative (DS 1-3)	4 (52)
PET positive (DS 4-5)	3 (29)
Response on PET-EOTI, n (%)	
PET negative (DS 1 - 3)	7 (100)
PET positive (DS 4–5)	0
Toxicity, n (%)	
Immune-mediated pneumonitis	1 (14)
Immune-mediated thyroiditis	2 (29)
Follow-up (months), median (rango)	16 (2 - 22)

DS: Deauville score; iPET: PET interim; PET-EOT: PET end-of-treatment; TMTV: Total metabolic tumor volume.

Introduction: Classical Hodgkin lymphoma (cHL) has high cure rates, although outcomes remain poorer in advanced stages and in patients with high baseline metabolic tumor burden (3). Novel first-line regimens combining immunotherapy and chemotherapy have improved efficacy and reduced toxicity (ECHELON-1, HD21 and SWOG S1826), but real-world data are still limited (1,2,4,5).

Objective: To evaluate the efficacy and safety of first-line Nivolumab-AVD in high-risk advanced cHL (stages III–IV and IIB with risk factors) with high metabolic tumor burden on baseline PET (metabolic tumor volume (MTV) and total lesion glycolysis (TLG)), at our center.

Materials and Methods: Retrospective study of patients with cHL treated with first-line Nivolumab-AVD (SWOG S1826 regimen) between 2024 and 2026. Clinical, metabolic imaging, response and survival data, were analyzed descriptively. Efficacy was assessed according to Lugano 2014 criteria, and adverse events (AEs) according to CTCAE v5.

Results: Seven of eight patients were analyzed; one was excluded due to grade 4 non-immune-mediated toxic hepatitis after cycle 1. Median age was 24 years (18–58), 52% were male, nodular sclerosis was the most frequent subtype (71%). None of the patients were EBER or HIV-positive. All patients had advanced disease (stages III–IV), except one high-risk stage IIB case. Median IPS was 4 and median MTV was 309. Extranodal involvement was present in all patients, while 86% had B symptoms, 71% bulky disease, and 43% splenic involvement.

After a median follow-up of 16 months, six patients completed treatment and one completed 3 cycles with complete metabolic response (CMR) on interim PET (iPET). Median iPET MTV was 0 (0–16.5); CMR was observed in 4 patients with Deauville score (DS) 2–3 while three patients obtained DS4. In this regard, recent studies such as HD21 have combined DS and MTV on iPET for a more accurate evaluation of response to immunotherapy. End-of-treatment PET (EOT-PET) showed a 100% CMR rate, with estimated 2-year progression-free survival and overall survival of 100%. All patients received G-CSF prophylaxis. Two patients developed grade 1–2 immune-mediated AEs after completing treatment (thyroiditis and pneumonitis). No consolidative radiotherapy was administered.

Conclusion: First-line Nivolumab-AVD demonstrated excellent real-world efficacy and favorable tolerability in high-risk advanced cHL across all ages, outperforming historical results with ABVD regimen.

P009: PRECISE-HL Trial: Personalized Reduction of Chemotherapy Intensity through ctDNA Evaluation in Advanced Hodgkin Lymphoma

Ryan Lynch¹, David Russler-Germain², Joseph Schroers-Martin³, Alison Moskowitz⁴, Reid Merryman⁵, Azra Borogovac⁶, Hongyan Du¹, Heather Rasmussen¹, Ranjana Advani³, Ash A. Alizadeh³, Philippe Armand⁵, Nancy Bartlett², Alex Herrera⁶, Sarah Rutherford⁷, David Kurtz⁸, Ted Gooley¹, Jenna Voutsinas¹, Ajay Gopal¹

¹Fred Hutch Cancer Center, ²Washington University School of Medicine, ³Stanford University, ⁴Memorial Sloan Kettering Cancer Center, ⁵Dana Farber Cancer Institute, ⁶City of Hope National Medical Center, ⁷Weill Cornell School of Medicine, ⁸Natera

Introduction: Nivolumab-AVD has become a new standard for untreated advanced stage Hodgkin lymphoma in North America. The PRECISE-HL trial will assess a response-adaptive CHL treatment approach utilizing PhasED-Seq to reduce the overall chemotherapy burden for patients with early MRD-negativity when treated with nivolumab-AVD (NCT06745076).

Methods: This is a multi-center phase 2, open label pilot study of six cycles of response-adapted therapy based on MRD testing by PhasED-Seq for untreated stage III or IV CHL. Patients will receive the combination of nivolumab (240 mg IV), doxorubicin (25 mg/m² IV), vinblastine (6 mg/m² IV) dacarbazine (375 mg/m² IV) on days 1 and 15 of 28-day cycles.

Blood samples for PhasED-Seq testing at baseline and post cycle 2 will be sent to Foresight Diagnostics for rapid processing (estimated turn-around time 10–14 days). For patients with undetectable MRD at cycle 3 day 1, the doxorubicin, vinblastine, and dacarbazine will be removed from Cycle 5 and Cycle 6 while continuing nivolumab. For patients with detectable or inconclusive MRD, treatment after interim assessment will continue with all 4 agents for 6 total cycles.

Planned enrollment is 125 patients. The primary endpoint is 1-year PFS in patients with undetectable MRD after 2 cycles of treatment. Secondary endpoints include 1-year PFS in MRD positive patients after 2 cycles of treatment, 2-year PFS in the overall cohort and stratified by MRD status, and best overall response as complete or partial response (CR/PR). Exploratory endpoints include MRD assessments at other timepoints and during follow up, patient reported outcomes, and cardiac biomarkers.

The primary efficacy benchmark for this trial is a 1-year progression-free survival (PFS) rate of ≥94% for interim ctDNA negative patients based on historical data from the S1826 study.

Additional key eligibility criteria include age 18+ and measurable disease per Lugano criteria. Key exclusion criteria include current or prior autoimmune disease except vitiligo or thyroid disease on stable replacement doses.

P010: Frontline Escalation to BrECADD in Advanced Hodgkin Lymphoma: Multicenter Real-World Experience

Tzvika Porges¹, Tsofia Levi², Tareq Buqai³, Eldad J. Dann⁴

¹Institute of Hematology, Soroka university medical center, Beer sheva, Israel, ²Department of Hematology and bone Marrow Transplantation, Rambam health care campus, Haifa, Israel, ³Institute of Hematology, Soroka university medical center, Beer sheva, Israel, ⁴Clin Prof of Hematology Technion Israel technical institute, Rambam Medical center, Haifa, Israel

Characteristic	Overall cohort, n = 9
Age, median, range, years	25, 20–50
Female sex, n percent	6, 66.7
Ann Arbor stage II, III, IV, n	4, 1, 4
IPS, median, range	2, 0–5
Initial regimen ABVD, AAVD, CHOP, n	6, 2, 1
Escalation for inadequate or partial response, n percent	7, 77.8
BrECADD cycles, median, range	4, 3–4
Completed planned BrECADD, n percent	8, 88.9
Dose reduction, n percent	2, 22.2
Neurotoxicity, n percent	0, 0
Grade 4 hematologic toxicity n,percent	6, 66.6
Complete metabolic response, n percent	9, 100
Relapse or progression, n percent	2, 22.2
Alive at last follow-up, n percent	9, 100
Follow-up, median, range, months	15.7, 5.1–30.7

Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine. AAVD, brentuximab vedotin, doxorubicin, vinblastine, dacarbazine. BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone. IPS, International Prognostic Score

Table 1: Baseline characteristics and treatment outcomes of patients who underwent frontline escalation to BrECADD.

Background: Response-adapted treatment escalation is an established strategy in advanced classical Hodgkin lymphoma for patients with inadequate early response to initial lower-intensity therapy. However, the published evidence for PET2-adapted escalation is based largely on escalation to escalated BEACOPP with The RATHL study and SWOG S0816 support escalation with 3- and 2-year progression-free survival of 67.5% and 64% respectively. BrECADD protocol has mainly been studied as an upfront intensive regimen and showed lower treatment-related morbidity than escalated BEACOPP with at least noninferior efficacy and a 4-year progression-free survival of 94.3 percent. Data on BrECADD as an escalation strategy in routine practice remain limited.

Methods: We conducted a multicenter retrospective real-world analysis of adults treated with BrECADD between July 1, 2023, and October 1, 2025, data cut off was 1.12.25. Within this cohort, we identified nine patients with advanced Hodgkin lymphoma who underwent escalation to

BrECADD during frontline therapy. Most patients escalated because of inadequate response to initial lower-intensity treatment. This subgroup was analyzed descriptively for treatment delivery, response, survival outcomes, and safety.

Results: Nine patients with advanced Hodgkin lymphoma underwent escalation to BrECADD after other regimen: ABVD in 6 patients, AAVD in 2, and CHOP in 1. Escalation was triggered by partial response in 7 patients, toxicity in 1, and revised diagnosis in 1. The median age was 25 and stage 4 disease was reported in 4 patients. Patients received a median of 4 BrECADD cycles, with 8 of 9 completing planned treatment and 2 requiring dose reduction. All 9 patients achieved complete metabolic response after BrECADD, 7 of them after 2 cycles. After a median follow-up of 15.7 months (range, 5.1–30.7), 2 patients had relapsed, and all patients were alive at last follow-up. Grade 4 hematologic adverse events were recorded in 6 patients with only one patient with Grade 3–4 non-hematologic toxicity. No ICU admission or neurologic toxicity was reported.

Conclusions: In this multicenter real-world series, frontline escalation to BrECADD was feasible and induced complete metabolic response in all patients. Although 2 relapses occurred during follow-up, there were no recorded death which bring the overall survival to 100%. These findings extend the limited literature on BrECADD beyond its use as upfront.

P011: Interim analysis of the A-AVD PET2 adapted in patients with stage IV classical Hodgkin lymphoma. The AVATAR program

Andrea Visentin¹, Alessandro Cellini¹, Francesco Angotzi¹, Martina De Ferrari¹, Mattia D'Antiga¹, Anna Giordano¹, Nicolo' Danesin¹, Marco Pizzi², Gaia Grassetto³, Federica Vianello⁴, Francesco Piazza¹, Andrea Gallamini⁵, Livio Trentin¹

¹Hematology unit, Department of Medicine, University of Padova, Azienda Ospedale - Università Padova, Padova, Italy, ²Pathology unit, Department of Medicine, University of Padova, Azienda Ospedale - Università Padova, Padova, Italy, ³Nuclear Medicine, Azienda Ospedale - Università Padova, Padova, Italy, ⁴Radiotherapy unit, Veneto Institute of Oncology IOV IRCCS, Padova, Italy, ⁵Research and Clinical Innovation Department, A. Lacassagne Cancer Center, Nice, France

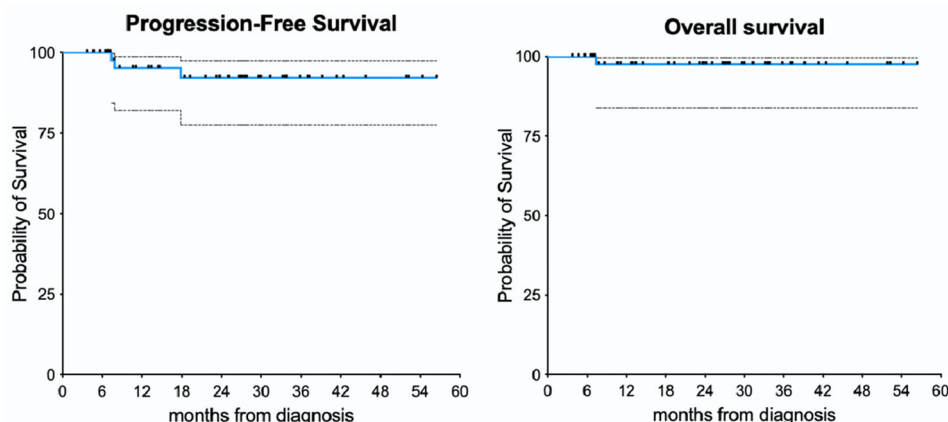


Figure 1: Probability of Survival.

Background: In the ECHELON-1 trial brentuximab-AVD (A-AVD) improved the progression-free survival (PFS) and overall survival (OS) stage IV classical Hodgkin lymphoma (cHL) compared to ABVD. This trial, alongside other real-life studies confirmed the predictive role of the 18FDG PET-CT scan after the two courses of A-AVD (PET2), with PET2 positivity (PET2+) associated with a higher risk of relapse. Recently in the COBRA trial almost 40% of the patients with a positive PET after 1 cycle of A-AVD escalated to BrECADD for 6 cycles with a 2-yr PFS of 89%. We hypothesized that escalation to BrECADD in PET2+ cases would reduce the number of patients requiring treatment intensification while improving their outcomes.

Methods: Patients with stage IV cHL aged 18–60 years were treated with A-AVD for 2 cycles according to Italian regulatory agency. Patients with a negative PET2 scan (Deauville score 1–3) continued A-AVD until cycle 6, whereas those with a positive PET2 scan (DS 4–5) received 4 cycles of BrECADD. Consolidative radiotherapy (cRT) was provided in case of focal residual disease at the end of treatment (EoT).

Results: Fifty patients with stage IV cHL have been enrolled since 2021, 46% were male, median age was 31 years (IQR 25–43), 62% had B symptoms, 38% an IPS > 3, 20% a bulky mass and 6% were HIV positive. Regarding histology, 70% had nodular sclerosis subtype, 4% mixed cellularity, 2% lymphocyte-rich, 2% lymphocyte depletion, 22% NOS. Only 10% of cases were PET2+ (6% DS 4, 4% DS 5). Among 90% PET2 negative cases, only 2 patients had a positive EoT PET, 1 with localized diseases received cRT achieving a complete remission. Among the 5 PET2+ patients, 1 patient with localized EoT PET positivity received cRT. Only 1 patient in both subgroups relapsed, after 2 and 9 months, respectively. After a median follow-up of 24 months the 2-yr PFS and OS were 92.2% and 97.6%. Only 1 HIV+ PET2 negative patient died of infection at cycle 5.

As expected, cytopenias, blood transfusion and fatigue were more common with BrECADD, while the rate of peripheral neuropathy (PN) was higher patients who received 6 cycles of A-AVD. Thus since February 2026, to reduce the incidence of PN, PET2-negative patients are receiving A-AD (i.e w/o vinblastine).

Conclusions: In our ongoing program, we confirmed the low rate of PET2+ after of A-AVD and provide initial results that 4 cycles of BrECADD can successfully rescue most PET2+ patients.

P012: KEYNOTE-204 final analysis: An open-label, phase 3 study of pembrolizumab (pembro) versus brentuximab vedotin (BV) in relapsed or refractory (R/R) classic Hodgkin lymphoma (cHL)

John Kuruvilla¹, Armando Santoro², Jan Walewski³, Robin Gasiorowski⁴, Nathalie Johnson⁵, Vladimir Melnichenko⁶, Valeria Buccheri⁷, Patricia Giacon⁸, Laura Maria Fogliatto⁹, Iara Goncalves¹⁰, Guilherme Perini¹¹, Sergey Alekseev¹², Neta Goldschmidt¹³, Iryna Kriachok¹⁴, Judyta Strzala¹⁵, Michael Dickinson¹⁶, Anna Lojko-Dankowska¹⁷, Andrew McDonald¹⁸, Muhit Ozcan¹⁹, Razi Ghorri²⁰, Doyun Park²⁰, Rushdia Yusuf²⁰, Pier Luigi Zinzani²¹

¹Princess Margaret Cancer Centre, Toronto, ON, Canada, ²IRCCS Humanitas Research Hospital- Humanitas Cancer Center, Milan, Italy, ³Maria Skłodowska-Curie National Research Institute of Oncology, ERN/EuroBloodNet, Warsaw, Poland, ⁴Concord Hospital, University of Sydney, Concord, NSW, Australia, ⁵Jewish General Hospital, Montreal, QC, Canada, ⁶Pirogov National Medical Surgical Center, Moscow, Russia, ⁷Hospital das Clínicas da FMUSP, São Paulo, Brazil, ⁸Casa de Saude Santa Marcelina, Sao Paulo, Brazil, ⁹Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil, ¹⁰Fundação Pio XII-Hospital de Câncer de Barretos, Sao Paulo, Brazil, ¹¹Hospital Israelita Albert Einstein, Sao Paulo, Brazil, ¹²Petrov Research Institute of Oncology, St. Petersburg, Russia, ¹³Hadassah Hebrew University Medical Center, Jerusalem, Israel, ¹⁴National Cancer Institute, Kyiv, Ukraine, ¹⁵Szpital Pomorskie, Gdynia, Poland, ¹⁶Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, ¹⁷Poznan University of Medical Sciences, Poznan, Poland, ¹⁸Alberts Cellular Therapy, Netcare Pretoria East Hospital, Pretoria, South Africa, ¹⁹Faculty of Medicine, Ankara University, Ankara, Türkiye, ²⁰Merck & Co., Inc., Rahway, NJ, USA, ²¹IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia "Seragnoli", Bologna, Italy

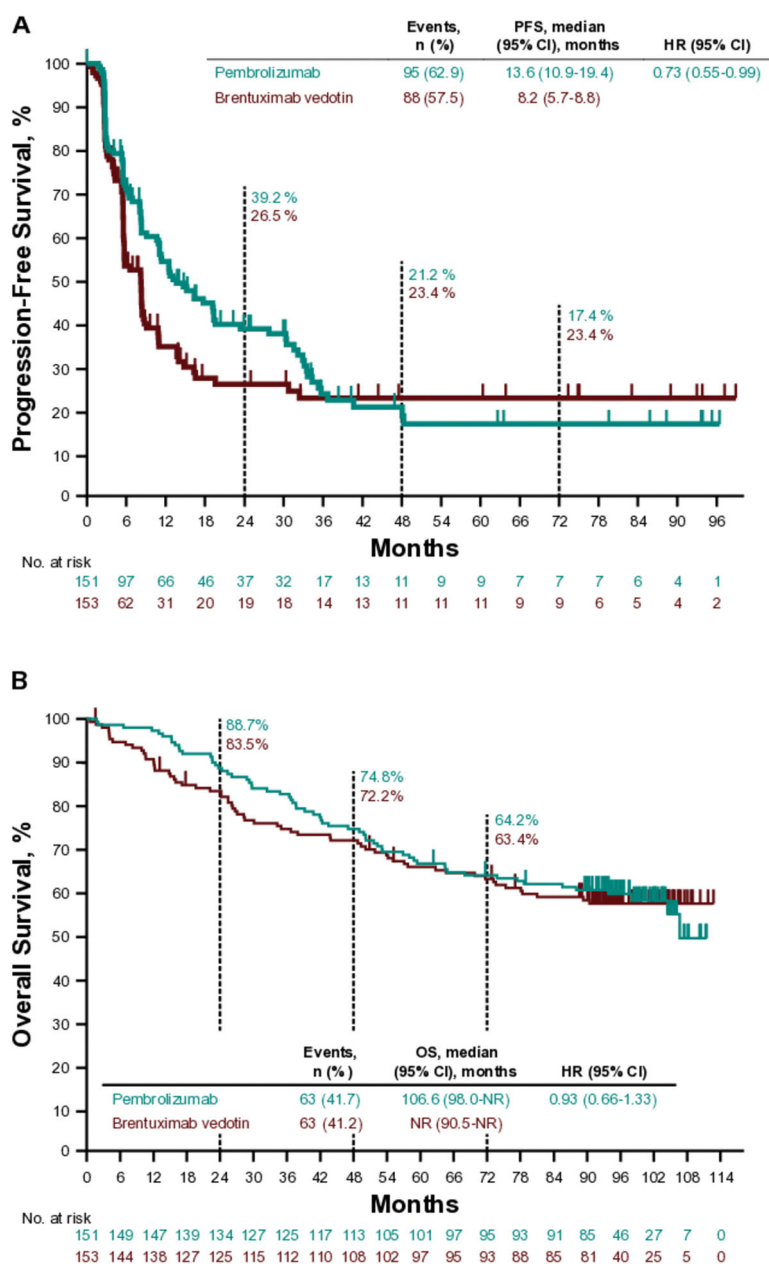


Figure 1: Kaplan-Meier estimates of (A) PFS per IWG 2007 by BICR including clinical and imaging data after auto-SCT or allo-SCT and (B) OS.

Background: At the second interim analysis of KEYNOTE-204 (NCT02684292), PFS was significantly improved with pembro vs BV in participants with R/R cHL (median PFS, 13.2 vs 8.3 months; HR, 0.65 [95% CI, 0.48–0.88]; $P = 0.0027$ [P value threshold for significance, 0.0043]). We report results from the final analysis.

Methods: Eligible participants aged ≥ 18 years with R/R cHL who were post-autologous stem cell transplant (auto-SCT) or ineligible for auto-SCT, had measurable disease, and an ECOG PS of 0 or 1, were randomly assigned 1:1 to pembro 200 mg or BV 1.8 mg/kg IV Q3W for 35 cycles. Participants were stratified by prior auto-SCT (yes vs no) and status after 1 L therapy (primary refractory vs relapsed < 12 months vs relapsed ≥ 12 months after 1 L). Dual primary end points were PFS per IWG 2007 criteria by BICR including clinical and imaging data after auto-SCT or allogeneic SCT (allo-SCT) and OS. ORR per IWG by BICR and safety were secondary. DOR per IWG by BICR was exploratory.

Results: 304 participants were randomized and 300 participants were treated (pembro, $n = 148$; BV, $n = 152$).

At data cutoff (Jan 14, 2026), median (range) follow-up was 97.6 months (90.6–113.9) for pembro and 97.7 months (90.1–114.3) for BV. Median PFS was 13.6 months for pembro and 8.2 months for BV (HR [95% CI], 0.73 [0.55–0.99]); median OS was 106.6 months and not reached (NR; HR [95% CI], 0.93 [0.66–1.33]), respectively (Figure). ORR (95% CI) was 65.6% (57.4–73.1; 40 complete responses, 59 partial responses) for pembro and 54.2% (46.0–62.3; 37 complete responses, 46 partial responses) for BV. Median (range) DOR was 24.9 months (0.0+ to 102.6) for pembro and 13.8 months (0.0+ to 96.2+) for BV. Treatment-related AEs occurred in 75.0% of participants for pembro and 77.0% for BV (grade 3–5, 19.6% and 25.0%). One participant in the pembro arm died due to treatment-related pneumonia. Subsequent therapies included auto-SCT (23.0% pembro, 24.3% BV), allo-SCT (14.2%, 12.5%), BV (47.0%, 13.1%), anti-PD-1 (21.9%, 49.0%), and other (62.9%, 65.4%).

Conclusions: PFS benefit with pembro at the interim analysis was maintained at the final analysis. OS was not statistically significantly improved with pembro vs BV. The converging OS Kaplan-Meier curves are likely due to receipt of effective subsequent therapies, including auto-SCT, allo-SCT, or anti-PD-1 agents. Results illustrate the limitations of using OS as a primary end point in cancers with rapidly changing therapeutic landscapes.

P013: Subcutaneous Pembrolizumab (Pembro) in Relapsed or Refractory Classic Hodgkin Lymphoma (cHL) or Primary Mediastinal Large B-cell Lymphoma (PMBCL): Additional Follow-Up From a Phase 2 Study

Elizabeth H. Phillips¹, Gabriel Barragán Ibáñez², Ewa Paszkiewicz-Kozik³, Wojciech Jurczak⁴, Mauricio Chandia Cabas⁵, Sergio Portiño⁶, Elifcan Aladag Karakulak⁷, Sebastian Giebel⁸, Anna Sureda⁹, Tae Min Kim¹⁰, Brenda González-García¹¹, Norma Gutiérrez¹², Sebastian Hidalgo¹³, Kirit Ardeshta¹⁴, Antonia Rodríguez Izquierdo¹⁵, Bastian Von Tresckow^{16,17}, Gina Song¹⁸, Jessica Flynn¹⁸, Katherine Ryland¹⁸, Rushdia Yusuf¹⁸, Muhit Ozcan¹⁹

¹Division of Cancer Sciences, University of Manchester and The Christie NHS Foundation Trust, Manchester, United Kingdom, ²Centro de Investigación Clínica de Oaxaca (CICLO), Oaxaca, Mexico, ³Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland, ⁴Maria Skłodowska-Curie National Research Institute of Oncology, Kraków, Poland, ⁵Biocenter, Concepción, Chile, ⁶Bradford Hill Clinical Research Center, Santiago, Chile, and Finis Terrae University, Faculty of Medicine, Santiago, Chile, ⁷Hacettepe University Faculty of Medicine, Ankara, Türkiye, ⁸Maria Skłodowska-Curie National Research Institute of Oncology, Gliwice, Poland, ⁹Institut Català d'Oncologia - L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain, ¹⁰Seoul National University Hospital, Seoul, Republic of Korea, ¹¹Health Pharma Professional Research, Mexico City, Mexico, ¹²Hospital Universitario de Salamanca, IBSAL, Centro de Investigación del Cáncer, Salamanca, Spain, ¹³Fundación Arturo López Pérez (FALP), Santiago, Chile, ¹⁴University College London Hospitals NHS Foundation Trust, London, United Kingdom, ¹⁵Hospital Universitario 12 de Octubre, Madrid, Spain, ¹⁶German Hodgkin Study Group, University of Cologne, Cologne, Germany, ¹⁷West German Cancer Center and German Cancer Consortium (DKTK partner site Essen), University Hospital Essen, University of Duisburg-Essen, Essen, Germany, ¹⁸Merck & Co., Inc., Rahway, NJ, USA, ¹⁹Ankara University School of Medicine, Ankara, Türkiye

Pembrolizumab PK exposures	N ^a	GM (95% CI)	Geometric % CV
C _{max} (ug/mL)	64	74.78 (67.66-82.65)	41.73
C _{trough} (ug/mL)	64	28.63 (25.22-32.51)	54.26
AUC _{0-6wks} (ug*day/mL)	64	2100.21 (1898.36-2323.53)	42.17
AUC ₀₋₆ , area under the concentration-time curve from time 0 to 6 weeks; C _{max} , maximum concentration; C _{trough} , trough concentration; CV, coefficient variation; GM, geometric mean; PK, pharmacokinetics.			
^a Number of participants who met per protocol population criteria.			

Table 1: PK exposures of pembrolizumab in cycle 1 following administration of subcutaneous pembrolizumab in participants with hematologic tumors.

Background: Subcutaneous pembro is approved outside the US for treatment of relapsed or refractory (R/R) cHL and PMBCL. Prior analysis of an open-label, phase 2 study (NCT06504394) evaluated pharmacokinetics (PK), efficacy, and safety of subcutaneous pembro in participants (pts) with R/R cHL or R/R PMBCL. At a median follow-up of 2.6 months, subcutaneous pembro 790 mg Q6W had a manageable safety profile and efficacy consistent with intravenous pembro. Additional follow-up are presented that includes complete cycle 1 data for all pts.

Methods: Eligible pts were ≥ 18 years with histologically confirmed, FDG-avid cHL or PMBCL per WHO criteria, radiographically measurable disease, and ECOG PS 0 or 1. Pts with cHL or PMBCL were anti-PD-1 naive and had disease that was refractory to, did not achieve CR with, or had relapsed after prior therapy. Pts with cHL received ≥ 1 multiagent regimen, and those with PMBCL received ≥ 2 prior therapies (including ≥ 1 rituximab-based regimen). Pts could enroll if they were ineligible for or had relapsed after stem cell transplant. Pts received subcutaneous pembro 790 mg Q6W for ≤ 18 cycles (~ 2 years) or until disease progression or other discontinuation criteria were met. Primary objectives included PK exposure measures during cycle 1 (C1) and ORR; secondary objectives included safety and duration of response (DOR). OS and PFS were exploratory objectives. ORR, DOR, and PFS were assessed per Lugano criteria by investigator.

Results: At data cutoff (January 28, 2026), 64 pts had enrolled and received ≥ 1 cycle of subcutaneous pembro ($n = 58$, cHL; $n = 6$, PMBCL). Median follow-up was 9.9 months (range, 1.4–15.0). PK exposures of subcutaneous pembro in pts with hematologic tumors were consistent with those with IV pembro (table). Overall, 57 pts with cHL and 4 with PMBCL had a baseline and postbaseline assessment. For pts with cHL ORR was 84% (95% CI, 72–93; 26 CR; 22 PR). Among those with PMBCL, the ORR was 75% (95% CI, 19–99; 1 CR and 2 PR). For pts with cHL, median DOR was 8.3 months (range, 0.0+–10.8+), median PFS was 11.0 (95% CI, 8.5–NR) and median OS was NR (95% CI, NR–NR). Among all pts, 12 (19%) had a grade 3 or 4 treatment-related AEs (TRAEs), and 3 (5%) discontinued due to a TRAE. No deaths due to TRAEs occurred.

Conclusion: With ≥ 9 months follow-up, the PK profile was consistent with the previous report; subcutaneous pembro Q6W continues to demonstrate durable responses with no new safety concerns.

P014: Changes in Patient Reported Outcomes and Treatment Tolerance with a Structured Diet and Exercise Plan

Michele Stanchina¹, Melissa Lopez-Pentecost², Akina Natori³, Juan Alderuccio¹, Asaad Trabolsi¹, Alvaro Alencar¹, Emily Panzner¹, Grey Freylersthe³, Tracy Crane³, Craig Moskowitz¹

¹Department of Medicine, Division of Hematology, University of Miami Miller School of Medicine, Miami, FL. Sylvester Comprehensive Cancer Center, Miami, FL, ²Department of Public Health Sciences, University of Miami Miller School of Medicine, Miami, FL. Sylvester Comprehensive Cancer Center, Miami, FL, ³Department of Medicine, Division of Medical Oncology, University of Miami Miller School of Medicine. Sylvester Comprehensive Cancer Center, Miami, FL

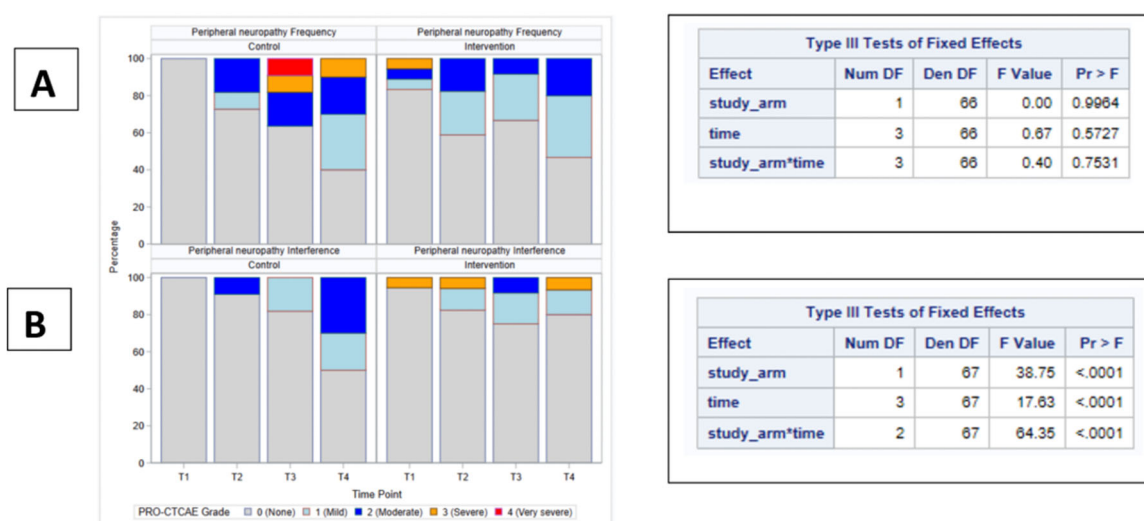


Figure 1: Graph A: Frequency of Peripheral Neuropathy in Control vs Intervention Group by PRO-CTCAE at Timepoints (T) 1–4 Graph B: The Amount of Interference in Daily Life Caused by Peripheral Neuropathy in Control vs Intervention Group by PRO-CTCAE at T1-4.

Background: Diet and exercise have shown benefits in a variety of cancers but evidence in lymphoma is limited. Here we explore the impact of a structured diet and exercise intervention during treatment on patient-reported outcomes (PRO) in patients (pts) with Hodgkin lymphoma (HL).

Methods: Patients with newly diagnosed lymphoma receiving six cycles of chemotherapy were enrolled on the Lifestyle Intervention of Food and Exercise for Lymphoma Survivors (LIFE-L) trial (NCT05839210) and randomized 2:1 to the intervention arm, where pts followed a Mediterranean diet and a home-based exercise regimen with weekly remote health coaching from a registered dietitian and exercise physiologist, or the control arm. Patient-Generated Subjective Global Assessment (PG-SGA) for malnutrition assessment, handgrip strength, and PRO-Common Terminology Criteria for Adverse Events (PRO-CTCAE) were completed at baseline, before cycle (C) 3 and C6, and 4 weeks post treatment. This is a secondary analysis of HL pts from LIFE-L. Descriptive statistics were used to summarize pt characteristics and generalized linear mixed-effects models evaluated changes in outcomes.

Results: 32 pts with HL were enrolled between 04/26/2023–10/2/2025. Pts were white (91%), Hispanic (84%), and had advanced stage HL (75%) with equal distribution of sex (male 50%). Groups were well balanced other than age; control group ($n = 13$) was younger than intervention group ($n = 19$), 39.8 (SD: 14.0) vs 43.1 (SD: 16.4) yrs old respectively ($p < 0.001$). PG-SGA was significantly different over time ($p < 0.001$) with a

trend towards significance between groups ($p = 0.056$), with the intervention arm reporting better nutritional status at baseline. Peripheral neuropathy differed between groups, timepoints, and their interaction (all $p < 0.001$), however, estimates were unstable with large odds ratios, suggesting model instability due to sparse data. Constipation severity varied over time ($p = 0.001$), but not between groups ($p = 0.771$). Fatigue frequency worsened over time ($p = 0.013$), particularly from baseline to C3, (OR 3.41, CI 95%, 1.10–10.56), as did depression severity ($p = 0.036$). No significant difference was observed for vomiting, anxiety, depression, cognition, insomnia or handgrip strength.

Conclusion: The LIFE-L study is among the first interventional trials evaluating a structured diet and exercise program in HL. These early results from this ongoing trial are promising and should be replicated in a more robust sample size.

P015: High efficacy and acceptable toxicity of BrECADD regimen in advanced-stage classical Hodgkin lymphoma

Heidi Mocikova¹, Lubica Gaherova¹, Barbara Brizova², Katerina Steinerova², Jozef Michalka³, Zdenek Kral³, Marie Lukasova⁴, Vit Prochazka⁴, Alice Sykora⁵, Pavla Stepankova⁵, Katarina Hradská⁶, Juraj Duras⁶, Blanka Vackova⁷, Jan Koren⁷, Tomas Kozak¹

¹Department of Haematology, Fakultni nemocnice Kralovske Vinohrady and Third Faculty of Medicine, Charles University, Prague, Czech Republic, ²Department of Clinical Hematology, University Hospital, Pilsen, Czech Republic, ³Department of Internal Medicine, Hematology and Oncology, University Hospital Brno, Faculty of Medicine, Masaryk University Brno, Czech Republic, ⁴Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Czech Republic, ⁵th Department of Internal Medicine-Hematology, University Hospital and Faculty of Medicine, Hradec Kralove, Czech Republic, ⁶Department of Hematooncology, University Hospital Ostrava and Faculty of Medicine, University of Ostrava, ⁷1st Department of Medicine, General University Hospital, 1st Faculty of Medicine, Charles University, Prague, Czech Republic

Background: The HD21 trial conducted by the German Hodgkin Lymphoma Study Group established BrECADD, a regimen including brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone, as the standard first-line therapy for advanced-stage classical Hodgkin lymphoma (cHL). Our retrospective analysis provides real-world data on the efficacy and toxicity of BrECADD regimen in patients with cHL in the Czech Republic.

Methods: Patient demographics and baseline characteristics were analyzed using descriptive statistics. PET/CT scans were performed before starting treatment, after completing two cycles of chemotherapy, upon the conclusion of treatment, and assessed according to the Lugano criteria. Overall survival (OS) and progression-free survival (PFS) were calculated utilizing the Kaplan-Meier method.

Results: A total of 97 patients, including 58 males, who received at least one cycle of the BrECADD regimen between November 2023 and February 2026, were evaluated. The median age was 32 (range 18–66) years. Among the 97 patients, 76 (78%) were classified as being in clinical stages III or IV, while 21 (21.6%) were in stage IIB with a massive mediastinal tumor and/or extranodal disease. Additionally, 18 patients (18.5%) had an International Prognostic Score 4–7. Overall 7.2% of patients did not complete the planned number of BrECADD cycles. A complete metabolic response was observed in 63.9% of cases after two cycles and increased to 84.5% by the end of the treatment. Only four (4.1%) patients received radiotherapy. During a median follow-up of 8.2 months three patients relapsed. The estimated 1-year PFS rate was 96.5% and the 1-year OS rate was 100%. Although the incidence of grade ≥ 3 neutropenia was high at 65%, the occurrence of grade ≥ 3 infections remained relatively low at 15.8%. Toxicity resulted in treatment reductions for 25.4% of patients. Brentuximab vedotin was prematurely discontinued in two (3.1%) patients due to grade ≥ 3 peripheral neuropathy.

Conclusion: The BrECADD regimen was well-tolerated, and our efficacy findings closely match those reported in the HD21 trial.

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P016: FENIX Score: A Novel PET-Derived Signature Predicting Neurotoxicity in Advanced Hodgkin Lymphoma Treated with A+AVD

Matteo Cristante^{1,2}, Federico Fallanca³, Teresa Calimeri¹, Andrés José María Ferreri^{1,2}, Fabrizio Marino¹

¹Strategic Program on Lymphomas, IRCCS San Raffaele Scientific Institute, Milano, Italy, ²Vita-Salute San Raffaele University, Milano, Italy, ³Nuclear Medicine, IRCCS San Raffaele Scientific Institute, Milano, Italy

Variable	OR	95% CI	p-value	Additional tests*
Age	1.03	0.97-1.09	0.357	MW: 0.286
Male sex	1.75	0.24-12.64	0.579	Fisher: 0.659
B Symptoms	0.63	0.11-3.71	0.605	Fisher: 0.673
Bulky disease	0.63	0.48-8.20	0.720	Fisher: 1.00
IPS	0.84	0.36-1.93	0.672	MW: 0.636
Hb	2.48	1.18-5.51	0.026	MW: 0.007
CRP	0.98	0.96-1.00	0.096	Fisher: 0.096
Albumin	1.09	0.92-1.30	0.312	Fisher: 0.153
Comorbidities**	1.50	0.22-10.08	0.677	Fisher: 0.523
FENIX score	1.04	0.98-1.10	0.141	MW: 0.017
FENIX score (high)	10.00	1.28-78.10	0.028	Fisher: 0.032
Multivariate Analysis				
FENIX score (high)	2.77	0.21-31.78	0.413	
Hb	2.14	0.92-4.95	0.077	

Table 1: Univariate analysis of peripheral neuropathy and characteristics. *Additional test includes Fisher's exact test and Mann-Whitney test.

**Comorbidities: hypertension (n = 4), diabetes (n = 1), hypertension+autoimmune thyroiditis (n = 1).

Background: Brentuximab vedotin plus AVD (A+AVD) is a standard treatment for advanced-stage Hodgkin lymphoma (HL), but peripheral neuropathy (PN) remains a frequent and clinically relevant toxicity. Reliable predictors are lacking. While PET-derived parameters are established prognostic biomarkers, their role in predicting treatment-related toxicity is largely unexplored.

Methods: We retrospectively analyzed 21 patients with stage IV HL treated with frontline A+AVD. Baseline PET/CT parameters included SUVmax, total metabolic tumor volume (TMTV4), and total lesion glycolysis (TLG4).

The FENIX score (FDG-based Extraction of Neurotoxicity Imaging index) was defined as a composite PET-derived index integrating focal metabolic activity and global tumor burden, calculated as $(\text{SUVmax}/\text{TMTV4} + \text{SUVmax}/\text{TLG4}) \times 100$, reflecting the relative metabolic intensity of the disease.

The primary endpoint was grade ≥ 2 PN. Continuous variables were compared using the Mann–Whitney test, while categorical variables were analyzed using Fisher's exact test. Receiver operating characteristic (ROC) analysis was performed to assess the discriminative performance and identify an optimal cut-off.

Results: Baseline PET showed heterogeneous tumor burden. Grade ≥ 2 PN occurred in 9/21 patients (42.9%).

FENIX score was significantly higher in patients developing PN ($p = 0.017$). ROC analysis demonstrated good discrimination (AUC 0.81).

Using an optimal cut-off of 8.7, FENIX identified patients at higher risk with 77.8% sensitivity and 83.3% specificity. PN incidence was higher in patients with high FENIX score (75.0% vs 23.1%, $p = 0.032$).

Among baseline clinical variables, only hemoglobin was associated with PN, while no significant associations were observed for other baseline characteristics.

Conclusion: The FENIX score, a PET-derived index integrating metabolic activity and tumor burden, predicts clinically relevant PN using baseline PET alone. The FENIX score reflects the relative metabolic intensity of the disease, integrating peak metabolic activity with both tumor mass and overall metabolic burden.

These findings support the role of PET-based biomarkers in identifying patients at increased risk of neurotoxicity and guiding personalized therapeutic strategies. The association with hemoglobin should be interpreted with caution given the small sample size. Prospective validation is warranted.

P017: Frontline Use of Nivolumab with Doxorubicin, Vinblastine, and Dacarbazine in Advanced-Stage Classical Hodgkin Lymphoma: A Real-World Analysis

Iľubica Gah rov  ¹, Tom    Koz  k¹, Jozef Mich  lka², Marcela Cermanov   ², Zden  k Kr  l², Blanka Vackov   ³, Jan Ko  en³, Alice S  korov   ⁴, Katar  na Hradsk   ⁵, Kate  rina Steinerov   ⁶, Marie Luk     ov   ⁷, Heidi M  cikov   ¹

¹Department of Haematology, Fakult  n   nemocnice Kralovske Vinohrady and Third Faculty of Medicine, Charles University, Prague, Czech Republic, ²Department of Internal Medicine, Hematology and Oncology, University Hospital Brno, Faculty of Medicine, Masaryk University Brno, Czech Republic, ³1st Department of Medicine, General University Hospital, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, ⁴4th Department of Internal Medicine– Hematology, University Hospital and Faculty of Medicine, Hradec Kralove, Czech Republic, ⁵Department of Hematooncology, University Hospital Ostrava and Faculty of Medicine, University of Ostrava, Czech Republic, ⁶Department of Clinical Hematology, University Hospital, Pilsen, Czech Republic, ⁷Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Czech Republic

Background: The combination of nivolumab with doxorubicin, vinblastine, and dacarbazine (N-AVD) represents a promising frontline therapeutic approach that has demonstrated high efficacy in the treatment of advanced-stage classical Hodgkin lymphoma (cHL). We assessed the real-world effectiveness and safety of frontline N-AVD treatment in patients with advanced-stage cHL.

Methods: A retrospective analysis was conducted on 61 cHL patients in clinical stages III/IV who received N-AVD treatment between 2023 and 2026 in the Czech Republic. Treatment response was assessed using 18F-FDG PET/CT imaging based on the Lugano criteria.

Results: Out of 61 patients 19 were aged <60 and 42 were ≥ 60 , with a median age of 67 years. Of the participants, 68.9% were diagnosed with stage IV disease and 75.4% presented with B symptoms. The PET-2 results showed rapid metabolic clearance in 85.7% of patients, whereas 11.9% demonstrated Deauville scores of 4 to 5. N-AVD demonstrated an overall response rate of 89.2%, with 86.5% of patients achieving a complete metabolic response at the end of treatment. After a median follow-up of 8.9 months, 5 (8.1%) patients progressed or relapsed, resulting in an estimated 1-year progression-free survival rate of 91.8%. Four patients died (two due to cardiotoxicity-related complications, one due to infection and one unknown cause) and the estimated 1-year overall survival rate was 93.4%. Grade ≥ 3 hematological toxicities were observed in 44.3% of cases (neutropenia 27.9%, anemia 11.5%, thrombocytopenia 4.9%). Non-hematologic toxicities including immune-related adverse events of grade ≥ 3 were reported in 16.4% of cases. Treatment discontinuation due to toxicity was reported in 11.5% of patients. This included two patients (3.2%) experiencing grade ≥ 3 neurotoxicity and one patient (1.6%) with grade ≥ 3 ulcerative colitis. Patients aged ≥ 60 years had higher rates of severe hematologic toxicities, while younger patients experienced more immune-related adverse events. Treatment discontinuation rates were similar across both age groups.

Conclusions: The frontline N-AVD regimen demonstrated excellent response rates in patients with advanced-stage cHL. Extended follow-up is necessary to better assess the durability of responses, long-term toxicity, and overall survival outcomes. This work was supported by the grant AZV NU22-03-00182 from the Ministry of Health of the Czech Republic and by the Cooperatio Program, research area "Oncology and Haematology".

P018: Interim PET remains clinically informative during frontline nivolumab-based therapy in advanced-stage classical Hodgkin lymphoma

Anna Kravtsova¹, Daria Koroleva¹, Olga Shchetsova¹, Madina Bagova¹, Aminat Magomedova¹, Oleg Margolin¹, Ekaterina Gitelzon¹, Alexey Subbotin², Evgeny Zvonkov^{1,3}, Yana Mangasarova^{1,3}

¹National Medical Research Center for Hematology, Moscow, Russia, ²N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russia, ³The Russian University of Medicine, Moscow, Russia

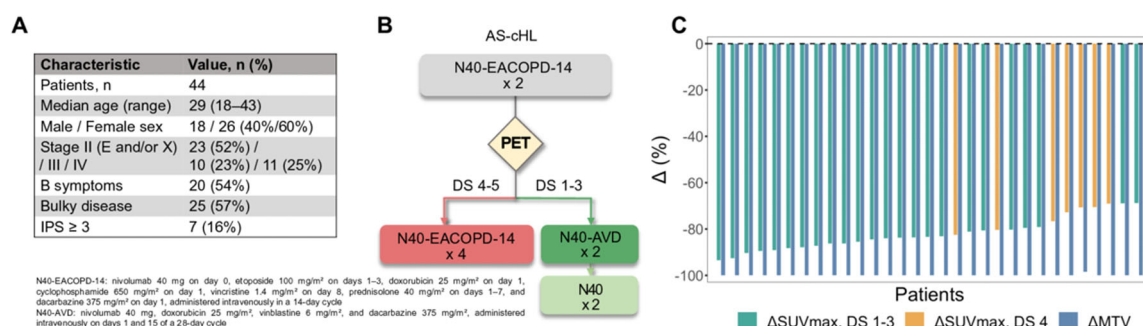


Figure 1: Baseline patient characteristics (A), study design (B) and quantitative PET response (C).

Background: Interim PET is essential for response-adapted frontline treatment in classical Hodgkin lymphoma, but its interpretation may be complicated by PD-1 blockade. We evaluated whether PET2, supported by quantitative PET parameters, remains informative for treatment adaptation during nivolumab-based treatment.

Methods: We conducted a prospective single-center study (NCT07209059) evaluating a PET-adapted nivolumab-based first-line strategy in advanced-stage classical Hodgkin lymphoma (AS-cHL). 44 previously untreated pts were enrolled.

All pts received two induction cycles of nivolumab 40 mg (N40) plus EACOPD-14. Patients achieving CMR (DS 1–3) at PET2 received N40-AVD consolidation followed by 2 cycles of N40, whereas patients with PMR (DS 4–5) continued N40-EACOPD-14 up to 6 cycles. RT was omitted in all patients. Quantitative PET analysis included changes in SUVmax (Δ SUVmax) and metabolic tumor volume (Δ MTV) and was available for 31 patients.

Results: All 44 pts completed induction therapy and underwent PET2 assessment. CMR was achieved in 36/44 patients (82%), while 8/44 (18%) demonstrated PMR. No DS5 cases were observed. All PMR cases showed low-volume residual uptake confined to mediastinal lesions. One patient experienced pseudoprogression after 2 cycles of N40-AVD.

Quantitative PET analysis demonstrated profound early metabolic responses. Median Δ SUVmax was –84.5% (IQR, –87.3% to –81.4%) in pts achieving PET2 CMR and –72.8% (IQR, –78.6% to –70.6%) in pts with PET2 PMR. Importantly, near-complete elimination of MTV was observed irrespective of PET2 category, with Δ MTV of 100% in 30/31 pts and 99% in the remaining patient.

At data cutoff, 38 patients had completed treatment and all achieved EOT CMR. No relapses or disease progression have been observed. Median follow-up was 10.2 months.

Conclusions: This PET-adapted nivolumab-based strategy demonstrated high early metabolic response rates and enabled chemotherapy de-escalation with radiotherapy omission in AS-cHL. Despite residual PET2 DS4 uptake, metabolic tumor burden was nearly completely eliminated, suggesting treatment-related inflammatory activity rather than substantial viable lymphoma. Quantitative PET parameters may help refine PET2 interpretation during PD-1-containing treatment regimens and improve response assessment beyond conventional Deauville scoring.

P019: Real-World Treatment Options and Outcomes of Hodgkin Lymphoma in Hungary

Zsófia Dr Miltényi¹, Fanni Borics¹, Dávid Tóthfalusi¹, Boglárka Fülöp-Dobó¹, László Imre Pinczés¹, Árpád Illés¹

¹University of Debrecen, Department of Hematology, Debrecen, Hungary

Background: Survival outcomes in Hodgkin lymphoma (HL) have markedly improved, with 80–90% of patients now curable. A nationwide initiative was launched in Hungary to evaluate real-world treatment patterns and compare them with international results. Since January 2021, 17 of 20 hematology centers have contributed data.

Aims: To assess epidemiology, treatment approaches, and survival outcomes of HL patients diagnosed between 2021–2023 in Hungary, with special focus on stage IV disease and the real-world introduction of brentuximab vedotin (A)+AVD.

Methods: Patients diagnosed and treated for HL between 01/01/2021 and 12/31/2023 were analyzed. Progression-free survival (PFS) and overall survival were evaluated by stage and treatment. A+AVD was accessible only for stage IV patients through individual reimbursement requests, typically allowing its use from cycle 3 after initial ABVD. Stage IV patients were grouped into: ABVD (n = 75);

ABVD → AVD with negative interim PET/CT (n = 15); A+AVD from cycle 1 (n = 6); ABVD → A+AVD following approval (n = 12). Interim PET/CT was evaluated using the Deauville score.

Results: A total of 385 HL patients were identified (204 female, 181 male). Of these, 361 had classical HL and received curative-intent therapy (187 early-stage, 149 advanced-stage). Sixteen patients received non-standard therapy due to age or comorbidities.

The 2-year PFS was 87.6% in early-stage and 79.9% in advanced-stage disease. Twenty-seven early-stage and 32 advanced-stage patients were refractory or relapsed. In stage III, 2-year PFS was 90.5%; in stage IV, 75.7% ($p = 0.024$), lower than international benchmarks. In stage IV, combined ABVD/AVD groups (1+2) achieved a 2-year PFS of 75.6%, while brentuximab-treated groups (3+4) reached 77.8%. No relapses or deaths occurred after 2 years in patients receiving any brentuximab vedotin. Group-specific 2-year PFS was: 76% (group 1), 73.3% (group 2), 50% (group 3), and 91.7% (group 4) ($p = 0.04$). Interim PET/CT was Deauville 4 in three patients each in groups 3 and 4.

Summary/Conclusion: Real-world PFS of stage IV HL patients in Hungary was inferior to outcomes from clinical trials. Nevertheless, adding brentuximab vedotin improved PFS even when initiated after initial ABVD cycles. Although subgroup numbers were small, the findings provide important real-world evidence supporting the use of brentuximab vedotin in advanced HL.

P020: Efficacy and Safety of the combination of Programmed Death-1 inhibitors (PD-1i) with chemotherapy for the treatment of classical Hodgkin's Lymphoma (cHL). A single center experience

Kassiani Papanastassi¹, Pavlos Triantafyllou¹, Chara Giatra¹, Natassa – Eleni Loutsidi¹, Alexandros Tolia¹, Antonis Patrinos¹, Eleni Tszilioni¹, Leonidas Kotsifas¹, Evaggelia Giannikou¹, Maria Vassiliou¹, Christos Massoutis², Phoebe Rondogianni³, Ioannis Baltadakis¹, Maria Bouzani¹

¹Hematology & Lymphoma Dpt, BMT Unit, Evangelismos General Hospital of Athens, Greece, ²Hematopathology Dpt, Evangelismos General Hospital of Athens, Greece,

³Nuclear Medicine Dpt, Evangelismos General Hospital of Athens, Greece

Background: Although efficacy and toxicity of the continuous treatment of PD-1i is well documented, less is known about their combination with chemotherapy.

Aim: Our aim is to provide real-world data on this topic.

Methods: We report outcomes and toxicities of 11 subjects treated with Nivolumab+AVD as 1L for advanced stage cHL (AS-cHL) and 6 other salvaged with Pembrolizumab+GVD for primary refractory disease.

Results: Between 2023–2026, 2 men and 9 women, median age 61 y (51–70), were newly diagnosed with AS-cHL. The subtypes were nodular sclerosis (NS) in 5, mixed cellularity (MC) in 3, lymphocyte-rich (LRcHL) in 3 cases. Ann Arbor stage was III in 8, IV in 3 patients. Seven patients completed 6 cycles, 3 interrupted due to toxicity and 1 is on treatment. iPET was performed in 9: DS2 n = 5, DS3 n = 2, DS1 n = 1, DS4 n = 1. EoT PET was performed in 8 patients: DS2 n = 4, DS3 n = 3, DS5 n = 1. All had GCSF prophylaxis. Treatment-related toxicities were observed in 7 patients: Acute heart failure, rash, hypothyroidism, thrombocytopenia with hemorrhagic manifestations, anemia, stomatitis, cataract. Febrile neutropenia requiring hospitalization was manifested in 4 (36%) and hepatotoxicity $\geq$ grade 3 in 4 (36%) patients. Among them a woman died due to liver failure, while delayed hepatic fibrosis occurring 6 months after treatment completion was observed in another case. With a mfollow up of 27.7 months (0.9–34), all patients but 1 are alive. The mPFS is 18.93 months (5.17–31.8) with 3 (27%) patients relapsing after achieving CR and 1 dying in CR. Median OS was not reached. Between 2024–2026, 3 men and 3 women, median age 51 y. (33–69) with primary refractory cHL-NS, after treatment with BrECADD (n = 2) and ABVD (n = 4) were salvaged with PembroGVD. The Ann Arbor stage was II (n = 1), III (n = 3) and IV (n = 2). One patient is on treatment and 5 completed it: Four achieved CMR and 3 underwent ASCT. A 4th patient manifested acute heart and renal failure, becoming ineligible for ASCT. The 5th subject showed resistant disease and died thereafter. One patient was intubated due to severe pulmonary toxicity and another 1 for aseptic meningitis, 2 developed hypothyroidism, 1 hepatotoxicity. With a mfollow up of 17.8 months (0.6–20.8), all patients but 1 are alive. MedianOS was not reached. Among patients who achieved CR nobody relapsed.

Conclusions: Combining PD-1i with chemotherapy is efficacious, but it demonstrates significant toxicity, more than it is described in the pivotal trials.

P021: Vanishing Bile Duct Syndrome as a Paraneoplastic Manifestation of Hodgkin Lymphoma

Elizaveta Kodrul¹, Larisa Filatova¹, Stanislav Volchenkov¹, Svetlana Elkhova¹, Alexander Lomazov¹, Leonid Kramynin¹, Anastasia Kolgotina¹, Anna Zverkova¹, Irina Ishmatova¹, Nikita Kolupaev¹, Alina Eliseeva¹, Ilya Zyuzgin¹

¹Federal State Budget Institution «N.N. Petrov National Medical Research Centre of Oncology»

Introduction: Vanishing bile duct syndrome (VBDS) is a rare, life-threatening paraneoplastic complication of Hodgkin lymphoma (HL), characterized by severe cholestasis and ductopenia. Its pathogenesis is linked to immune dysregulation within the tumor microenvironment and cytokine-mediated cholangiocyte damage.

Objective: To describe the clinical and laboratory features, diagnostic approach, and response to therapy in a patient with HL complicated by VBDS.

Materials and Methods: We report a case of a 31-year-old patient with classical HL complicated by VBDS. The clinical presentation included weakness, nausea, generalized lymphadenopathy (cervical, axillary, mediastinal, intra-abdominal), pruritus, lower back pain, fever up to 39°C persisting for 2 months and progressive jaundice. Prior to hospitalization, the patient had been taking paracetamol 500 mg and ketorolac 20 mg daily for month to relieve fever and lower back pain. Laboratory findings revealed leukocytosis ($25 \times 10^9/L$), eosinophilia, ESR 55 mm/h, total bilirubin 186 mg/dL, direct bilirubin 154 mg/dL, ALT 334 U/L, AST 287 U/L, LDH 824 U/L, and GGT 308 U/L. Mechanical biliary obstruction was

excluded by abdominal ultrasound and CT. Test for viral hepatitis, HIV, herpes viruses and syphilis is negative results. Given the history of prolonged NSAID use, a probable diagnosis of drug-induced liver injury was made. Ursodeoxycholic acid and ademetionine were administered. However, this therapy proved ineffective. Further diagnostic workup was therefore pursued. Liver biopsy confirmed VBDS, demonstrating greater than 50% loss of interlobular bile ducts, with no histological evidence of primary sclerosing cholangitis, autoimmune liver disease or infiltration by lymphoma cells.

Results: Treatment with the DHAP regimen was initiated. Fever resolved by day 7. After the first cycle of chemotherapy, all disease-related symptoms completely resolved, with significant decreases in bilirubin, GGT, ALP, and aminotransferase levels. After the third cycle, PET-CT confirmed a complete metabolic response, and all laboratory parameters normalized. No hepatic failure was observed.

Conclusion: VBDS associated with HL represents a paraneoplastic syndrome. Timely performance of liver biopsy is essential for establishing the diagnosis and guiding treatment. In patients with HL presenting with cholestasis that cannot be attributed to other causes, a comprehensive diagnostic evaluation for VBDS should be systematically undertaken.

P022: Association of Patlak-derived dynamic FDG PET parameters with Deauville response categories and kinetic heterogeneity of residual PET-positive findings in classical Hodgkin lymphoma: a prospective single-center pilot study

Gregor Horňák¹, Veronika Hanáčková², Marie Lukášová², Jaroslav Ptáček³, Vít Procházka², Milan Kamínek¹

¹Department of Nuclear Medicine, University Hospital Olomouc, Palacký University Olomouc, Czech Republic, ²Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacký University Olomouc and University Hospital Olomouc, Czech Republic, ³Department of Medical Physics and Radiation Protection, University Hospital Olomouc, Palacký University Olomouc, Czech Republic

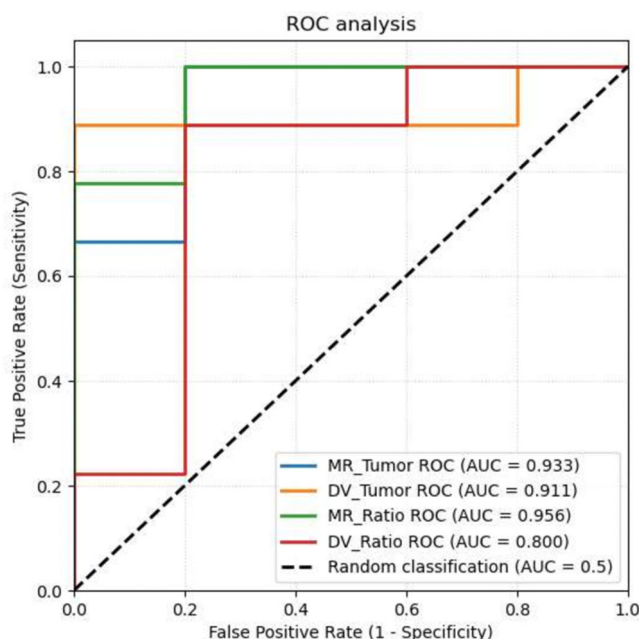


Figure 1: ROC analysis of Patlak-derived MRFDG and DVFDG for discrimination between DS 1–3 and DS 4–5 cHL lesions. Ratio parameters are shown as exploratory metrics.

Background: FDG PET/CT interpreted using the Deauville score (DS) is the standard method for response assessment in classical Hodgkin lymphoma (cHL). However, visual assessment of residual uptake is limited by inflammatory changes and suboptimal specificity. Dynamic FDG PET/CT with Patlak kinetic modeling enables quantitative evaluation of tracer kinetics beyond SUV metrics.

Aim: To assess the association between Patlak-derived FDG PET parameters and Deauville response categories and to explore kinetic heterogeneity among residual PET-positive lesions in cHL.

Methods: In this prospective single-center pilot study, patients with cHL undergoing interim or end-of-treatment FDG PET/CT with residual uptake (Aug 2025–May 2026, University Hospital Olomouc) were included.

Dynamic PET/CT was performed on a Siemens Biograph Vision 600 scanner. Patlak analysis with population-based input function was used to calculate metabolic rate of FDG (MRFDG) and distribution volume (DVFDG). One dominant mediastinal lesion per scan was analyzed.

Scans were classified as PET-negative (DS 1–3) or PET-positive (DS 4–5). MRFDG and DVFDG were compared between groups; ROC analysis and intra-group variability were assessed.

Results: Fourteen examinations were included; 5 were DS 1–3 and 9 DS 4–5.

MRFDG was higher in PET-positive vs PET-negative scans (12.34 ± 6.72 vs 4.59 ± 2.00 ; $p = 0.009$), with a 2.7-fold difference. DVFDG was also increased (208.83 ± 81.48 vs 110.95 ± 18.99 ; $p = 0.006$).

MRFDG and DVFDG showed strong discrimination (AUC 0.93 and 0.91, respectively). PET-positive scans showed marked heterogeneity in MRFDG (4.73–24.21) and DVFDG (105.84–389.39) despite identical DS.

Conclusions: Patlak-derived FDG PET parameters correlate with Deauville categories and reveal substantial kinetic heterogeneity among residual PET-positive cHL lesions. Dynamic PET may provide additional quantitative information beyond visual assessment. Further outcome-based validation is required.

P023: Real-World Effectiveness and Safety of the BrECADD Regimen in Advanced Hodgkin Lymphoma. A Multicenter Observational Study of the Polish Lymphoma Research Group

Justyna Rybka¹, Tomasz Wróbel¹, Anna Czyż¹, Kacper Bułdyś¹, Iwona Grygoruk-Wiśniowska², Monika Długosz-Danecka², Mateusz Sawicki³, Katarzyna Malesa³, Jarosław Dybko³, Ewa Paszkiewicz-Kozik⁴, Michał Kurlapski⁵, Kamila Kruczkowska-Tarantowicz⁶, Agnieszka Kołkowska-Leśniak⁷, Ewa Lech-Marañda⁷, Emilia Migryt-Rogala⁸, Justyna Gil⁹, Agnieszka Kopacz¹⁰, Anna Kopińska¹¹, Agnieszka Janus¹², Agnieszka Giza¹³, Jan Maciej Zaucha⁵

¹Department and Clinic of Hematology, Cellular Therapies and Internal Medicine, Wrocław Medical University, Wrocław, Poland, ²Maria Skłodowska-Curie National Institute of Oncology State Research Institute in Krakow, Krakow, Poland, ³Department of Hematology, Lower Silesian Center for Oncology, Pulmonology and Hematology, Wrocław, Poland, ⁴Department and Clinic of Lymphatic System Cancers, National Research Institute of Oncology in Warsaw, Warsaw, Poland, ⁵Department of Hematology and Transplantation, Medical University of Gdansk and University Clinical Center in Gdansk, Gdansk, Poland, ⁶Department of Internal Medicine and Hematology, Military Institute of Medicine - National Research Institute, Warsaw, Poland, ⁷Department of Hematology, Institute of Hematology and Transfusion Medicine in Warsaw, Warsaw, Poland, ⁸Department and Clinic of Hematooncology and Bone Marrow Transplantation University Clinical Hospital No. 1 in Lublin, Medical University of Lublin, Lublin, Poland, ⁹Department of Hematology and Oncology, Specialist Hospital in Brzozów, Podkarpackie Oncology Center, Brzozów, Poland, ¹⁰Department of Hematology, Fryderyk Chopin University Clinical Hospital in Rzeszów, Poland, ¹¹Hematology and Bone Marrow Transplantation Clinic of the Medical University of Silesia in Katowice, Poland, ¹²Department of General Hematology and Internal Diseases of the Hematology Clinic in Łódź, Poland, ¹³Department and Clinic of Hematology, Jagiellonian University Medical College in Kraków, Poland

N, n (%)	61 (100.0)
Female	30 (49.2)
Male	31 (50.8)
Age at diagnosis, years, mean ± SD	33.58 ± 10.79
CS, n (%)	
2	1 (1.6)
3	14 (23.0)
4	46 (75.4)
IPS, n (%)	
Low risk	23 (37.7)
High risk	38 (62.3)
General symptoms, n (%)	43 (70.5)
Extranodal location, n (%) *	45 (75.0)
No of cycles, mean ± SD	4.00 ± 1.41
No of cycles, n (%)	
1	2 (3.3)
2	10 (16.4)
3	4 (6.6)
4	29 (47.5)
5	2 (3.3)
6	14 (23.0)

Table 1: Clinical data of patients treated with BrECADD.

Introduction: The BrECADD regimen has demonstrated high efficacy in patients with advanced Hodgkin lymphoma (HL).

Aim: The aim of this observational study conducted by the Polish Lymphoma Research Group (PLRG) was to assess the efficacy and safety of the BrECADD regimen in patients with advanced HL treated in real-world clinical practice.

Materials and methods: Clinical data from patients with HL treated in 12 hematology centers in Poland were retrospectively evaluated. The analysis included 61 patients: 30 women and 31 men, diagnosed with advanced-stage HL. The mean age was 33 years. According to the Ann Arbor classification, 15 patients had stage III disease and 46 had stage IV. B symptoms were present in 43 patients (70.5%), while extranodal involvement was confirmed in 45 patients (75%).

Statistical analyses were performed using R software. Categorical variables were presented as n (%), while continuous variables were expressed as mean $\pm$ standard deviation due to their normal distribution. Normality of distribution was assessed using the Shapiro–Wilk test and additionally verified by skewness and kurtosis analyses.

Results: The median number of administered cycles was 4. Interim PET/CT assessment after 2 cycles was performed in 53 patients and demonstrated complete remission (CR) in 40 patients (75%) and partial remission (PR) in 12 patients (22.6%). Disease progression (PD) was observed in 1 patient. PET/CT assessment after 4 cycles was available in 39 patients and confirmed CR in 34 patients (87%), while PD was observed in 2 patients (5%). Progression-free survival (PFS) in the overall analyzed cohort was 97.1% at 6 months. Grade 3–4 neutropenia occurred in 40 patients (89%), thrombocytopenia with platelet count below 20 G/L was observed in 13 patients (21%). Febrile neutropenia developed in 13 patients (21%). Dose reduction of brentuximab vedotin was required in 12 patients (19%), whereas dose reductions of other agents (cyclophosphamide and etoposide) were necessary in 19 patients (31%).

Conclusion: Our preliminary real-world data confirm the high efficacy of the BrECADD regimen in patients with advanced HL, with high complete remission rates and excellent short-term PFS. Although hematologic toxicity was frequent, adverse events were manageable and consistent with the known safety profile of the regimen. These findings support the implementation of BrECADD as an effective first-line treatment option for advanced HL in Poland.

P024: Anthracycline-containing regimens confer better survival in risk-matched, advanced stage older patients with classic Hodgkin lymphoma; comorbidity, not age, predicts cardiac toxicity

Aisling Barrett¹, Amy Kirkwood², Pam McKay³, Wendy Osborne⁴, Nimish Shah⁵, Fatima Jamil³, Ravindu De Silva⁵, Joanna Fawcett⁴, Nicola Crosbie⁶, Jacinta Hardman⁶, Sarah Idris⁷, Chenxi Lee⁷, Edward Truelove⁸, Amjad Hmaid⁸, Sunil Iyengar⁹, Laura McDonald⁹, Fiona Miall¹⁰, Heather Laing¹⁰, Georgina Talbot¹¹, Syed Hasan¹¹, Shuyang Dai¹¹, Anna Santarsieri¹², Sai Lon Wann¹², Maria Marzolini¹³, James Paterson¹³, Sarah Lawless¹⁴, David Waddell¹⁴, Rachel Trickey¹⁵, Tessa Davies¹⁵, Vivek Radhakrishnan¹⁶, Srishma Sridhar¹⁶, Elizabeth H. Phillips¹⁷, Chiara Dallatorre¹⁷, Peter Toth¹⁸, Pierre McCarthy¹⁸, Emily Chernucha¹⁹, Moitreyo Pandit¹⁹, Laura Percy²⁰, Jack Easton²⁰, Rory McCulloch²¹, Julia Wolf²¹, Matthew Wells²², David Quinn²², Andrea Kuhn²³, Charlotte Subklewe^{23,24}, Lucy Cook²⁵, Oscar Atkins²⁵, Eve Gallop-Evans²⁶, Katja Williams²⁶, Cathy Burton²⁷, Graham P. Collins²⁸

¹Nuffield Department of Population Health, University of Oxford, Oxford, UK, ²CR UK and UCL Cancer Trials Centre, UCL Cancer Institute, University College London, London, UK, ³Beatson Cancer Centre, Glasgow, UK, ⁴The Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK, ⁵Norfolk and Norwich University Hospitals NHS Foundation Trust, Norfolk, UK, ⁶University Hospitals Plymouth NHS Trust, Plymouth, UK, ⁷Barking, Havering and Redbridge University Hospitals NHS Trust, Barking, UK, ⁸Barts Health NHS Trust, London, UK, ⁹The Royal Marsden NHS Foundation Trust, London, UK, ¹⁰University Hospitals of Leicester NHS Trust, Leicester, UK, ¹¹University Hospitals of North Midlands NHS Trust, North Midlands, UK, ¹²Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK, ¹³University College London Hospitals NHS Foundation Trust, London, UK, ¹⁴Belfast Health and Social Care Trust, Belfast, UK, ¹⁵Aneurin Bevan University Health Board, Newport, UK, ¹⁶University Hospital Southampton NHS Foundation Trust, Southampton, UK, ¹⁷The Christie NHS Foundation Trust, Manchester, UK, ¹⁸Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, ¹⁹Nottingham University Hospitals NHS Trust, Nottingham, UK, ²⁰University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK, ²¹Gloucestershire Hospitals NHS Foundation Trust, Gloucestershire, UK, ²²The Clatterbridge Cancer Centre NHS Foundation Trust, Liverpool, UK, ²³King's College Hospital NHS Foundation Trust, London, UK, ²⁴Department of Hematology, Oncology, and Tumor Immunology, Charité, Universitätsmedizin Berlin, Berlin, Germany, ²⁵Imperial College Healthcare NHS Trust, London, UK, ²⁶University Hospital of Wales, Cardiff, UK, ²⁷Leeds Teaching Hospitals NHS Trust, Leeds, UK, ²⁸Oxford University Hospitals NHS Foundation Trust, Oxford, UK

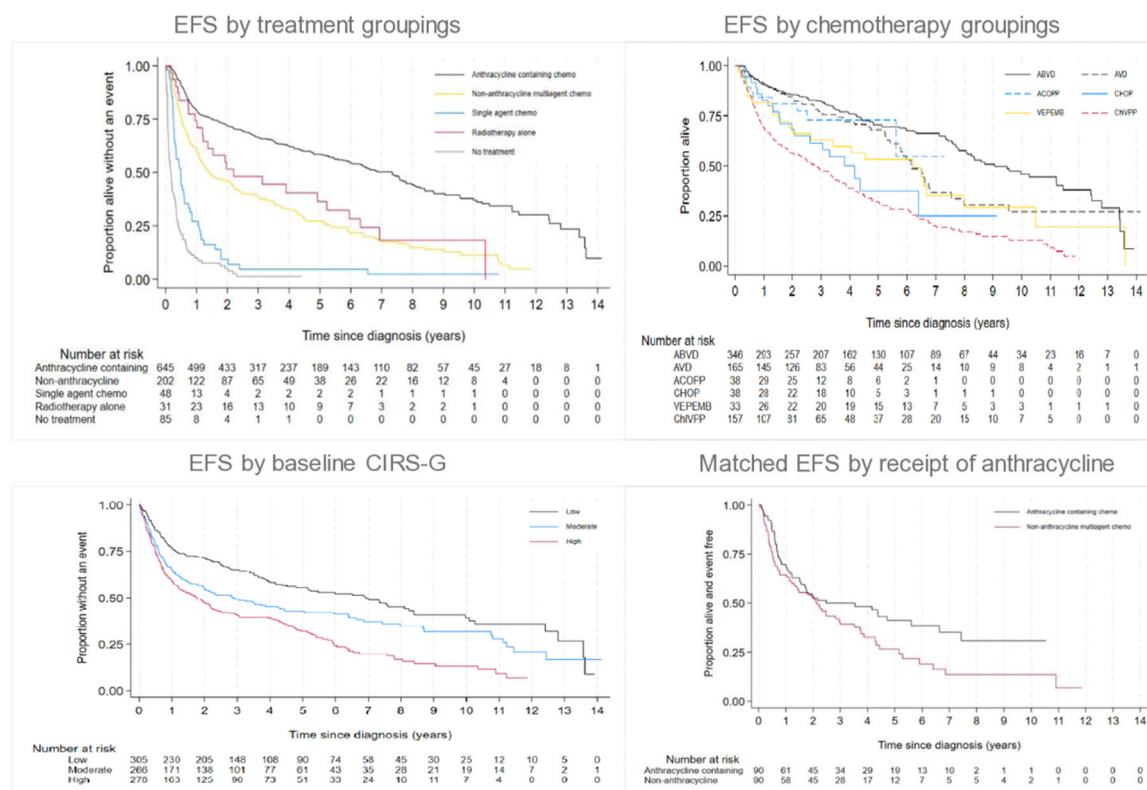


Figure 1: Event-free survival of older classic Hodgkin lymphoma patients.

Introduction: Older (≥ 60 year old (y)) patients with classical Hodgkin lymphoma (cHL) have worse outcomes than their younger counterparts. The interplay between comorbidities, treatment choice and outcomes has been incompletely examined.

Methods: This is a retrospective cohort study with contribution from 24 UK sites. Eligible ≥ 60 y cHL patients were diagnosed from 2010–23. Baseline factors were compared using Kruskal Wallis and Fisher's exact tests. Overall survival (OS) and event-free survival (EFS) were assessed using Kaplan-Meier survival analysis with groups compared using Cox regression. Binary endpoints were compared using logistic regression.

Results: A total of 1011 eligible patients were registered to the study: 645 receiving anthracycline-containing chemotherapy (antra), 202 multiagent chemotherapy without antra (non-antra), 48 single-agent, 31 radiotherapy alone and 85 with no treatment. Antra was used more commonly and radiotherapy less commonly in the more recent era (2020–23 $p = 0.002$ compared to pre-2020). Antra patients had lower CIRS-G score at diagnosis ($p < 0.0001$).

The median follow up was 5.3 years. OS and EFS varied significantly by CIRS-G score at baseline, treatment groups and type of chemotherapy delivered (all $p < 0.0001$).

Upfront dose modification was more common in the non-antra group ($p = 0.002$), older patients ($p < 0.0001$), prior cardiac history ($p = 0.016$) and higher CIRS-G score ($p = 0.007$); it did not protect against later treatment changes when groups were adjusted for age, CIRS-G and treatment group.

There was increased risk of treatment-related cardiac toxicity if prior cardiac history, but only in the non-antra group ($p = 0.0092$). CIRS-G with omission of cardiac scores was more predictive in antra but the interaction was not significant ($p = 0.11$). No significant difference was seen with increasing age ($p = 0.15$). There was increased risk of infectious admission in the non-antra group ($p = 0.002$), higher CIRS-G score ($p = 0.008$) and increased age at diagnosis ($p = 0.005$).

When advanced stage patients were matched for international prognostic score factors, CIRS-G and age band the non-antra group had inferior OS (HR 1.59, $p = 0.021$) and EFS (1.45, $p = 0.046$) compared to antra.

Discussion: Anthracycline use is preferable in older cHL patients. A comorbidity-focused approach to treatment selection may improve outcomes whilst maintaining acceptable toxicity.

P025: Validation of the Hodgkin lymphoma Simplified Frailty Score for Patients Receiving Modern Regimens

Katherine Sobol¹, Efrat Luttwak¹, Tiffany Chang¹, Nivetha Ganeson¹, Pallawi Torka¹, Alison Moskowitz¹

¹Memorial Sloan Kettering Cancer Center

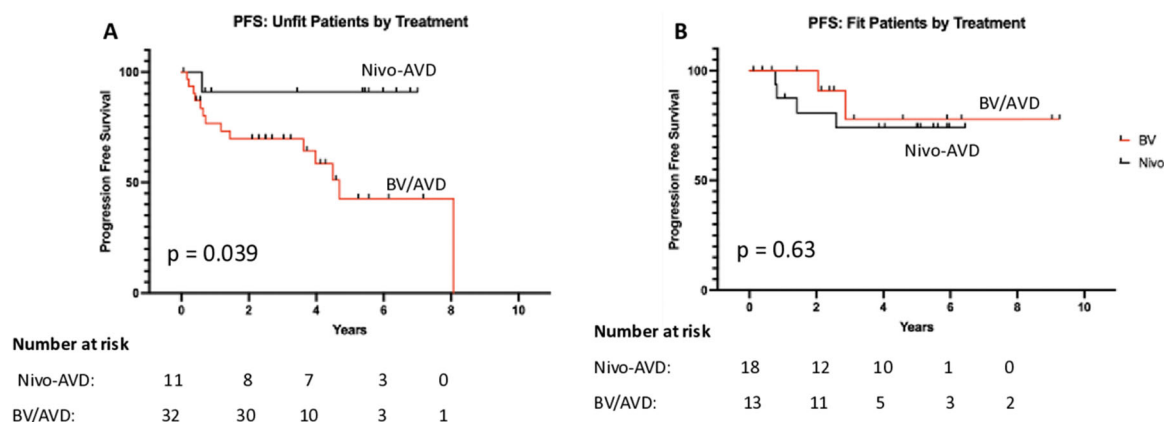


Figure 1: A. PFS for unfit patients treated with BV-based therapy versus Nivo-based therapy B. PFS for fit patients treated with BV-based therapy versus Nivo-based therapy.

Background: Treatment of classic Hodgkin lymphoma (cHL) in older patients (≥ 60 years) is challenging due to frailty, comorbidities, and poor tolerance to standard therapies. Front-line regimens incorporating either brentuximab vedotin (BV) or nivolumab (nivo) demonstrated improved outcomes. A simplified frailty score combining age (≥ 70), Charlson Comorbidity Index (CCI (0–2 vs 3 or higher)), and Eastern Cancer Oncology Group (ECOG ≥ 2) predicted outcomes in older patients treated with conventional curative treatment (Lia, et al. Haematologica 2025). We assessed the utility of the simplified frailty score in patients treated with newer regimens containing either BV or nivo.

Methods: We identified consecutive patients age ≥ 60 at the time of cHL diagnosis treated with curative-intent treatment consisting of BV or nivo in combination (or sequentially) with AVD chemotherapy, treated from June 2014 to February 2025. Each frailty criterion contributed one point for an index ranging from fit (0), unfit (1–2), and frail (3). The primary outcomes were progression-free survival (PFS) and overall survival (OS) analyzed using Kaplan-Meier methods and log-rank tests.

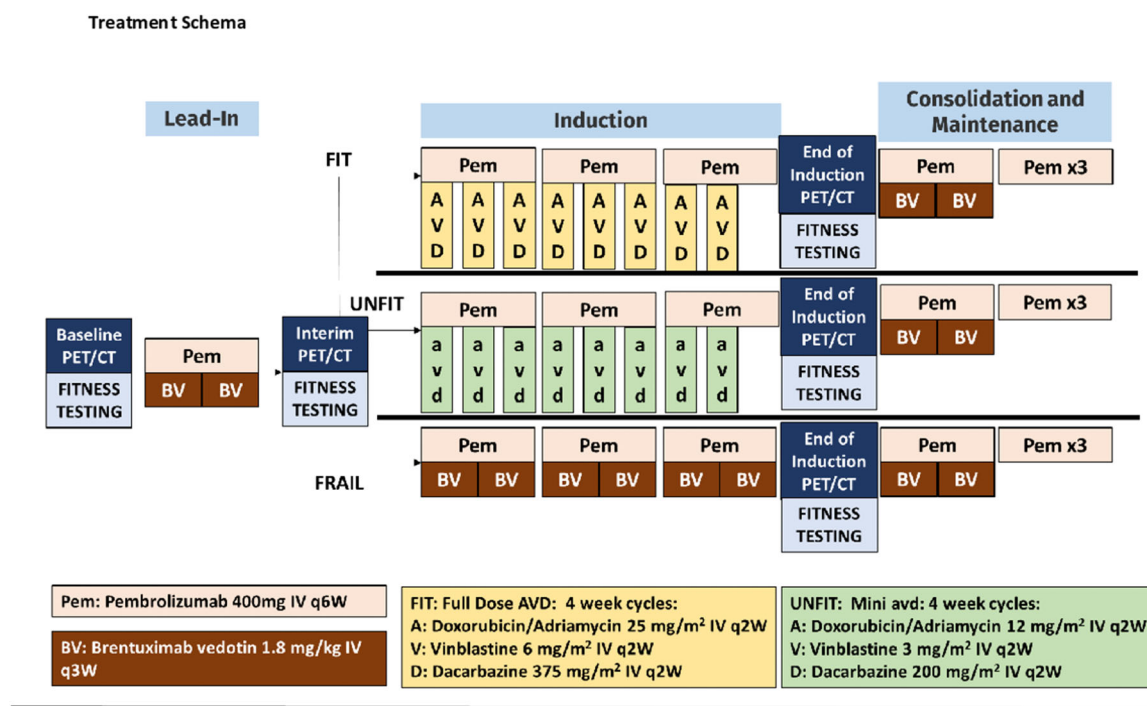
Results: Among 75 patients, median age was 69 (60–82); 29 (39%) received nivo-based therapy and 46 (61%) BV-based (67% sequential; 33% combined). There were 31 (41%) fit patients, 43 (57%) unfit patients, and one frail patient. 5-year PFS and OS were 65% and 85%, respectively. The 5-year PFS for fit and unfit patients were 74% and 59% ($p = 0.10$); the 5-year OS were 100% and 72% ($p = 0.009$). Treatment with nivo-based, BV-sequential, or BV-combined therapy was associated with 5-year PFS of 80%, 54%, and 53%, respectively ($p = 0.16$ for nivo-based vs BV-sequential, $p = 0.039$ for nivo-based vs BV-combination). For unfit patients, PFS was significantly improved for patients treated with nivo-based therapy compared to BV-based therapy (5-year PFS 91% vs 43%, $p = 0.039$), however OS was not significantly different (5-year OS 89% vs 61%, $p = 0.24$). For fit patients, outcomes were similar regardless of treatment; 5-year PFS, OS were 74%, 100% and 78%, 100%, for patients treated with nivo-based therapy and BV-based therapy, respectively (Figure).

Conclusion: These findings aid in validating the simplified frailty score in patients treated with modern therapy and suggest that nivo-based therapy is particularly beneficial for unfit elderly patients. Treatment choice is less likely to impact outcomes for fit patients.

P026: Fitness-adapted, pembrolizumab-based therapy for untreated classical Hodgkin Lymphoma (cHL) patients (Pts) 60 years of age and above: a multicenter prospective study

Craig Portell¹, Bethany Horton¹, David Brighton¹, Jakub Svoboda², Victor Orellana-Noia³, Andrew M. Evens⁴

¹University of Virginia, ²University of Pennsylvania, ³City of Hope National Medical Center, ⁴Rutgers Cancer Institute of New Jersey



Fitness Assessment

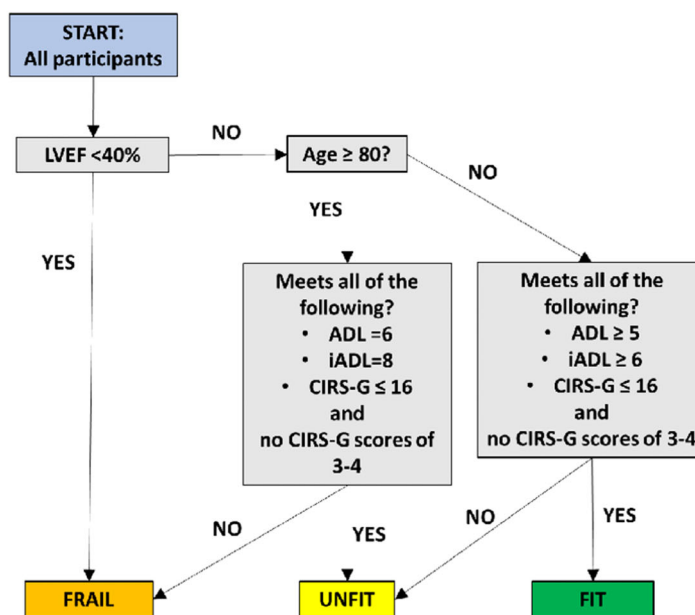


Figure 1: Treatment Schema and Fitness assignment.

Background: cHL occurs in a bimodal age distribution with 20–30% of diagnoses occurring in Pts aged ≥60 years. Outcomes have improved in the recent era. However, treatment related toxicities are common, especially for unfit and frail pts. We designed a multicenter prospective study utilizing fitness-based assessments to assign targeted cHL therapy.

Methods: Subjects had untreated cHL with an age ≥60 years and ECOG performance status (PS) of 0–1 or PS of 2 if decline was cHL-related. Those with Grade ≥2 neuropathy, known additional malignancy, and active inflammatory disease were excluded.

All subjects were treated with brentuximab vedotin (BV) and pembrolizumab (Pem) for 6 weeks (Figure). Thereafter, fitness assessment, comprising activities of daily living (ADLs), instrumental ADLs, and Cumulative Illness Rating Scale-Geriatric scores were repeated. Subjects were grouped into Fit, Unfit and Frail adapted from Merli et al JCO 2021. All patients continued Pem, with additional treatment based on fitness: Fit (full dose AVD x4 cycles), Unfit (half-dose “mini” AVD x4 cycles), and Frail (BV x18 weeks). Primary objectives were to assess safety and efficacy. Target sample size was 44 participants. The study was registered on clinicaltrials.gov (NCT05404945) and supported by a research grant from Merck Sharp & Dohme LLC.

Results: Enrollment occurred from 7/2022 to 12/2025 at 3 US institutions. Due to slow enrollment and a new standard therapy for fit older cHL Pts (S1826 study: Rutherford et al JCO 2025), the study closed early. Ten pts consented to the trial and 8, with a median age of 81 years (range 66–85), were treated. After BV/Pem lead-in, 3 were allocated to the frail arm, 4 were allocated to the unfit arm, and 1 was allocated to the fit arm. 75% (n = 6) completed induction. All subjects responded; best response was CR in 75% (n = 6) and PR in 25% (n = 2). Five related SAE's occurred in 37.5% (n = 3) of subjects. No new toxicities were identified or Grade 5 events. One subject remains on treatment.

Conclusions: Treatment with Bv/Pem-based therapy for newly-diagnosed older cHL Pts based on fitness assessments was feasible. This study also introduced a new “mini-AVD” regimen for unfit cHL Pts. Responses rates were robust in this small cohort; however, the study was closed prematurely. Further study is warranted for older cHL pts with therapy tailored according to fitness.

P027: Cost-effectiveness analysis of N-AVD vs BrECADD in advanced-stage classic Hodgkin lymphoma

Jowon Laura Kim¹, Amar H. Kelkar², Susan Parsons³, Alison Moskowitz⁴, Kishan Patel⁴, Adrienne Nedved¹, Arushi Khurana¹, Jc C. Villasboas Bisneto¹, Jonas Paludo¹, Jithma P. Abeykoon¹, Yun Kyoung Tiger¹, Paul J. Hampel¹, Yucai Wang¹, Yi Lin¹, N. Nora Bennani¹, Luis F. Porrata¹, Gita Thanarajasingam¹, Carrie A. Thompson¹, Patrick B. Johnston¹, Ivana N. Micallef¹, Thomas M. Habermann¹, Thomas E. Witzig¹, Philippe Armand¹, Stephen M. Ansell¹, Urshila Durani¹

¹Division of Hematology, Mayo Clinic, Rochester, Minnesota, ²Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts, ³Division of Hematology/Oncology, Tufts Medical Center, Boston, Massachusetts, ⁴Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York

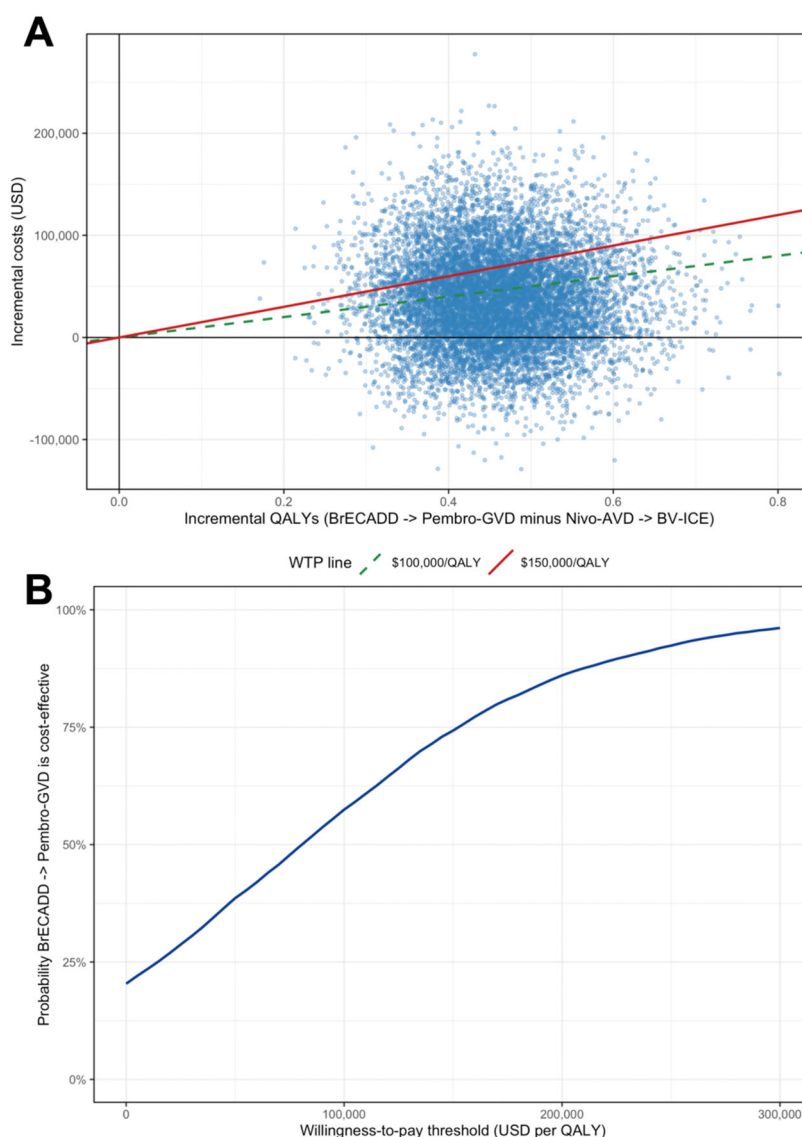


Figure 1: Probabilistic sensitivity analyses with (A) cost effectiveness plane (B) cost effectiveness acceptability curve.

Background: Recent trials have established Nivolumab(N)-AVD and BrECADD as parallel standards in advanced-stage classic Hodgkin lymphoma (cHL). Many factors influence the choice of frontline regimen, including comorbidities, stage, toxicities, and reimbursement decisions. We compared the cost-effectiveness of the two strategies from a US payer perspective over a lifetime horizon.

Methods: A 5-state Markov model was developed: progression-free after first-line therapy (PF1), salvage therapy +/- ASCT for first progression (PD1), progression-free after salvage and ASCT (PF2), second progression (PD2), and death. Patients who relapsed after N-AVD were assumed to receive Brentuximab-based salvage, while patients who relapsed after BrECADD were assumed to receive Pembrolizumab-based salvage. Costs and utilities were discounted at 3% annually. Transition probabilities were derived from digitized and extrapolated survival curves. Main outcomes were incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit (INMB). Sensitivity analyses were performed to test the validity of the base case conclusions.

Results: In the base case, BrECADD increased discounted quality-adjusted life years (QALYs) by 0.50 and life-years by 0.36 at an incremental cost of \$39,307, yielding an ICER of \$79,298/QALY and an INMB of \$35,046 at a willingness-to-pay (WTP) threshold of \$150,000/QALY. In probabilistic sensitivity analysis (10,000 simulations), the ratio-of-means ICER was \$84,241/QALY, and the probability that BrECADD was cost-effective was 74.3% at a WTP of \$150,000/QALY. In one-way sensitivity analyses, the base case conclusion was most sensitive to varying frontline regimen efficacy, frontline costs, and the time horizon. In two-way sensitivity analyses, BrECADD was no longer preferred when N-AVD 5-year PFS was increased to 91.3%, when BrECADD drug costs were increased by 125%, or when the time horizon was shortened to 26 years. In a structural sensitivity analysis assigning Pembrolizumab-based salvage after both N-AVD and BrECADD, the ICER for BrECADD rose to \$176,019/QALY.

Conclusion: BrECADD was cost-effective compared with N-AVD at a WTP threshold of \$150,000/QALY. This finding remained consistent across most deterministic and probability sensitivity analyses.

P028: First-line BrECADD in routine clinical practice: excellent treatment deliverability and early efficacy in advanced-stage classical Hodgkin lymphoma

Ida Hude Dragičević¹, Klaudia Babić čukman², Sandra Bašić-Kinda^{1,2}, Barbara Dreta¹, Dino Dujmović¹, Josip Batinić^{1,2}, Margareta Dobrenić^{3,2}, Lea Galunić-Bilić^{4,2}, Igor Aurer^{1,2}

¹Department of Internal Medicine, Division of Haematology, University Hospital Center Zagreb, Zagreb, Croatia, ²University of Zagreb School of Medicine, Zagreb, Croatia,

³Department of Nuclear Medicine and Ionizing Radiation Protection, University hospital Center Zagreb, Zagreb, Croatia, ⁴Department of Oncology and Radiotherapy, University Hospital Center Zagreb, Zagreb, Croatia

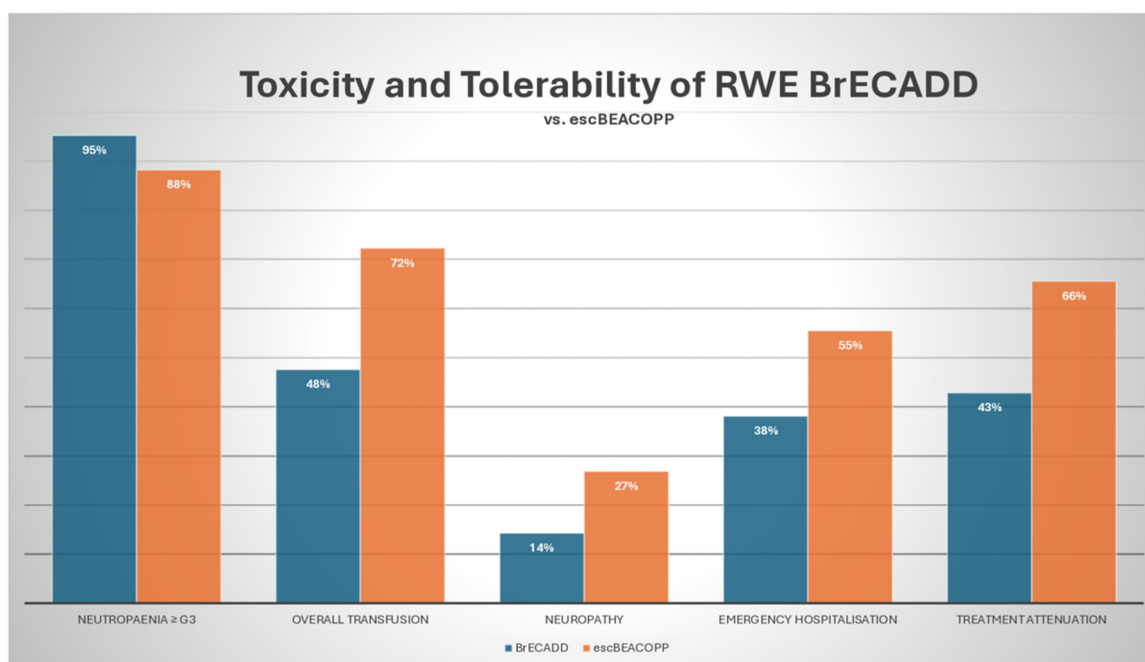


Figure 1: Significant reductions were observed in overall transfusion requirements and treatment attenuation. Differences in neuropathy and emergency hospitalization were not statistically significant. Rates of neutropaenia ≥G3 were similar between cohorts.

Background: BrECADD became the preferred first-line treatment for advanced-stage (AS) classical Hodgkin lymphoma (cHL) following HD21. However, real-world data remain limited.

Aim: To evaluate efficacy, treatment deliverability, and toxicity of first-line BrECADD in routine clinical practice and compare toxicity outcomes with a historical escalated BEACOPP (escBEACOPP) cohort.

Methods: We retrospectively analyzed all patients with AS cHL treated with first-line BrECADD at the University Hospital Centre Zagreb (2023–2025). Toxicity findings were compared with an escBEACOPP cohort treated between 2015 and 2025. Toxicity endpoints included grade ≥ 3 neutropenia, transfusion requirements, treatment modifications, peripheral neuropathy, and hospitalizations. Multivariable logistic regression adjusted for age, stage, and ECOG performance status was used to evaluate factors associated with transfusion requirements and treatment modifications.

Results: Twenty-one patients received first-line BrECADD. Median age was 27 years (19–60); 86% had stage IV disease and 71% extranodal involvement. Interim PET2 was available in 19 pts, with 18/19 achieving complete metabolic remission (CMR). Most pts received 4 cycles (4 received 6 cycles).

At a median follow-up of 15 months, all patients achieved CMR, with progression-free and overall survival rates of 100%.

Treatment modifications occurred in 43% of patients; however, no cycle delays or treatment discontinuations were observed. Grade ≥ 3 neutropenia occurred in 95% of patients, hospitalization for febrile neutropenia in 33%, red blood cell transfusions in 19%, platelet transfusions in 33%, and peripheral neuropathy in 14%.

Compared with escBEACOPP ($n = 119$), BrECADD-treated patients received fewer treatment cycles (median 4 vs 6, $p < 0.001$).

Overall transfusion requirements were lower with BrECADD (48% vs 72%; $p = 0.039$). In multivariable analysis, BrECADD remained independently associated with lower odds of transfusion requirement (OR 0.37, 95% CI 0.14–0.98; $p = 0.046$) and superior treatment deliverability (OR 2.73, 95% CI 1.01–7.41; $p = 0.048$).

Conclusions: In routine clinical practice, first-line BrECADD demonstrated excellent efficacy and tolerability. Despite frequent hematologic toxicity, treatment completion was universal and no treatment delays occurred. Compared with escBEACOPP, BrECADD was associated with reduced transfusion requirements and better preservation of planned treatment intensity.

P029: Ten-year follow-up of ECHELON-1: overall survival and long-term safety with Brentuximab vedotin plus AVD versus ABVD in patients with previously untreated advanced classic Hodgkin lymphoma

Stephen M. Ansell¹, David J. Straus², Joseph M. Connors³, Wojciech Jurczak⁴, Won Seog Kim⁵, Andrea Gallamini⁶, Marco Picardi⁷, Tatyana Feldman⁸, Kerry J. Savage³, Radhakrishnan Ramchandren⁹, Pier Luigi Zinzani¹⁰, Jeremy S. Abramson¹¹, Graham P. Collins¹², Jonathan W. Friedberg¹³, Andrew Grigg¹⁴, Mehmet Turgut¹⁵, Martin Hutchings¹⁶, Ranjana Advani¹⁷, Adriana Scheliga¹⁸, Andrew M. Evens¹⁹, Rizvan Bush²⁰, Farhad Sedarati²⁰, Fei Jie²¹, Michelle Fanale²¹, John Radford²²

¹Mayo Clinic, Rochester, MN, USA, ²Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA, ³BC Cancer, Centre for Lymphoid Cancer, Vancouver, BC, Canada, ⁴Maria Skłodowska-Curie National Research Institute of Oncology, Krakow, Poland, ⁵Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, ⁶Antoine-Lacassagne Cancer Center, Nice, France, ⁷Federico II University Medical School, Naples, Italy, ⁸John Theurer Cancer Center, Hackensack Meridian Health, Hackensack, NJ, USA, ⁹University of Tennessee Graduate School of Medicine, Knoxville, TN, USA, ¹⁰University of Bologna, Bologna, Italy, ¹¹Massachusetts General Hospital, Boston, MA, USA, ¹²Oxford University Hospitals NHS Foundation Trust, Oxford, UK, ¹³Wilmot Cancer Institute, University of Rochester, Rochester, NY, USA, ¹⁴Health, Melbourne, VIC, Australia, ¹⁵Ondokuz Mayıs University, Samsun, Turkey, ¹⁶Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, ¹⁷Stanford University, Stanford, CA, USA, ¹⁸Rede Americas Group, Rio de Janeiro, Brazil, ¹⁹Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA, ²⁰Takeda Development Center Americas, Inc. (TDCA), Cambridge, MA, USA, ²¹Pfizer Inc., Bothell, WA, USA, ²²University of Manchester and the Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK

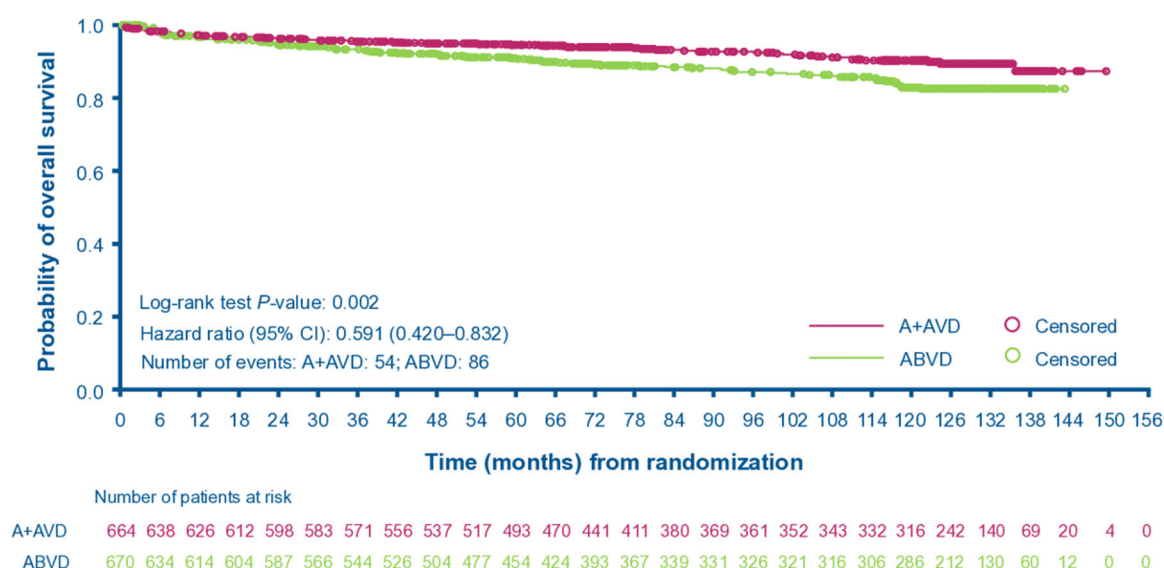


Figure 1: Kaplan-Meier plot of overall survival.

Background: The phase 3 ECHELON-1 study (NCT01712490) compared brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine (A+AVD) with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) in patients (pts) with previously untreated stage III/IV classic Hodgkin lymphoma (cHL). A 7-year follow-up (FU) analysis showed durable progression-free survival and overall survival (OS) benefits, and no new safety signals with A+AVD versus ABVD. We report 10-year FU data from ECHELON-1.

Methods: Pts were assigned 1:1 to receive up to 6 cycles of A+AVD (n = 664) or ABVD (n = 670) on days 1 and 15, every 28 days. OS was investigator-assessed in the intent-to-treat population (data cut-off [DCO] December 16, 2025). Long-term safety was evaluated in all pts who received ≥ 1 dose of any study medication (A+AVD, n = 662; ABVD, n = 659) and included subsequent anti-cancer therapies, secondary malignancies, peripheral neuropathy (PN) resolution/improvement, and pregnancies.

Results: At DCO, with a median FU of 120 months (95% CI 117.0–121.2), estimated 10-year OS rates were 90.3% (95% CI: 87.3–92.6) with A+AVD and 84.9% (95% CI: 81.4–87.8) with ABVD (hazard ratio 0.59 [95% CI 0.42–0.83]; P = 0.002; Figure). A+AVD was associated with proportionally fewer deaths than ABVD (8% vs 13%). In the A+AVD and ABVD arms, 21% and 25% of pts had ≥ 1 subsequent anti-cancer therapy, respectively; chemotherapy was most common (13% A+AVD; 17% ABVD). Secondary malignancies were reported in 5% of pts (A+AVD) and 7% pts (ABVD), which included solid tumors (4% A+AVD; 4% ABVD) or hematological malignancies (2% A+AVD; 3% ABVD). Treatment-emergent PN was ongoing in 116/443 (26%) pts who originally reported PN in the A+AVD arm (15% grade 1; 8% grade 2; 3% grade 3; <1% grade 4) and in 56/286 (20%) pts in the ABVD arm (13% grade 1; 5% grade 2; 1% grade 3). PN resolved or improved in 86% of pts with A+AVD (74% resolved/12% improved) and 87% of pts with ABVD (80%/7%). Median (range) time to complete PN resolution and improvement was 36 (0–507) and 42 (8–392) weeks with A+AVD, and 17 (0–530) and 22 (2–213) weeks with ABVD, respectively. Pregnancies occurred in 94 pts (A+AVD, n = 60; ABVD, n = 34) and 87 partners of male pts (n = 42; n = 45). Live births were reported in 77 pts (A+AVD, n = 51; ABVD, n = 26) and 77 partners of male pts (n = 37; n = 40), with no stillbirths reported.

Conclusion: In this 10-year FU, A+AVD demonstrated a sustained OS benefit vs ABVD in advanced cHL, with manageable long-term safety.

P030: Outcome and Prognostic Value of PET-2 in Stage IV Classical Hodgkin Lymphoma Treated with Frontline Brentuximab Vedotin Plus AVD: A Real-World Multinational GELTAMO-GATLA Study

Jose Ignacio Trucco^{1,2}, Marta Peña^{3,4}, Maria Teresa Marti^{3,4}, Laura Korin^{5,2}, Maria Rocio Figueroa Mora^{6,4}, Carmen Martinez^{7,4}, Guadalupe Antelo Perez^{8,2}, Marta Zerga^{9,2}, Maria Belen Navarro^{10,4}, Carolina Mahuad^{9,2}, Cecilia Carpio^{11,4}, Carmen Maria Alonso Prieto^{12,4}, Lorena Fiad^{13,2}, Maria Jimena Cannata-Ortiz^{14,4}, Malena Rocca^{15,2}, Nicolas Kellenher^{16,4}, Mariana Rosenhain^{17,2}, Blanca Sanchez Gonzalez^{18,4}, Luciano Salvano^{19,2}, Lucia Villalon Blanco^{20,4}, Javier Romano^{21,2}, Veronica Musso^{22,2}, Alessandra Comai^{23,4}, Fernando Warley^{24,2}, Carlos Santorum^{25,2}, Florencia Negri Aranguren^{26,2}, Maria Orlova^{27,2}, Amalia Cerutti^{28,2}, Valeria Drouet^{29,2}, Lautaro Sardu^{30,2}, Trinidad Viviani², Julia Valerga Couste², Eva Domingo-Doménech^{3,4}, Anna Sureda^{3,4}, Astrid Pavlovsky^{31,32,2}

¹Hospital Universitario Austral, ²GATLA, ³ICO Hospital Duran I Reinalds, ⁴GELTAMO, ⁵Instituto Alexander Fleming, ⁶Clinica Universitaria de Navarra, ⁷Hospital Clinic de Barcelona, ⁸CEMIC, ⁹Hospital Aleman de Buenos Aires, ¹⁰Hospital Universitario Puerta de Hierro Majadahonda, ¹¹Hospital Universitario Vall D Hebron, ¹²Hospital Arnau de Vilanova, ¹³Hospital italiano La Plata, ¹⁴Hospital Universitario de la Princesa, ¹⁵Hospital Allende, ¹⁶Hospital Josep Trueta, ¹⁷Hospital General de Agudos Enrique Tornu, ¹⁸Hospital del Mar, ¹⁹Clinica Universitaria Reina Fabiola, ²⁰Hospital Universitario Fundacion Alcorcon, ²¹Hospital Nacional Alejandro Posadas, ²²Centro Privado de Oncologia Milstein, ²³Hospital General de Catalunya, ²⁴Universidad del Hospital Italiano de Buenos Aires, ²⁵Hospital Cesar Milstein, ²⁶Instituto Privado de Hematología y Hemoterapia, ²⁷Hospital Italiano de Buenos Aires, ²⁸Sanatorio Británico, ²⁹Hospital Carlos Durand, ³⁰Hospital El Cruce, ³¹Centro de Hematología Pavlovsky, ³²FUNDALEU

Fig 1. Overall Survival

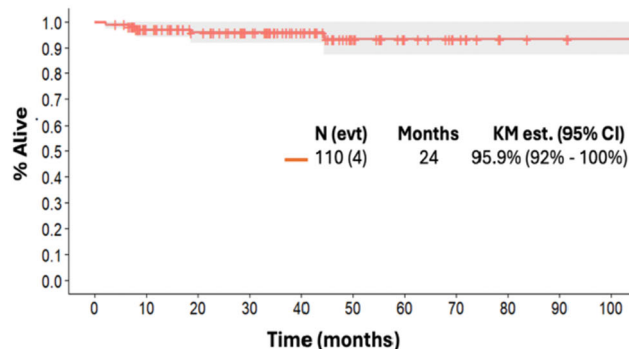


Fig 2. Event-Free Survival

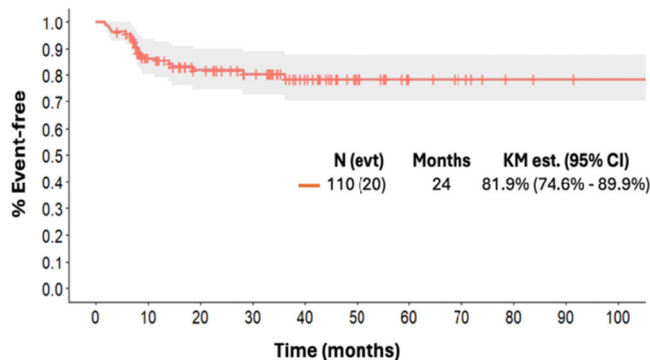
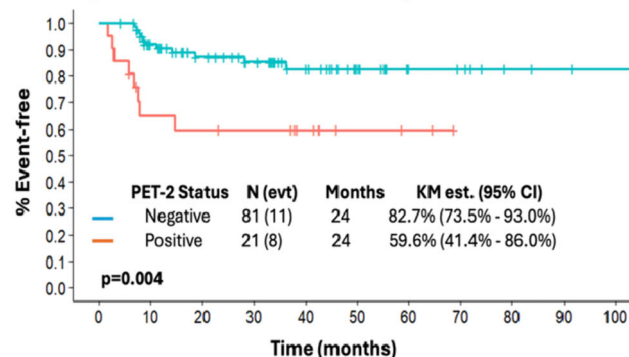


Fig 3. Event-Free Survival according to PET-2 status



Background: Real-world evidence of the benefit of Bv AVD vs. ABVD in stage IV cHL remains limited, and the prognostic value of interim PET (PET-2) is not clearly defined.

Aims: Evaluate metabolic complete remission (mCR) rate, 2-year EFS, OS, toxicity and the prognostic value of PET-2 in stage IV cHL pts treated with frontline Bv-AVD in routine clinical practice within a GELTAMO and GATLA collaboration.

Methods: Retrospective multicentre cohort of stage IV cHL patients (≥ 16 years) treated with frontline Bv-AVD (2/2019–3/2025) at 30 centres in Spain and Argentina. PET-2 (after ≥ 2 cycles) mCR was DS1–3. EFS/OS calculated with Kaplan-Meier. EFS/OS predictors were assessed by uni/multivariable Cox models including age (< 60 vs ≥ 60), IPS (1–3 vs 4–7), B symptoms, bulky (Bx) disease, PET-2 status, and ≥ 2 extranodal (EN) sites.

Results: 110 pts were included. Median age was 40.4 yrs (range 27.8–53.5); 80.6% ECOG 0–1, 69.1% B symptoms and 53.6% ≥ 2 EN sites. Bx disease in 28.2%; 38.2% IPS ≥ 4 . Median of Bv doses was 12. PET-2 was done in 102/110 pts (92.7%) achieving 79.2% mCR. EOT PET was done in 98/110 (89.1%), 88.8% mCR rate. Consolidative RT was delivered in 4.7% pts. At a median follow-up of 28.3 m for EFS and 34 m for OS, 2-year EFS was 81.9% [95%CI 74.6%–89.9%] and 2-year OS was 95.9% [CI95% 92%–100%]. mCR at PET-2 was associated with improved EFS (83.0% vs. 57.4%; $p = 0.002$) but not OS. IPS ≥ 4 and ≥ 2 EN sites involvement were associated with shorter OS (85.5% vs. 98.2%, $p = 0.05$ and 88.6% vs. 100%, $p = 0.04$ respectively). In multivariable analysis, PET-2 positivity remained independently associated with shorter EFS (HR 3.52; $p = 0.007$), without significant impact on OS. 48% pts developed neutropenia ($\geq G3$ 35%) with a median of 1 cycle; 14% $\geq G3$ febrile neutropenia. Peripheral neuropathy developed in 34% of the pts, mostly G1–2 (27%).

Conclusions: This large binational real-world study, restricted to pts with stage IV cHL, demonstrates that frontline Bv-AVD achieves favorable outcomes, with 2-year EFS and OS rates of 81.9% and 95.9%, respectively, consistent with ECHELON-1. To our knowledge, it represents the largest real-world series in stage IV pts and the first to show that PET-2 positivity independently predicts inferior EFS with

Bv-AVD, although the implications for treatment adaptation require prospective validation. This collaborative GELTAMO–GATLA analysis provides a relevant benchmark for future PET-adapted strategies in this high-risk population.

P031: Multistate Modeling of Disease Trajectories for Advanced-Stage Hodgkin Lymphoma Patients Receiving PET Response-Adapted Therapy

Zhu (jenny) Cui¹, Hocine Tighiouart¹, Nicholas Counsell², Sara Rossetti³, Jenica Upshaw⁴, Amy Kirkwood⁵, Hongli Li⁶, Ranjana Advani⁷, Olivier Casanovas⁸, James Cerhan⁹, Massimo Federico¹⁰, Andrea Gallamini¹¹, Hervé Ghesquieres¹², Eliza Hawkes¹³, David Hodgson¹⁴, Martin Hutchings¹⁵, Peter Johnson¹⁶, Brian Link¹⁷, Eric Mou¹⁷, John Radford¹⁸, Kerry J. Savage¹⁹, Deborah Stephens²⁰, Pier Luigi Zinzani²¹, Matthew Maurer⁹, Cedric Rossi⁸, Andrew M. Evens²², Susan Parsons¹, Angie Mae Rodday¹

¹Tufts Medical Center, Boston, MA, USA, ²Cancer Research UK and University College London Cancer Trials Centre, University College London, UK, ³Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark, ⁴Beth Israel Deaconess Medical Center, Boston, MA, USA, ⁵Cancer Research UK and University College London Cancer Trials Centre, University College London, UK, ⁶Southwest Oncology Group Statistical Center, Fred Hutchinson Cancer Research Center, Seattle, WA, ⁷Stanford University, Stanford, CA, USA, ⁸University Hospital F. Mitterrand and Inserm UMR 1231, Dijon, France, ⁹Mayo Clinic, Rochester, MN, USA, ¹⁰University of Modena and Reggio Emilia, Modena, Italy, ¹¹A. Lacassagne Cancer Center, Nice, France, ¹²Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Pierre Benite, France, ¹³Australasian Lymphoma and Related Diseases Registry, Monash University, Melbourne, Australia, ¹⁴Princess Margaret Cancer Centre and University of Toronto, Toronto, Canada, ¹⁵Rigshospitalet and Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, ¹⁶University of Southampton, Southampton, UK, ¹⁷University of Iowa, Iowa City, IA, USA, ¹⁸Christie NHS Foundation Trust, and NIHR Manchester Biomedical Research Centre, Manchester, UK, ¹⁹BCCancer, Centre for Lymphoid Cancer, Vancouver, BC, Canada, ²⁰University of North Carolina, Chapel Hill, NC, USA, ²¹Università di Bologna, Bologna, Italy, ²²Rutgers Cancer Institute, New Brunswick, New Jersey, USA

Table. Multivariable transition specific hazard ratios from multistate model.

Disease State Transition	N	Variables	HR (95% CI)
Diagnosis → Treatment Failure	216	A-HIPI ¹	1.44 (1.28 – 1.61)
		escBEACOPP2 ²	0.61 (0.40 – 0.93)
Diagnosis → Death	15	A-HIPI	2.47 (1.71 – 3.55)
Remission → Treatment Failure	169	A-HIPI	1.30 (1.13 – 1.50)
		escBEACOPP2	0.39 (0.22 – 0.67)
		Neg iPET ²	0.55 (0.38 – 0.78)
Remission → Death	7	A-HIPI	1.75 (0.96 – 3.16)
Treatment Failure → Death	70	A-HIPI	1.45 (1.19 – 1.77)
		escBEACOPP2	0.61 (0.28 – 1.36)
		Neg iPET	0.57 (0.35 – 0.91)

A-HIPI: advanced-stage Hodgkin lymphoma international prognostic index; **escBEACOPP:** escalated bleomycin, etoposide, doxorubicin (Adriamycin), cyclophosphamide, vincristine (Oncovin), procarbazine, and prednisone; **CI:** confidence interval; **HR:** hazard ratio; **iPET:** interim positron emission tomography computed tomography.

¹ A-HIPI ranged from 1–100, with higher values indicating greater risk of 5-year PFS events and was modeled per 1 standard deviation increase.

² Treatment and iPET were only modeled in transitions with at least five patients per group.

Table 1: Multivariable transition specific hazard ratios from multistate model.

Background: Despite recent advances in advanced-stage (AS) classical Hodgkin lymphoma (cHL), PET-adapted chemotherapy remains a first-line option where access to novel agents is limited. Many regimens begin with 2 cycles of escalated BEACOPP (escBEACOPP2) or ABVD (ABVD2), followed by interim PET (iPET)-guided treatment. There have been no direct comparisons of PET-adapted regimens initiated with escBEACOPP2 vs ABVD2. We used rigorous multistate model (MSM) methodology to assess transition specific impacts of treatment (escBEACOPP vs ABVD), baseline HL International Prognostic Index (A-HIPI) risk score, and iPET result.

Methods: We pooled individual data from 4 clinical trials of newly-diagnosed stage IIB-IV cHL patients (ages 18–60 years (y)) treated with PET-adaptive escBEACOPP2 (n = 363 from AHL2011) or ABVD2 (n = 1917 from SWOG0816, RATHL, HD0607) regimens. The 5 y MSM implemented with a Cox model had 4 states: diagnosis, sustained remission at 1 y, treatment failure, and death. We assessed the impact of treatment on transitions (except binary sustained remission at 1 y) that involved ≥ 5 pts per group, adjusting for A-HIPI for all transitions and iPET for post-remission transitions.

Results: The escBEACOPP2 group was younger (age 32 (SD 11) vs 34 y (SD 11)), had fewer females (39% vs 47%), less stage IIB disease (12% vs 28%), more bulk (57% vs 25%), and higher baseline disease risk according to A-HIPI (25.1 (SD 6.3) vs 22.7 (SD 6.3)). After adjusting for A-HIPI, escBEACOPP2 was associated with lower hazard of treatment failure within 1 y (aHR 0.61, 95%CI 0.40–0.93) and post-remission failure (aHR 0.39, 95%CI 0.22–0.6; see Table). Negative iPET was associated with lower hazards of post-remission failure (aHR 0.55, 95%CI 0.38–0.78) and death after first-line treatment failure (aHR 0.57, 95%CI 0.35–0.91), independent of baseline A-HIPI score and initial chemotherapy.

Conclusions: iPET-adapted treatment with escBEACOPP was associated with lower rates of both early treatment failure and post-remission relapse versus ABVD, after adjustment for baseline disease risk. Negative iPET was independently associated with a lower risk of post-remission treatment failure and death following frontline treatment failure, regardless of chemotherapy regimen or A-HIPI score. MSM offers a dynamic assessment of disease trajectories by capturing transitions between remission, treatment failure and death, and it provides a comprehensive framework to inform clinical decision-making.

P032: ABVD versus a risk-stratified and a response adapted strategy-addressing the dilemma in Advanced Hodgkin Lymphoma: A Phase III Randomized Study

Hasmukh Jain^{1,2}, Aravind Padmanabhan^{1,2}, Alok Shetty^{1,2}, Lingaraj Nayak^{1,2}, Bhausaheb Bagal^{1,2}, Jayashree Thorat^{1,2}, Thomas Eipe^{1,2}, Supriya More^{1,2}, Nisha Khatakar^{1,2}, Prasanth Ganesan³, Sreeraj Vasudevan⁴, Jayant Goda^{1,2}, Sumeet Gujral^{1,2}, Tanuja Shet^{1,2}, Jyothi Kode^{1,2}, Archi Agrawal^{1,2}, Venkatesh Rangarajan^{1,2}, Sneha Shah^{1,2}, Neha Sharma^{1,2}, Epari Sridhar^{1,2}, Siddhartha Laskar^{1,2}, Manju Sengar^{1,2}

¹Tata Memorial Centre, Dr. E Borges Road, Parel, Mumbai - 400 012 India, ²Homi Bhabha National Institute, Training School Complex, Anushaktinagar, Mumbai - 400 094 India, ³Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), Puducherry - 605 006 India, ⁴Amala Institute of Medical Sciences, Thrissur - 680 555 India

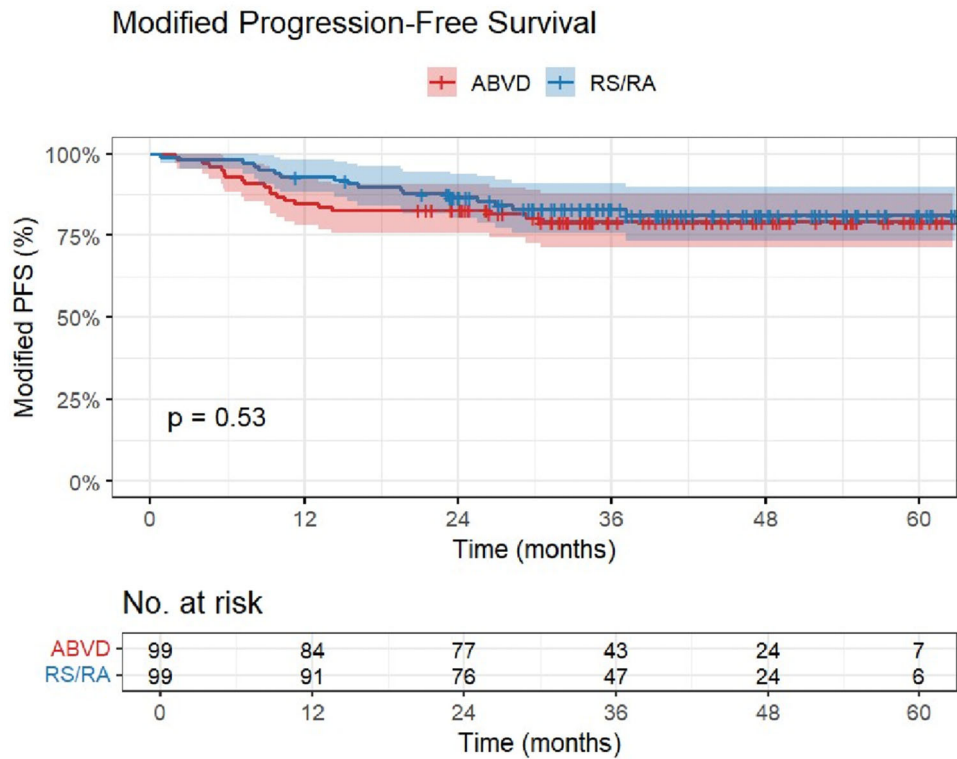


Figure 1: Modified progression-free survival (mPFS) according to treatment arm. Kaplan–Meier curves showing mPFS in patients randomized to standard ABVD therapy versus the risk-stratified, response-adapted (RS/RA) strategy.

Background: Outcomes with ABVD in advanced-stage cHL remain suboptimal in resource-limited settings. Although escBEACOPP improves disease control, concerns regarding toxicity and resource utilization limit its use. We evaluated a risk-stratified, response-adapted (RS/RA) strategy based on International Prognostic Score (IPS) and interim PET response against standard ABVD in a phase III randomized study.

Methods: Patients aged 15–60 years with newly diagnosed advanced-stage cHL were enrolled. They were randomized 1:1 to receive standard ABVD (Arm A) or a risk-stratified, response-adapted strategy (Arm B) using RATHL (IPS 0–2) and GHSG HD18 (IPS 3–7) approaches with interim PET-guided treatment modification. The primary endpoint was 3-year modified PFS, defined as progression, relapse, death, non-complete response, or initiation of subsequent anticancer therapy.

Results: Between September 2022 and July 2024, 200 patients were enrolled; 2 were excluded for protocol ineligibility, and 198 patients were analysed. The median age was 27 years (range, 15–58), and 140 (70.7%) were male. Baseline characteristics included B symptoms in 154 (77.8%), ECOG performance status 0–1 in 181 (91.4%), extranodal disease in 116 (58.5%), bulky disease in 82 (41.4%), stage III/IV disease in 169 (85.3%), and high-risk patients were 53/99 in Arm A and 56/99 in Arm B.

The 3-year mPFS was 79.1% (95% CI, 71.2–87.7) in Arm A and 83.0% (95% CI, 75.7–91.0) in Arm B ($p = 0.53$). The 3-year OS was 96.8% (95% CI, 93.3–100.0) and 93.6% (95% CI, 88.2–99.3), respectively ($p = 0.72$). After a median follow-up of 38 months (range, 1–63), 37 events were observed, including 20 in Arm A and 17 in Arm B (including 1 death due to septic shock). The median time to relapse was 9.9 months (range, 1.9–37.1). Post relapse 15/36 patients received a nivolumab based regimen as salvage and 11/36 patients received bone marrow transplantation.

No new safety signals were observed. Six patients receiving escBEACOPP were switched to ABVD/AVD due to toxicity. In Arm B, 3 low-risk patients had a positive interim PET scan and were escalated to escBEACOPP, of whom 2 subsequently had progressive disease.

Conclusion: Standard ABVD achieved comparable outcomes to RS/RA strategy, with no significant differences between the groups. However, the final results comparing patient reported outcomes and resource utilization will help determine the optimal frontline treatment strategy for advanced cHL.

P033: Evaluating the outcomes of elderly Hodgkin Lymphoma patients: a focus on sequential Brentuximab-AVD

Alessandro Cellini¹, Francesco Angotzi¹, Martina De Ferrari¹, Nicolo' Danesin¹, Mattia D'Antiga¹, Arianna Bevilacqua¹, Anna Giordano¹, Marco Pizzi², Filippo Crimi³, Gaia Grassetto⁴, Federica Vianello⁵, Francesco Piazza¹, Livio Trentin¹, Andrea Visentin¹

¹Hematology Unit, Department of Medicine, University of Padova, Padova, Italy, ²Surgical Pathology and Cytopathology Unit, Department of Medicine, University of Padova, Padova, Italy, ³Institute of Radiology, Department of Medicine, University of Padova, Padova, Italy, ⁴Nuclear Medicine Unit, Department of Medicine, University of Padova, Padova, Italy, ⁵Radiotherapy Unit, Veneto Institute of Oncology IOV IRCCS, Padova, Italy

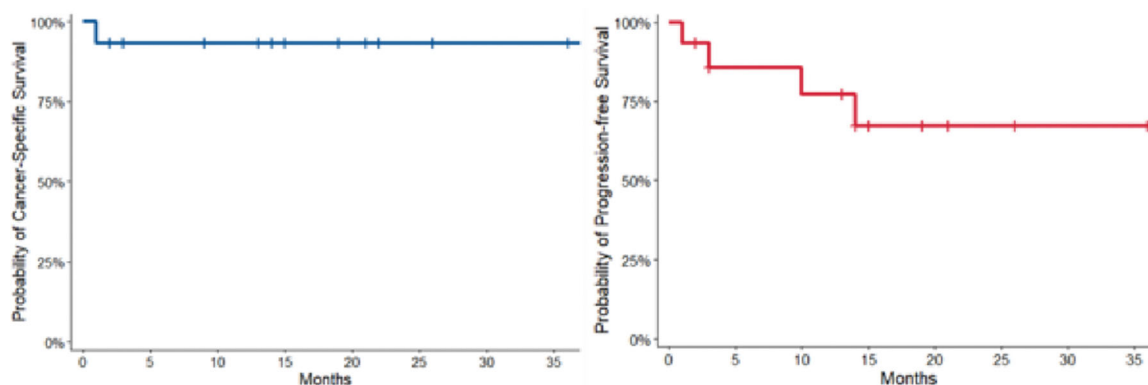


Figure 1: Cancer-specific (left) and Progression-free survival (right) in the whole cohort.

Background: Older patients with classical Hodgkin lymphoma (cHL) have inferior outcomes and limited tolerance to conventional chemotherapy, due to poor performance status (PS) and possibly due to differences in the underlying disease biology. Sequential brentuximab vedotin (BV) before and after AVD (sBV-AVD) has shown promising activity in older patients, but real-world data remain limited.

Aim: To assess the outcomes of elderly cHL patients treated with sBV-AVD in a real-world setting.

Methods: A single-centre, retrospective study was conducted at our tertiary centre, enrolling consecutive cHL patients treated with sBV-AVD between Jan 2022 and Mar 2026 (AM Evens, JCO 2018). Primary endpoints were overall- and cancer-specific survival (censoring non-HL deaths, CSS), as well as event-free survival (EFS), with events defined as progression, death or the start of a new therapy.

Results: Fifteen patients were enrolled in the study, with 13 (86%) having stage IV disease. Median age at enrollment was 72 years (60–86), and 8 (53%) were female. Most subjects (80%) presented with B symptoms, whereas only 2 (13%) had bulky disease. Median ECOG PS at baseline was 2, with 9 (60%) individuals having a PS ≥ 3 . After a median follow-up of 15 months (range 1–52), 2 subjects died (one from HL progression and one from a second primary malignancy) and 2 experienced progression. Fifteen-month EFS and OS were 67% (95% CI 45–100) and 83% (95% CI 63–100), respectively, while 15-month CSS was 93% (95% CI 81–100). An improvement in PS after the 2 lead-in BV doses was documented in all but 3 patients (one who died shortly after the 1st BV infusion, and one who started BV with a PS of 0; Wilcoxon $p < 0.001$), and median PS were 2 and 1 before and after the lead-in BV.

Overall, the sequential regimen was well tolerated. Infections were the most common adverse event, with 7 total cases being reported across 5 patients, 2 of which were septic events happening during the BV lead-in. Notably, no cases of febrile neutropenia were recorded. Peripheral neuropathy was documented in 6 patients (3 G2, 3 G1), appearing in half the cases after the second lead-in BV infusion.

Conclusion: sBV-AVD appeared to be effective and well tolerated in this real-world cohort of elderly cHL patients. Of note, the initial BV infusions were associated with a notable improvement in patient performance, which led to full delivery of the following AVD cycles with only mild complications.

P034: Netupitant/palonosetron for prevention of chemotherapy-induced nausea and vomiting in Hodgkin lymphoma treated with ABVD or BV-AVD: a single-centre observational study

Alessandro Cellini¹, Francesco Angotzi¹, Ivan Zatta², Martina De Ferrari¹, Andrea Serafin¹, Arianna Bevilacqua¹, Nicolo' Danesin¹, Giovanni Leone¹, Mattia D'Antiga¹, Anna Giordano¹, Francesco Piazza¹, Francesca Temporin³, Livio Trentin¹, Andrea Visentin¹

¹Hematology Unit, Department of Medicine, University of Padova, Padova, Italy, ²Department of Transfusion Medicine, Ospedale Ca' Foncello, Treviso, Italy, ³Department of Pharmacy, University Hospital of Padova, Padova, Italy

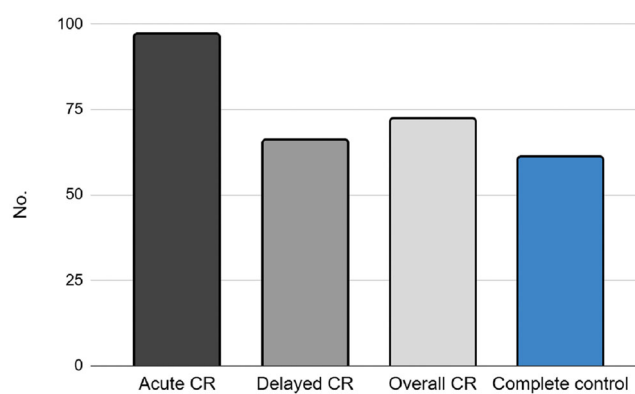


Figure 1: Histogram depicting the proportion of patient achieving acute, delayed and overall CR as well as the percentage of complete control obtainment.

Background: ABVD and brentuximab vedotin-AVD (BV-AVD) represent the standard-of-care therapeutic regimens for the treatment of classical Hodgkin lymphoma (HL) and require effective prophylaxis against chemotherapy-induced nausea and vomiting (CINV). Fixed-dose oral netupitant/palonosetron (NEPA) combines an NK1 receptor antagonist and a second-generation 5-HT₃ receptor antagonist, but HL-specific data remain limited. We evaluated the effectiveness of NEPA-based prophylaxis in patients receiving first-line ABVD or BV-AVD.

Methods: We performed a retrospective single-centre observational study including patients with HL treated at the University Hospital of Padova between 2021 and 2024. Patients who escalated to BEACOPP or salvage therapy after interim PET were excluded to assess CINV outcomes across ABVD/BV-AVD treatment. NEPA was administered with or without dexamethasone according to physician choice. The primary endpoint was complete response (CR), defined as no emesis and no rescue antiemetic use, during the overall phase from 0–120 hours after chemotherapy. Secondary endpoints were acute CR (0–24 hours), delayed CR (24–120 hours) and complete control (CR with no more than mild nausea).

Results: One hundred patients were included; 54% were female and median age was 33 years. Seventy-one patients received ABVD and 29 received BV-AVD, for a total of 1040 chemotherapy administrations evaluable for CINV. NEPA plus dexamethasone was used in 73 patients and NEPA alone in 27. Acute-phase control was high, with acute CR in 97 [95%CI 91–99] patients. The 3 subjects who did not obtain acute CR also experienced acute vomiting. Overall-phase CR was 72% (95%CI 62–80), while complete control was achieved in 61% (95%CI 51–71). Delayed nausea occurred in 34% (95%CI 25–44), was predominantly mild-to-moderate in severity, and was not accompanied by vomiting. Rescue antiemetics were required in 26 (95%CI 18–36). Delayed CINV occurred mainly during the first cycle, accounting for 25/34 (73%; 95%CI 56–87) of delayed events, with no recurrence of the symptoms being reported in all but 2 subjects.

Conclusion: In this single-centre HL cohort, NEPA-based prophylaxis provided high acute-phase protection and low rates of vomiting during ABVD and BV-AVD. Delayed nausea remained the main residual unmet need. These findings support NEPA as a feasible antiemetic strategy in this setting and justify prospective evaluation of risk-adapted prophylaxis.

P035: In-Field Recurrence Patterns Following Consolidation Radiotherapy after BrECADD in Advanced-Stage Hodgkin Lymphoma: A Secondary Analysis of the Randomized Phase 3 GHSG HD21 Trial

Johannes Rosenbrock^{1,2}, Maja Supprian^{1,3}, Michael Oertel^{1,4}, Justin Ferdinandus^{1,3}, Hishan Tharmaseelan^{1,3}, Christian Peter Jaworek^{1,3}, Simone Ferdinandus², Jasmin Weindler⁵, Paul J. Bröckelmann^{1,3}, Hendrik Dapper², Carsten Kobe^{1,5}, Michael Fuchs^{1,3}, Emmanouil Fokas², Peter Borchmann^{1,3}, Hans Theodor Eich^{1,4}, Christian Baues^{1,6}

¹German Hodgkin Study Group (GHSG), ²Department of Radiation Oncology and Cyberknife Center, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany, ³Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf, Faculty of Medicine and University Hospital Cologne, University of Cologne, Germany, ⁴Department of Radiation Oncology, University Hospital Muenster, Muenster, Germany, ⁵Department of Nuclear Medicine, Faculty of Medicine and University Hospital Cologne, University of Cologne, Germany, ⁶Department of Radiation Oncology, Ruhr-University Bochum, Marien Hospital Herne, Herne, Germany

Purpose/Objective: While the GHSG HD21 trial demonstrated superior efficacy for the BrECADD regimen over escalated BEACOPP (eBEACOPP) in advanced-stage Hodgkin lymphoma (HL), the necessity of routine consolidation radiotherapy (RT) for end-of-treatment PET (EOT-PET)-positive patients remains debated. This analysis evaluates the role of consolidation RT by assessing patterns of in-field recurrence following both chemotherapy regimens.

Materials/Methods: Data from advanced-stage HL patients receiving consolidation RT in the randomized phase 3 HD21 trial were retrospectively analyzed. Following central review recommendation, EOT-PET-positive patients received 30 Gy RT. To determine the role of consolidation RT, EOT-PET scans and subsequent imaging were analyzed in relapsed patients to identify in-field recurrences. Descriptive statistics were performed on baseline and treatment characteristics. In-field recurrence rates were calculated using cumulative incidence functions.

Results: EOT-PET-positivity occurred at an identical rate of 17% in both treatment arms (n = 127/734 after eBEACOPP vs n = 125/739 after BrECADD). RT was administered to 112 EOT-PET-positive patients in the eBEACOPP group and 104 patients in the BrECADD group. Image analysis revealed that local treatment failure was rare in both groups: in-field relapses occurred in only 5 patients after eBEACOPP and 2 patients after BrECADD. The 60-month cumulative incidence of in-field recurrence was 4.5% (95% CI, 0.6–8.4) for eBEACOPP compared to just 2.0% (95% CI, 0.0–4.8) for BrECADD (HR, 0.43; 95% CI, 0.08–2.21).

Conclusion: Consolidation RT following frontline BrECADD provides outstanding local control even for EOT-PET-positive patients. Notably, the in-field recurrence rate was numerically lower after BrECADD than after eBEACOPP (2.0% vs. 4.5%). While EOT-PET positivity rates were identical between arms, they increased compared to the GHSG HD15 trial. Collectively, these findings suggest that in the era of modern PET technology with enhanced spatial resolution and highly effective systemic therapy, a distinct subset of EOT-PET-positive patients may not profit from consolidation RT. However, this must be carefully weighed against the excellent local efficacy of RT and the risk of undertreatment. To safely de-escalate RT, future trials should integrate advanced metrics like metabolic tumor volume or minimal residual disease assessment to precisely identify those who truly derive a therapeutic benefit.

P036: Interim PET-Adapted De-escalation Chemotherapy Regimen for Advanced Stage Classical Hodgkin Lymphoma Using Brentuximab Vedotin, Pembrolizumab, Doxorubicin, and Dacarbazine: Phase 2 Study—Updated Follow-up

Hun Ju Lee¹, Gregory Ravizzini¹, Jennifer Ramos¹, Javier Retamales¹, Ayushi Chauhan¹, Luis Fayad¹, Ranjit Nair¹, Jason Westin¹, Jared Henderson¹, Christopher Flowers¹, Michael Wang¹, Luis Malpica¹

¹MD Anderson Cancer Center

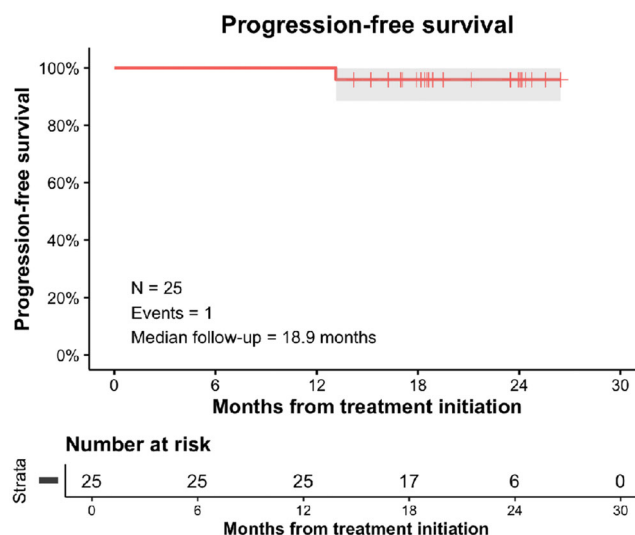


Figure 1: PFS Curve.

Background: Brentuximab vedotin(Bv), nivolumab, and pembrolizumab (P) have changed frontline therapy for advanced-stage classical Hodgkin lymphoma (AS cHL). GHSG HD18/HD21 showed PET-adapted strategies can reduce treatment without compromising efficacy. We evaluated BvP+AD with PET-adapted de-escalation to reduce chemotherapy exposure.

Methods: Pts with newly diagnosed AS or stage II bulky (≥ 10 cm) cHL received 3 cycles BvP+AD (Bv 1.2 mg/kg, P 400 mg Q6W, doxorubicin/dacarbazine standard dosing). P was dosed C1D1, C2D15, C4D1, and C5D15. Pts with interim PET DS1–2, or DS3 with $\geq 90\%$ TMTV reduction after cycle 3, received 3 additional cycles BvP only. Pts with DS4–5 or DS3 with $<90\%$ TMTV reduction completed 6 total cycles BvP+AD. Primary endpoint was EOT CR rate; secondary endpoints included safety, ORR, and PFS.

Results: 25 pts enrolled: median age 30 (17–64), female 48% (12); stage II bulky 32% (8), stage III/IV 68% (17); non-Hispanic White 64% (16), IPS ≥ 3 20% (5), extranodal disease 52% (13). All pts completed interim PET: DS1 2, DS2 16, DS3 7; all DS3 pts had $\geq 90\%$ TMTV reduction. All pts de-escalated to BvP only. EOT PET: DS1 5, DS2 15, DS3 2, DS4 3. EOT CR was 88% (22/25). Of 3 pts with DS4, all achieved CR by subsequent PET follow-up. At median follow-up 18.9 mo (14.2–26.4), 24/25 pts (96%) remain progression-free, with 1 progression at 13.3 mo (Figure 1). No consolidative RT was administered.

AEs: Most common any-grade AEs were PSN 80% (20), nausea 80% (20), fatigue 60% (15), ALT increased 56% (14), and alopecia 56% (14). PSN was G1 in 54% (16), G2 in 16% (4), and no G3; PSN resolved in 40% (8/20) by last follow-up. G3 AEs included ALT elevation (3), AST elevation (1), neutropenia (2), diarrhea (1), and generalized muscle weakness (1); all resolved. No neutropenic fever occurred. IMAEs included thyroid dysfunction 16% (4), G2 pneumonitis 1, and G3 diarrhea 1. Three SAEs occurred: fever, suspected pneumonitis, and UTI/fever. Two pts discontinued P for G3 LFT abnormalities; 4 had Bv dose reduction for G2 PSN.

Conclusions: BvP+AD with PET-adapted de-escalation showed favorable safety and durable efficacy in frontline AS cHL. All pts met de-escalation criteria, reducing anthracycline/alkylator exposure by 50%, with no RT, 88% EOT CR, and 96% progression-free at 18.9 mo. Longer follow-up and larger cohorts are needed.

P037: PET-Adapted EACODD-14 Regimen in Early Unfavorable and Advanced Stages of Classical Hodgkin Lymphoma: Efficacy and Survival in the Multicenter HL-Russia-1 Study

Nikita Shorokhov¹, Elena Demina¹, Gayane Tumyan², Valeria Spirko², Elena Pavluchenko³, Kamil Kaplanov⁴, Alena Bobrova⁴, Elena Baryakh^{5,6}, Diana Ivanova^{5,6}, Natalia Mikhailova⁷, Evgeniya Borzenkova⁸, Tatyana Pospelova⁹, Maria Voytko⁹, Olga Smirnova¹⁰, Elsa Kankumasheva¹¹, Elsa Siraeva¹¹, Vitaliy Kanin¹², Alexandra Saidullaeva¹³, Arina Adolf¹⁴, Irina Matveeva¹⁵, Nikita Mochkin¹, Vladimir Melnichenko¹, Vladislav Sarzhevskiy¹

¹Department of Hematology and Chemotherapy with Bone Marrow and Hematopoietic Stem Cell Transplantation Unit, Pirogov National Medical and Surgical Center, Moscow, Russia, ²Department of Antitumor Drug Therapy and Hematology, NN Blokhin National Medical Research Center of Oncology, Moscow, Russia, ³Department of Hematology and Chemotherapy, EE Eichwald Clinic, Mechnikov North-Western State Medical University, Saint Petersburg, Russia, ⁴Hematology Department N.11, Botkin Moscow Multidisciplinary Scientific and Clinical Center, Moscow, Russia, ⁵Department of Hematology and Chemotherapy, Moscow City Clinical Hospital 52, ⁶Sechenov University, Moscow, Russia, ⁷Division of Clinical Oncology, RM Gorbacheva Research Institute, Pavlov University, Hematology and Transplantology Department, Saint Petersburg, Russia, ⁸Hematology Department, RM Gorbacheva Research Institute, Pavlov University, Hematology and Transplantology Department, Saint Petersburg, Russia, ⁹Department of Internal Medicine, Hematology and Transfusiology, Novosibirsk City Hospital N. 2, Novosibirsk, Russia, ¹⁰Department of Chemotherapy, MZ Sigal Republican Clinical Oncology Dispensary, Kazan, Russia, ¹¹Department of Chemotherapy N.1, Republican Clinical Oncology Dispensary, Ufa, Russia, ¹²Chemotherapy Department, Regional Clinical Center of Oncology, Khabarovsk, Russia, ¹³Hematology Department, Tver Regional Clinical Oncology Center, Tver, Russia, ¹⁴Department of Chemotherapy with Bone Marrow and Hematopoietic Stem Cell Transplantation Unit, Irkutsk Regional Oncology Center, Irkutsk, Russia, ¹⁵Department of Hematology, Volzhsky Branch of Regional Clinical Oncology Dispensary, Volgograd, Russia

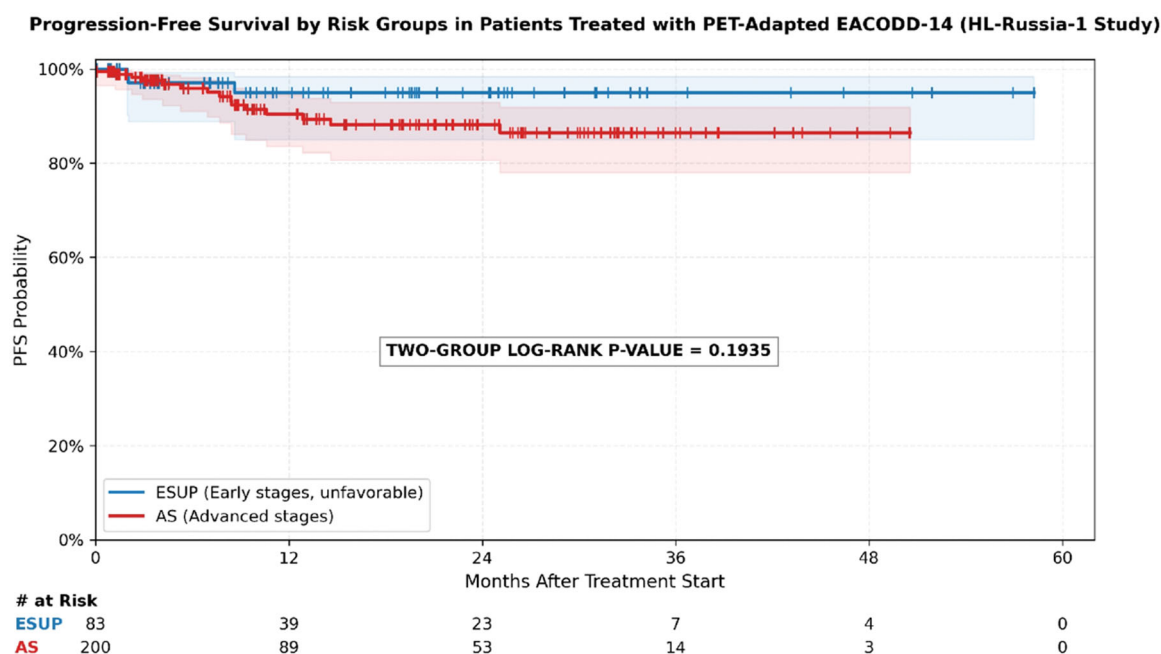


Figure 1: Progression-Free Survival by Risk Groups in Patients Treated with PET-Adapted EACODD-14 (HL-Russia-1 Study).

Background: Optimal first-line treatment for classical Hodgkin lymphoma (cHL) requires balancing efficacy and toxicity. The intensive EACODD-14 regimen (a modification of EA(50)COPP-14 substituting procarbazine/prednisone with dacarbazine/dexamethasone) demonstrated high efficacy and manageable toxicity in single-center trials. HL-Russia-1 evaluates PET-adapted approach in a real-world multicenter setting across Russia.

Aims: To assess the real-world effectiveness, PET-response dynamics, and survival outcomes of the PET-adapted EACODD-14 in patients (pts) with early stages unfavorable prognosis (ESUP) and advanced stages (AS) of cHL.

Methods: HL-Russia-1 (NCT04638790) is a prospective multicenter study. ESUP received 2 cycles of EACODD-14; PET-2-negative pts proceeded to 2 cycles of AVD, while PET-positive pts received 2–4 additional cycles of EACODD-14. AS pts received 6 cycles of EACODD-14. Consolidation involved-site radiotherapy (ISRT) was indicated for bulky disease, residual masses ≥ 2.5 cm, or PET-positive residual lesions. Primary neutropenia prophylaxis with pegG-CSF was recommended. Survival was analyzed using the Kaplan-Meier method.

Results: Between Nov 2020 and Apr 2026, 13 centers enrolled 349 pts. We analyzed 283 pts with ESUP and AS treated with EACODD-14.

Baseline: Median age was 30 years (18–64), 59.3% male. AS 64.1%, ESUP 26.6%. Pts with ESFP received ABVD and were excluded. IPS >2 for AS: 33.1%.

PET Response: PET-2 evaluable in 243 pts (85.9%); complete metabolic response (CMR, DS 1–3) in 64.7%. PET-4 and PET-6 CMR rates were 74.3% and 88.9%.

Radiotherapy: RT performed in 36.3% of pts; omitted in 44.6% of ESUP and 71.5% of AS pts with CMR and residual masses <2.5 cm.

Efficacy & Survival: EOT remission rate 93.5%. With a median follow-up of 9.4 months (range 1–58.2), the estimated 2-year progression-free survival (PFS) for the entire EACODD-14 cohort is 90.3% (95% CI: 84.6%–93.9%). For ESUP, 2-year PFS is 95.0% (95% CI: 84.9%–98.4%), and for AS, it is 88.2% (95% CI: 80.6%–92.9%). Overall survival is 100%. Treatment failures occurred in 18 pts.

Conclusion: Updated HL-Russia-1 confirms that PET-adapted EACODD-14 is highly effective and feasible in a real-world multicenter setting. High early metabolic response rates allow safe radiotherapy omission in a significant proportion of pts, minimizing long-term toxicity without compromising PFS. This platform demonstrates robust outcomes across federal and regional centers.

P038: Frontline nivolumab-AVD in older patients with advanced classical Hodgkin lymphoma: real-world experience from a single Italian centre

Tanja Lazic^{1,2}, Stefano Luminari¹, Alberto Bavieri^{1,2}, Silvia Gambaro^{1,2}, Maria Elena Nizzoli^{1,2}, Laura Arletti¹, Angela Ferrari¹, Fiorella Ilariucci¹, Francesco Merli¹

¹Hematology Unit, Azienda USL-IRCCS, Reggio Emilia, Italy, ²Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy

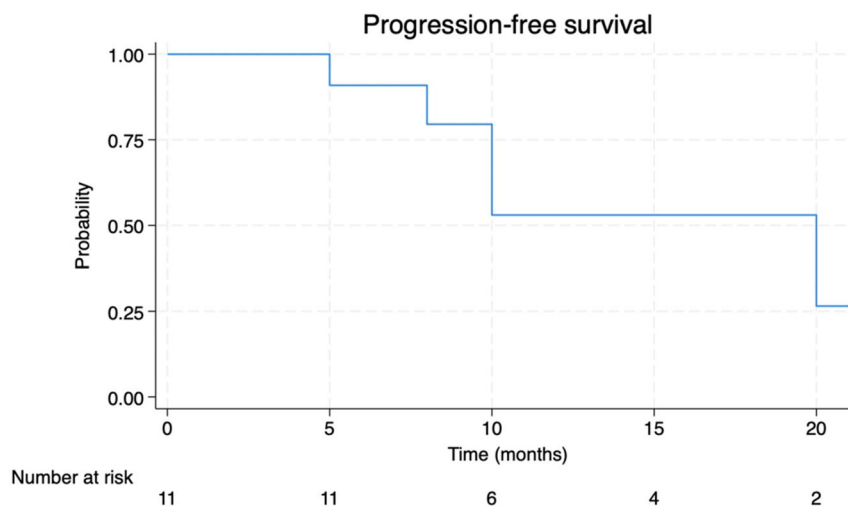


Figure 1: Estimated 18-month PFS.

Background: Older patients with advanced classical Hodgkin lymphoma (cHL) are underrepresented in clinical trials because of comorbidities and frailty. Although the phase III S1826 study demonstrated improved efficacy and tolerability of nivolumab plus AVD (N-AVD) compared with brentuximab vedotin-AVD, real-world evidence remains limited. We report updated outcomes of elderly patients treated with frontline N-AVD at our institution.

Methods: We retrospectively evaluated consecutive patients aged >60 years with stage III-IV cHL treated with frontline N-AVD. Treatment consisted of nivolumab (240 mg, days 1 and 15) combined with AVD every 28 days for six cycles. Chemotherapy dose reductions were allowed at physician discretion. Responses were assessed by PET-CT. Overall response rate (ORR) included complete and partial response (CR, PR), was assessed at end-of-treatment (EOT). Progression-free survival (PFS) was defined from treatment start to progression or death from any cause. Adverse events were graded according to CTCAE ver.5.0.

Results: Eleven patients were included (median age of 71 years, range 65–85); eight (73%) were male. All had stage III–IV disease. Median IPS was 3 (range 2–5), with 64% high-risk disease (IPS ≥ 3). AVD dose attenuation was required in five patients (four at 50% and one at 75% of standard dose), while nivolumab was administered at full dose in all cases. Interim PET showed CR in six patients (54%), PR in four (36%), and progressive disease (PD) in one patient. At EOT, ORR was 72% (CR 63%, PR 9%); three patients experienced PD. After a median follow-up of 18 months (range 5–25), estimated 18-month PFS was 53%. Most progression events occurred within the first 10 months of treatment. One patient died from PD beyond 18 months. Progressions occurred in both dose-attenuated and full-dose groups. The most frequent toxicity was neutropenia, occurring in nine patients (82%), including grade ≥ 3 in seven (64%). Infections included pneumonia ($n = 2$) and urinary tract ($n = 1$). Immune-related adverse events occurred in two patients (hypothyroidism and interstitial pneumonitis).

Conclusions: In this real-world series of elderly patients with advanced cHL, frontline N-AVD demonstrated considerable response rates despite dose attenuation. Early progression remained common, likely reflecting the greater frailty and comorbidity burden of patients treated in routine practice compared with those enrolled in clinical trials.

P039: Has Frontline Brentuximab Vedotin Plus AVD Altered the Historical Adverse Prognostic Impact of Stage IV Disease in Classical Hodgkin Lymphoma? A Dual-Center Real-World Experience

Martha Berliner¹, Tanja Lazic², Roberta Sciarra³, Alessandro Mazzacane³, Sofia Pedrali¹, Nicolò Rampi⁴, Chiara Rusconi⁴, Luca Arcaini³, Stefano Luminari², Manuel Gotti³

¹Department of Molecular Medicine, University of Pavia, Pavia, Italy, ²Department of Hematology Oncology IRCCS Arcispedale Santa Maria Nuova, Reggio Emilia, Italy,

³Department of Hematology Oncology Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, ⁴Department of Hematology Oncology ASST Melegnano e della Martesana, Melegnano, Italy

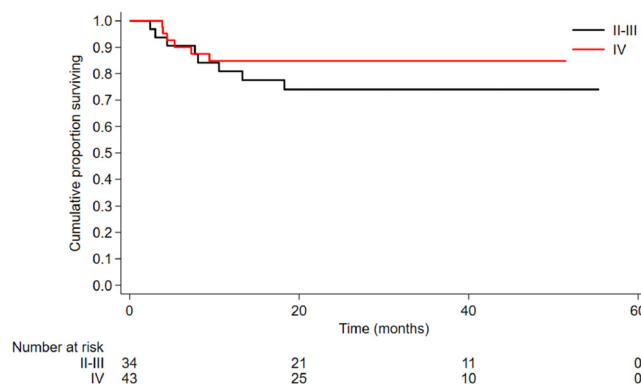


Figure 1: Kaplan-Meier of PFS by stage in 77 cHL patients. Stage IV (BV-AVD) vs IIB–III (ABVD-based); 24-month PFS 84.9% vs 74.0%.

Background: Advanced-stage classical Hodgkin lymphoma (cHL) is traditionally associated with progressively worse outcomes with increasing stage, with stage IV disease showing inferior progression-free survival (PFS). Since 2021 strategies have evolved at our institutions according to national treatment authorization, while maintaining a PET-oriented approach: stage IIB–III patients were treated with ABVD-based regimens, while stage IV patients received frontline brentuximab vedotin plus AVD (BV-AVD). We investigated whether this therapeutic shift has altered the prognostic impact of stage on PFS.

Methods: We retrospectively analyzed consecutive patients with newly diagnosed cHL stage IIB–IV treated across two Italian centers from September 2021 onward. All patients were managed according to a PET-oriented treatment strategy. PFS was calculated from first-line treatment initiation to progression, relapse, death, or last follow-up using Kaplan–Meier estimates. Exploratory Cox proportional hazards models were performed to identify variables associated with PFS.

Results: Seventy-seven patients were included; median age at diagnosis was 37 years (IQR 27–53), and 55.8% presented with stage IV disease. B symptoms were present in 76.7%, extranodal involvement in 57.3%, and bulky disease in 49.3%.

After a median follow-up of 32 months (IQR: 16–46 months), 14 PFS events were observed. Overall estimated PFS at 24 months was 79.8% (95%CI: 68.2%–87.6%).

Contrary to historical expectations, stage IV patients did not show inferior outcomes compared with stage IIB–III disease. Estimated 24-month PFS was 84.9% in stage IV and 74.0% in stage IIB–III patients (univariable Cox model, HR = 0.60; 95%CI 0.21–1.72; $p = 0.338$).

Exploratory univariable Cox models identified leukocytosis $\geq 15 \times 10^9/L$ (HR = 4.36; 95%CI: 1.38–13.83; $p = 0.012$) and bulky disease (HR = 3.84; 95%CI: 1.06–13.97, $p = 0.041$) as variables associated with worse PFS.

Conclusions: In this dual-center real-world PET-guided cohort, stage IV cHL did not retain its historically adverse prognostic impact and showed numerically superior PFS to stage IIB–III disease. Despite the limitations of retrospective design, sample size, and stage-based treatment allocation, these findings suggest that frontline BV-AVD may mitigate the traditional prognostic disadvantage of stage IV disease. Prospective validation is needed.

P040: Hyperbilirubinemia in Classical Hodgkin Lymphoma: Impact of Severity on Hepatic Recovery and Clinical Outcomes

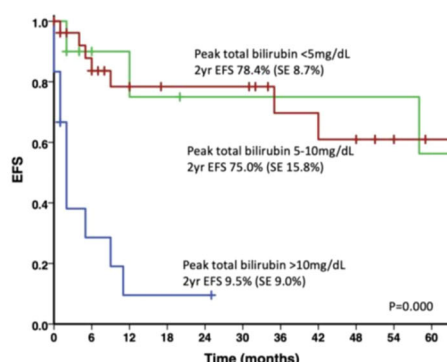
Yash Patel¹, Kavitha Lakshmi¹, Anu Korula¹, Vikram Mathews¹

¹Christian Medical College Vellore

Table 1: Univariable and multivariable analysis for factors affecting event-free survival

Univariable analysis				Multivariable analysis		
Parameter	HR	CI	P value	HR	CI	P value
Age	1.0	0.98-1.05	0.218	-	-	-
Sex	0.6	0.24-1.62	0.343	-	-	-
Baseline bilirubin (severe)	8.4	2.93-24.35	0.000	3.1	0.65-14.9	0.155
Baseline bilirubin (moderate)	0.9	0.24-3.83	0.973	-	-	-
Persistent LFT abnormality	23.4	6.24-88.36	0.000	30.5	4.56-204.8	0.000
Non-ABVD therapy	6.2	2.04-18.8	0.001	-	-	-
Non-cholestatic pattern	2.7	1.05-6.91	0.037	1.4	0.35-5.57	0.619
Hepatic involvement with lymphoma	0.48	0.19-1.16	0.48	-	-	-

Figure 1: Two-year event-free survival in patients based on baseline bilirubin value



Background: Hyperbilirubinemia, particularly severe hyperbilirubinemia, is uncommon in classical Hodgkin lymphoma (cHL) and is not incorporated into conventional prognostic scoring systems. Delivery of first-line chemotherapy is challenging because of concerns regarding altered hepatic metabolism and drug toxicity. These patients are under-represented in clinical trials, and evidence to guide management remains limited. We evaluated treatment approaches, hepatic recovery, and outcomes in patients with cHL presenting with baseline hyperbilirubinemia.

Methods: We retrospectively analysed patients with newly diagnosed cHL treated between January 2010 - December 2025 with baseline hyperbilirubinemia (total bilirubin >2 mg/dL), further stratified into mild (2–5 mg/dL), moderate (5.1–10 mg/dL), and severe (>10 mg/dL) hyperbilirubinemia. Clinical outcomes included normalization of liver function and event-free survival (EFS).

Results: Of 1541 patients treated during the study period, 50 (3.2%) had hyperbilirubinemia at presentation, of whom 28 (56%), 10 (20%), and 12 (24%) patients had mild, moderate, and severe hyperbilirubinemia, respectively. Corticosteroid bridging was used in 23 patients, predominantly in moderate/severe hyperbilirubinemia ($p < 0.001$), only 3 patients achieved sufficient hepatic recovery to receive standard ABVD.

Following chemotherapy, liver function normalized in 67.9% and 80% of patients with mild and moderate hyperbilirubinemia, respectively. Median time to normalization was 12 and 100 days; only one patient with severe hyperbilirubinemia achieved normalization.

The 2-year EFS was 78.4%, 75.0%, and 9.5% in patients with mild, moderate, and severe hyperbilirubinemia, respectively (log-rank $p < 0.001$).

On univariable analysis, severe hyperbilirubinemia (HR 8.4, $p < 0.001$), non-cholestatic liver injury (HR 2.7, $p = 0.037$) and persistent liver dysfunction (HR 23.4, $p < 0.001$) were associated with inferior EFS. On multivariable analysis, only persistent liver dysfunction remained independently associated with inferior EFS (HR 30.5, 95% CI 4.6–204.8; $p < 0.001$).

Conclusions: Severe hyperbilirubinemia identifies an ultra-high-risk subgroup of patients with cHL characterized by poor hepatic recovery and markedly inferior EFS. Persistent liver dysfunction following treatment initiation was the strongest predictor of adverse outcome. Prospective studies evaluating alternative therapeutic strategies for this rare and vulnerable population.

P041: Interim and End-Of-Treatment (EoT) PET/CT Assessment after Nivolumab, Doxorubicin, Vinblastine, and Dacarbazine (N-AVD) In Advanced-stage Classical Hodgkin Lymphoma (cHL): A Single-center Experience

Piperidou Alexia¹, Athanasios Liaskas¹, Anastasia Kopsaftopoulou¹, Maria Dimitrakoudi¹, Eliana Konstantinou¹, Marina Belia¹, Maria Arapaki¹, Rodanthi Fioretzaki¹, Aikaterini Kolotsiou¹, Alexandros Machairas¹, Georgia Poultzaki¹, Chrysovalantou Chatzidimitriou¹, John Asimakopoulos¹, Angeliki Georgopoulou, Calliope Zerzi¹, Panayiotis Tsafaridis¹, Fotios Panitsas¹, Aikaterini Benekou¹, Panayiota Petsa¹, Helen Plata¹, Aikaterini Bitsani¹, Maria Dimou¹, Marina Siakantaris¹, Maria Angelopoulou¹, Theodoros Vassilakopoulos¹

¹Department of Hematology and Bone Marrow Transplantation, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece

Background: Based on the randomized SWOG S1826 trial, N-AVD demonstrated superior disease control compared with BV-AVD in stage III/IV classical Hodgkin lymphoma. We adopted N-AVD as first-line therapy for advanced cHL starting in July 2023. Although PET/CT is a cornerstone of response assessment in cHL, checkpoint inhibitors may increase false-positive (FP) findings. We evaluated our institutional experience with PET/CT after first-line N-AVD. **Methods:** We retrospectively analyzed patients with cHL treated with first-line N-AVD. Interim PET (iPET) after 2 cycles and end-of-treatment (EoT) PET/CT were assessed according to the Deauville Score (DS), with DS4-5 considered positive.

Results: Median age was 29 years (range 16–79), 13% were ≥60 years, 51% were male, 44% had B symptoms, 63% had nodular sclerosis, and 64% had stage IV disease. Four patients (10%) had positive iPET, all DS4; three converted to negative EoT scans, suggesting FP iPET findings, whereas one developed progressive disease confirmed by subsequent PET/CT (DS5) having received BrECADD after N-AVDx3. Among 36 iPET-negative patients, 7/36 (19%) had positive PET/CT (5 with DS4, 2 with DS5). Three DS4 cases became negative on repeat imaging after three months, while two DS4 and two DS5 cases represented true treatment failure confirmed by serial imaging and/or biopsy. Salvage treatment included BrESHAP followed by autologous stem-cell transplantation in two patients and radiotherapy for localized disease in one patient. One DS5 case was ultimately diagnosed as metachronous diffuse large B-cell lymphoma necessitating chemotherapy initiation. An additional patient relapsed within 12 months despite negative iPET and EoT PET/CT. Overall 6/40 patients have experienced treatment failure so far (15%). With a median follow-up of 20.7 months, estimated 2-year progression-free survival was 82%.

Conclusions: N-AVD demonstrated high efficacy with a low rate of iPET positivity and no interim DS5 scans. Interestingly, most treatment failures occurred despite negative iPET, whereas several EoT-positive scans proved false positive, highlighting the limitations of PET/CT interpretation after checkpoint inhibitor-based therapy. Therefore, PET/CT results should be evaluated within the broader clinical context, and isolated metabolic findings should not automatically prompt treatment modification without careful consideration.

P042: Association of quantitative FDG-PET parameters and serum TARC with outcome in advanced classic Hodgkin lymphoma: A biomarker analysis of the EORTC-1537-COBRA trial

Sophie Teesink¹, Lydia Visser¹, Laure Musekera², Anna Sureda³, Susana Carvalho⁴, Andrey Vranovsky⁵, Annika Loft⁶, Anne Arens⁷, Sanne Tonino⁸, Ward Sents², Cédric Mallien², Berthe Aleman⁹, Walter Noordzij¹⁰, Catherine Fortpied², Martin Hutchings¹¹, Arjan Diepstra¹, Wouter Plattel¹²

¹Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Netherlands, ²EORTC Headquarters, Brussels, Belgium, ³Clinical Hematology Department, Institut Català d'Oncologia - L'Hospitalet, Institut de Investigacions Biomèdiques de Bellvitge (IDIBELL), Universitat de Barcelona, Barcelona, Spain, ⁴Instituto Português de Oncologia de Lisboa, Lisbon, Portugal, ⁵Department of Oncohematology, National Cancer Institute, Bratislava, Slovakia, ⁶Department of Clinical Physiology and Nuclear Medicine, Rigshospitalet, University Hospital of Copenhagen, Copenhagen, Denmark, ⁷Department of Medical Imaging, Radboud University Medical Center, Nijmegen, Netherlands, ⁸Department of Hematology, Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands, ⁹Department of Radiation Oncology, the Netherlands Cancer Institute, Amsterdam, Netherlands, ¹⁰Department of Nuclear Medicine & Molecular Imaging, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ¹¹Department of Haematology, Rigshospitalet, University Hospital of Copenhagen, Copenhagen, Denmark, ¹²Department of Hematology, University Medical Center Groningen, Groningen, Netherlands

Table 1. Distribution of patients according to interim PET response (Deauville score), sTARC status, and metabolic tumour volume.

Interim assessment	sTARC - MTV -	sTARC + MTV -	sTARC - MTV +	sTARC+ MTV +
DS 1 – 3 (n = 74)	61 (82%)	13 (18%)	x	x
DS 4 – 5 (n = 53)	31 (58%)	13 (25%)	5 (9%)	4 (7.5%)

Table 1: Distribution of patients by interim PET response (Deauville score 1–3 vs 4–5), sTARC status (threshold for sTARC positive was set at >1000 pg/ml) and MTV (Calculated by using SUV threshold of 4.0; MTV+ indicates MTV > 0 cm³, MTV– indicates MTV = 0 cm³).

Background: In classic Hodgkin lymphoma (cHL), FDG-PET is used for staging and response assessment using Deauville Score (DS). However, the positive predictive value of an interim PET (iPET) DS 4 is restricted. Quantitative PET parameters such as metabolic tumour volume (MTV), provide objective measures of tumour burden. Serum Thymus and Activation-Regulated Chemokine (sTARC), highly expressed by Hodgkin Reed-Sternberg cells, has emerged as a biomarker for disease monitoring. We evaluated the association between quantitative PET parameters, sTARC, and outcome in the EORTC-1537-COBRA trial.

Methods: The trial enrolled advanced stage cHL patients. Baseline and early interim FDG-PET-scans were centrally reviewed and scored using DS. After one cycle of A-AVD, patients with a positive iPET (DS 4–5) were escalated to intensified treatment. Quantified PET parameters were derived by semiautomatic segmentation. TARC was measured in serum by ELISA at multiple timepoints. Elevated sTARC was predefined as >1000 pg/ml. Associations were assessed using Pearson correlation and Kaplan Meier estimates were performed to analyse correlation with modified progression-free survival (mPFS), the primary endpoint.

Results: At baseline, 95% of evaluable patients showed elevated sTARC levels, resulting in 127 patients included in this analysis. sTARC declined rapidly after one cycle of A-AVD, with only 24% showing elevated sTARC at interim assessment. In contrast, 42% of patients remained iPET-positive according to DS. Using a SUV4.0 threshold, residual MTV was detected in 7% of patients (Table 1). Residual MTV did not identify a subgroup of total patients with a significantly worse mPFS. Elevated sTARC correlated with adverse mPFS. Available follow-up data indicate that sTARC remained normalized in 99 of 111 (89%) patients without a mPFS event. Sequential follow-up data will be presented at the conference.

Conclusion: Despite a substantial proportion of patients remaining iPET-positive based on DS, residual measurable MTV was uncommon after one cycle of A-AVD. No significant association with worse outcome was found, probably due to treatment intensification in iPET-positive patients. Available data indicate that sTARC remained normalized in most patients without a mPFS event during follow-up and sTARC levels were associated with outcome. These findings suggest that sTARC complements PET and support further investigation of sTARC-guided disease monitoring in cHL.

P043: Lung Function Assessment by Diffusing Capacity of the Lungs For Carbon Monoxide (DLCO) Measurement in Patients With Classical Hodgkin Lymphoma Receiving First-line Treatment With Nivolumab-AVD

Athanasios Liaskas¹, Alexia Piperidou¹, Georgia Poultsaki¹, Maria Dimitrakoudi¹, Anastasia Kopsaftopoulou¹, Rodanthi Fioretzaki¹, Alexandros Machairas¹, Marina Belia¹, Maria Arapaki¹, Eliana Konstantinou¹, Giannis Assimakopoulos¹, Panayiotis Tsafaridis¹, Fotios Panitsas¹, Aikaterini Bitsani¹, Maria Dimou¹, Marina Siakantaris¹, Maria Angelopoulou¹, Theodoros Vassilakopoulos¹

¹Department of Hematology and BMT, National and Kapodistrian University of Athens, "Laikon" General Hospital of Athens

Background: Nivolumab-AVD (NAVD) has shown outstanding efficacy in patients with advanced-stage classical Hodgkin Lymphoma (cHL), establishing a new standard of care. Pneumonitis is a well-recognized complication of bleomycin in patients previously treated with ABVD. Similarly, treatment with immune checkpoint inhibitors, can also lead to pneumonitis through an immune-mediated mechanism, raising concerns about potential pulmonary impairment during therapy.

Methods: The study included patients with stage III and IV cHL treated with NAVD as a first-line therapy. Single-breath Diffusing Capacity of the Lungs for Carbon Monoxide corrected for Hemoglobin (DLCOc-SB) measurements were performed at predefined time points: prior to treatment initiation, after four cycles of NAVD, and at treatment completion. Clinical evaluation and symptom assessment were constantly performed during treatment and afterwards to correlate functional changes with clinical findings.

Results: Among 40 patients who had completed treatment with NAVD up to the time of the present analysis, 19 had baseline and interim DLCOc-SB assessments and 10/19 also had at least 1 post-treatment assessment. Media age was 28 years (range 16–79), with 11% aged ≥60 years. The median value of DLCOc-SB at baseline was 83.8% of the predicted value [(IQR) 79.5–95.7%; range 55.8–120.8%], while after four cycles of NAVD it was 80% (IQR 74.4–89.2%; range 56.3–117.2%). In fact 16/19 patients had a reduction in DLCOc-SB by a median of 4.5% (range 0.5–10.12%) and 3 had an increase of 0.3–3.7%. The difference was statistically significant ($p < 0.001$). In the 10 patients with available post-treatment assessment the median DLCOc-SB was 82.9% (IQR 65.2–93.6%; range 49.3–106.3%) versus 83.3% (IQR 71.7–96.6%; range 55.8–120.8%) at baseline ($p = 0.33$) and 78.9% (IQR 67.7–91.2%; range 56.3–117.2%) at the interim assessment ($p = 0.96$). Comparing the baseline and post-treatment evaluation, 7/10 patients had a reduction in SLCOc-SB by a median of 5.1% (range 0.1–30.2%) and 3 had an increase of 6.8–8.8%. Comparing the interim and post-treatment evaluation, 5/10 patients had a reduction in DLCOc-SB by a median of 10.0% (range 0.6–27.6%) and 5/10 had an increase of 1.4–12.4% (median 9.8%). None of the patients developed clinical symptoms of pneumonitis and only 1/19 had a reduction in SLCOc-SB by >20%.

Conclusion: NAVD has a favorable pulmonary safety profile.

P044: HIV-associated Hodgkin lymphoma: real-world treatment outcomes and infectious complications – a multicentre study by the Polish Lymphoma Research Group

Agnieszka Giza¹, Magdalena Zapala², Joanna Drozd-Sokolowska³, Magdalena Witkowska⁴, Jan Maciej Zaucha⁵, Malgorzata Sobczyk-Kruszelnicka⁶, Anastazja Szlauer-Stefanska⁶, Anna Kopinska⁷, Magdalena Zawartko⁸, Magdalena Witak-Jedra⁹, Kamil Wisniewski¹⁰, Kamil Wdowiak¹¹, Jarosław Grzyb¹², Anna Parfieniuk-Kowerda¹³, Natalia Leńczuk¹⁴, Alicja Wandolowicz¹³, Monika Joks¹⁵, Justyna Rybka¹⁶, Judyta Strzala¹⁷, Agnieszka Szeremet¹⁸, Aleksandra Szymczak¹⁹, Marcin Czarnecki¹⁹, Marta Głuchowska², Jarosław Dybko¹⁸, Dagmara Zimowska-Curylo¹, Ewa Lech-Maranda¹⁰, Tomasz Sacha¹, Miłosz Parczewski²⁰, Monika Bociaga-Jasik²¹

¹Department of Hematology, Jagiellonian University Medical College, Faculty of Medicine, Jakubowskiego 2, Krakow, Poland, ²Haematology and Internal Medicine Clinical Department, The University Hospital, Krakow, Poland, ³Department of Hematology, Transplantation and Internal Medicine, University Clinical Centre, Medical University of Warsaw, Stefana Banacha 1a, Warsaw, Poland, ⁴Department of Hematology, Medical University of Lodz, Lodz, Poland, ⁵Department of Hematology, Transplantation and Cellular Therapies, University Clinical Center, Gdansk, Poland, ⁶Maria Skłodowska-Curie National Research Institute of Oncology, Gliwice Branch, ⁷Department of Hematology and Bone Marrow Transplantation, Medical University of Silesia Katowice, Katowice, Poland, ⁸Department of Hematology, Provincial Hospital, Szczecin, Poland, ⁹Department of Infectious, Tropical Diseases and Acquired Immune Deficiency, Provincial Hospital, Szczecin, Poland, ¹⁰Department of Hematology, Institute of Hematology and Transfusion Medicine, Warsaw, Poland, ¹¹Internal Medicine and Oncology Department, Medical University of Silesia, Katowice, Poland, ¹²Hematology Clinic, Fryderyk Chopin University Clinical Hospital in Rzeszów, Rzeszow, Poland, ¹³Department of Infectious Diseases and Hepatology, Medical University of Białystok, Białystok, Poland, ¹⁴Department of Haematology, Internal Medicine and Angiology with Haematopoietic Cell Transplantation Unit, Medical University of Białystok, Białystok, Poland, ¹⁵Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Poznan, Poland, ¹⁶Department of Hematology, Cellular Therapies, and Internal Medicine, Wrocław Medical University, Wrocław, Poland, ¹⁷Department of Hematology and Bone Marrow Transplantation, Polish Red Cross Maritime Hospital Gdynia, Poland, ¹⁸Lower Silesia Centre for Oncology, Pulmonology and Hematology in Wrocław, Wrocław, Poland, ¹⁹Department of Infectious Diseases, Liver Diseases and Acquired Immune Deficiencies, Wrocław Medical University, Wrocław, Poland, ²⁰Department of Infectious, Tropical Diseases and Immune Deficiency, Pomeranian Medical University, Szczecin, Poland, ²¹Department of Infectious Diseases, Jagiellonian University Medical College, Faculty of Medicine and Clinic of Infectious Diseases Clinical Department, The University Hospital, Krakow, Poland

Background: HIV-associated Hodgkin lymphoma (HL) is uncommon and remains clinically challenging despite the availability of antiretroviral therapy (ART). Contemporary cohorts suggest favourable outcomes with standard HL treatment and effective HIV care, but real-world data from Central and Eastern Europe are limited.

Methods: We retrospectively analysed 12 adults with HIV-associated HL treated in 10 Polish haematological centres between 2007 and 2026, representing 12.2% of the Polish Lymphoma Research Group HIV-positive lymphoma cohort (12/98).

Results: All patients were male; median age was 39.5 years. HIV and HL were diagnosed concurrently in 1 patient; 11/12 had known HIV infection and were receiving ART before HL diagnosis. CD4 count and HIV RNA at HL diagnosis were available in 6/12; median CD4 count was 296 cells/ μ L. Advanced disease (Lugano III–IV) was present in 11/12 and bone marrow involvement in 3/12. Importantly, 6/12 patients had clinically significant infectious complications before HL treatment, including CMV reactivation, oesophageal candidiasis, *Pneumocystis jirovecii* pneumonia and pulmonary tuberculosis.

First-line treatment consisted of ABVD in 11/12 patients and BV-AVD in 1/12. Infections and/or severe neutropenia complicated treatment, leading to dose reduction in 1 patient, prolonged intervals in 3 and hospitalisation in 3. Complete remission (CR) was achieved in 9/12; 4 of these patients relapsed, while 3/12 had primary refractory disease. Overall, 7/12 required second-line therapy and 1 underwent high-dose chemotherapy followed by autologous stem cell transplantation. Median time to relapse was 17.7 months.

Additional events illustrated diagnostic and immune-related complexity: syphilis mimicked PET-positive nodal relapse in one patient in CR on the end of treatment, while immune thrombocytopenia developed after first-line therapy in another patient and preceded subsequent HL relapse. During a median follow-up of 41 months, 4/12 patients died (33.3%), mainly due to lymphoma progression, including hemophagocytic lymphohistiocytosis and CSN relapse.

Conclusions: Despite favourable outcomes reported in ART-era cohorts, this real-world series shows that HIV-associated HL may still follow a clinically challenging course. Infectious and immune-related events may complicate PET-based assessment and follow-up. These findings underscore the need for clinical vigilance, HIV/immunological assessment and standardised infection prophylaxis.

P045: Frontline BV-AVD in Classical Hodgkin Lymphoma: A Multicenter Real-World Comparison with the ABVD Regimen

Fatma Keklik Karadag¹, Merve Yukse², Umut Yılmaz³, Meral Ulukoylu Menguc⁴, Denis Çetin¹, Ajda Gunes¹, Batuhan Bulan³, Taner Tan⁵, Sureyya Yigitkaya⁶, Hacer Berna Afacan Ozturk⁷, Ezel Elgün⁸, Deniz Gören⁹, Ulviyya Hasanzade¹⁰, Hale Bulbul Dilmen¹¹, Utku İltar¹², Merve Ecem Erdogan Yon¹³, Guldane Cengiz Seval², Ozan Salim¹², Orhan Kemal Yücel¹², Ekin Kircali², Zafer Serenli Yeğen¹⁴, Haşim Atakan Erol¹⁵, Ayşe Uysal¹⁶, Burak Deveci¹⁷, Omur Kayıkcı¹⁸, Zehra Narlı Özdemir¹¹, Esin Oğuz Kozan¹⁹, Mehmet Baysal²⁰, Ayşe Hilal Eroğlu Küçükçiler²¹, Zuhale Demirci¹, İrfan Yavasoglu²¹, Pelin Aytan¹⁹, Deniz Özmen İbis³, Murat Ozbalak¹⁰, Fahir Ozkalemkas⁸, Ahmet Kursad Gunes⁷, Ömür Gökmen Sevindik⁶, Gulsum Ozet¹³, Zafer Gulbas²², Olga Meltem Akay⁵, Muhlis Cem Ar³, Ahmet Emre Eskazan³, Elif Birtas Atesoglu²³, Burhan Ferhanoglu⁵, Guray Saydam¹, Muhit Ozcan², Ozgur Mehtap¹⁵

¹Ege University Department of Hematology, Izmir, Türkiye, ²Ankara University Department of Hematology, Ankara, Türkiye, ³Istanbul University-Cerrahpaşa Medical School, Department of Hematology, Istanbul, Türkiye, ⁴Marmara University, Department of Hematology, Istanbul, Türkiye, ⁵Koc University, Department of Hematology, Istanbul, Türkiye, ⁶Istanbul Medipol University, Department of Hematology, Istanbul, Türkiye, ⁷Ankara Etlik city Hospital, Department of Hematology, Ankara, Türkiye, ⁸Bursa Uludağ University, Department of Hematology, Bursa, Türkiye, ⁹Halic University, Sisli Memorial Hospital, Department of Hematology, Istanbul, Türkiye, ¹⁰Istanbul University Medical School, Department of Hematology, Istanbul, Türkiye, ¹¹Izmir City Hospital Department of Hematology, Izmir, Türkiye, ¹²Akdeniz University, Department of hematology, Antalya, Türkiye, ¹³Ankara Bilkent City Hospital, Department of Hematology, Ankara, Türkiye, ¹⁴Bursa Doruk Hospital, Department of Hematology, Bursa, Türkiye, ¹⁵Kocaeli University, Department of Hematology, Kocaeli, Türkiye, ¹⁶Firat University, Department of Hematology, Elazığ, Türkiye, ¹⁷Antalya Medstar Hospital, Department of Hematology, Antalya, Türkiye, ¹⁸Bahçelievler Memorial Hospital, Department of Hematology, Istanbul, Türkiye, ¹⁹Mersin University, Department of Hematology, Mersin, Türkiye, ²⁰Tekirdağ Namık Kemal University, Department of Hematology, Tekirdağ, Türkiye, ²¹Adnan Menderes University, Department of Hematology, Aydın, Türkiye, ²²Anadolu Sağlık Grubu Hospital, Department of Hematology, Kocaeli, Türkiye, ²³Yeditepe University, Department of Hematology, Istanbul, Türkiye

Background: For decades, the ABVD regimen remained the global gold standard for advanced-stage classical Hodgkin lymphoma (cHL). In the ECHELON-1 trial, brentuximab vedotin (BV) combined with AVD (BV+AVD) showed higher progression-free survival (PFS) and overall survival (OS) rates in patients with advanced stage compared to the standard ABVD regimen. We evaluated the clinical outcomes of a multicenter cohort treated with first-line BV-AVD and compared them against the long-term historical outcomes of patients treated with the ABVD regimen.

Methods: This multicenter, retrospective cohort study enrolled adult patients with newly diagnosed cHL across 20 centers in Turkey receiving first-line BV+AVD, with ABVD-treated patients as the internal control cohort from Ege University and external validation cohort of advanced-stage from different center. Survival outcomes were estimated using the Kaplan-Meier method and compared with the log-rank test, with Cox regression tests used for multivariate analyses.

Results: A total of 275 patients were analyzed: 123 in the BV-AVD group (median age 46, range 18–83) and 152 in the ABVD group (median age 39, range 18–81). The BV-AVD cohort exhibited a significantly higher risk profile, with a greater prevalence of advanced-stage disease (90% vs. 68%; $p < 0.001$), B symptoms (59% vs. 44.7%; $p = 0.019$), and bone marrow involvement (24% vs. 12%; $p = 0.006$). Median follow-up was 1.4 years for BV-AVD and 4.9 years for ABVD. In the overall cohort, the 2-year PFS and OS rates were higher in the BV-AVD group, though the difference did not reach statistical significance (PFS: 83.5% vs. 78.4%, $p = 0.7$; OS: 96.7% vs. 89.1%, $p = 0.1$). However, in a subgroup analysis of advanced-stage patients, while 2-year PFS remained comparable (81.8% vs. 66.7%; $p = 0.08$), the 2-year OS was significantly superior in the BV-AVD arm (95.6% vs. 81.8%; HR: 3.97, 95% CI: 1.3–12.1, $p = 0.015$). Regarding safety, neuropathy and grade 3–4 hematological toxicities were more frequent in the BV-AVD group. Consequently, the utilization of G-CSF was significantly higher in the BV-AVD cohort (77.2% vs. 41.1%; $p < 0.001$).

Conclusion: Our data suggests that BV-AVD is a robust and effective frontline regimen for advanced-stage HL in a real-world setting. By successfully managing a higher-risk patient population and providing a superior survival advantage in advanced stages, BV-AVD justifies its position as the new standard of care, provided that hematological toxicities are managed.

Biology and pathology

T046: Functional characterization of STAT6 mutations as oncogenic drivers in classical Hodgkin lymphoma (cHL)

Luisa Tasselli¹, Rafael L. B. Coan¹, Valentina Pensato¹, Francois Le Dily², Barbara G. Müller-Coan¹, Valentina Pettirossi¹, Enrique Blanco², Alessandro Cupola¹, Laura Pasqualucci³, Luciano Di Croce², Enrico Tiacci¹

¹Center of Hemato-Oncology Research, Dip. of Medicine and Surgery, Perugia University and Perugia Hospital, Italy, ²Centre for Genomic Regulation (CRG), Barcelona, Spain,

³Institute for Cancer Genetics and Department of Pathology, Columbia University, NY, United States

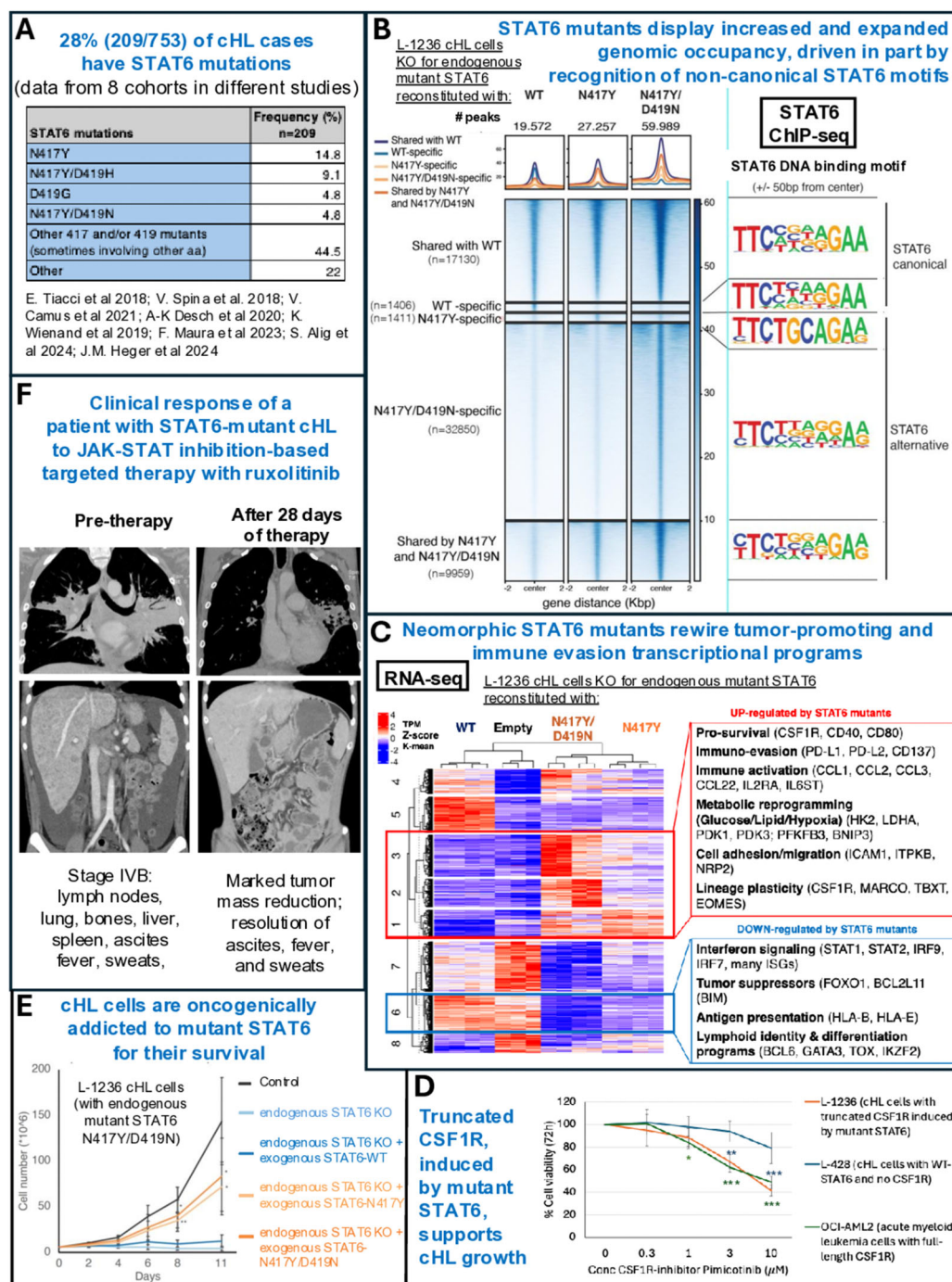


Figure 1: STAT6 mutations in cHL (A). Aberrant genomic binding (B), transcriptional rewiring (C) and clone growth promotion (D) by mutant STAT6. Oncogenic addition of cHL to mutant STAT6 (E). JAK-STAT inhibitor-based therapy in a STAT6-mutant cHL case (F).

Background: cHL is largely curable but a subset of patients still dies of this lymphoma, underscoring the need to better define its drivers for enabling targeted therapies. Mutations in the DNA-binding domain of the STAT6 transcription factor occur in ~30% of cHL cases (Tiacchi et al. Blood 2018), yet how they contribute to cHL pathogenesis is unclear.

Methods: We studied the most frequent STAT6 mutations (N417Y, D419G/H/N, and double mutants, Fig. 1A) in cHL cell lines expressing endogenous or exogenous wild-type (WT) or mutant STAT6 through an integrated multi-omics approach combining chromatin binding (ChIP-seq), chromatin accessibility and regulatory profiling (ATAC-seq; Cut&Run for H3K27ac), 3D genome organization (Hi-C-seq), and transcriptomic analyses (RNA-seq).

Results: Compared to WT, each STAT6 mutant showed stronger and expanded genomic occupancy, at least in part through neomorphic binding to non-canonical ("alternative") STAT6 DNA motifs (Fig. B), leading to increased chromatin accessibility, activation of regulatory elements including super-enhancers (SEs), and increased long-range chromatin interactions at multiple loci. These alterations established aberrant transcriptional programs (Fig. C) promoting proliferation, metabolic adaptation, immune evasion (including upregulation of PD-L1/PD-L2) and lineage plasticity, while repressing interferon signaling and tumor suppressors.

Notably, mutant STAT6 newly generated a SE overlapping the locus of the myeloid receptor tyrosine kinase CSF1R, leading to expression of a novel truncated isoform lacking the ligand-binding domain but retaining the kinase domain, consistent with potential constitutive activity. Indeed, viability of STAT6-mutant cHL cells was impaired by the clinical-grade CSF1R-specific inhibitor pimicotinib (Fig. D).

Consistently, knock-out of endogenous mutant STAT6 induced cHL cell apoptosis, which was rescued only by exogenous mutant (but not WT) STAT6 (Fig. E), indicating oncogenic addiction to mutant-specific programs. Finally, a young patient with STAT6-mutant cHL not responding to 9 prior therapies (including nivolumab) achieved a rapid and marked clinical response to treatment with the JAK/STAT inhibitor ruxolitinib combined with nivolumab.

Conclusions: We functionally dissected the role of STAT6 mutations in cHL pathogenesis and provided a mechanistic rationale for therapeutic strategies targeting the JAK/STAT axis and key downstream effectors like CSF1R.

T047: Artificial intelligence predicts EBV status and reveals prognostic morphology phenotypes in advanced-stage classic Hodgkin lymphoma

Hishan Tharmaseelan¹, Daniel Winderl², Steffen Gretser³, Julia Richter³, Justin Ferdinandus¹, Peter Borchmann¹, Michael Altenbuchinger², Wolfram Klapper³

¹University of Cologne, Faculty of Medicine and University Hospital of Cologne, Department I of Internal Medicine, and Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf (CIO ABCD), and German Hodgkin Study Group (GHSG), Cologne, Germany, ²Department of Medical Bioinformatics, University Medical Center Göttingen, Göttingen, Germany, ³Department of Pathology, Hematopathology Section and Lymph Node Registry, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

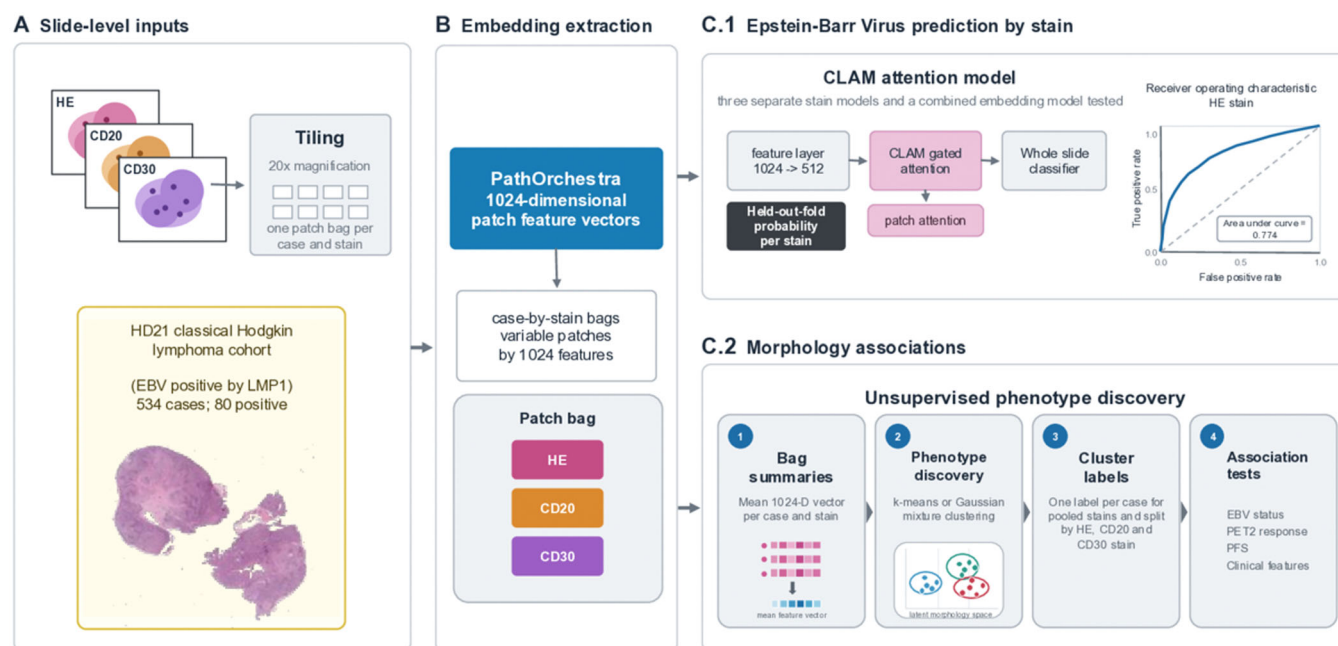


Figure 1: Workflow of the AI analyses to unveil histologic subtypes and EBV status from whole-slide imaging.

Background: Epstein–Barr virus (EBV) status and morphologic heterogeneity characterize the histopathologic phenotype of classic Hodgkin lymphoma (cHL). We asked whether artificial intelligence (AI) models trained on self-supervised histology foundation-models can (i) predict EBV status without testing for the virus and (ii) define clinically meaningful clusters from routine stains.

Methods: We analyzed 935 advanced stage cHL cases from the German Hodgkin Study Group HD21 trial. Embeddings were generated from H&E, CD30 and CD20 staining Whole-slide imaging (WSI) using the general pathology foundation model Pa-thOrchestra. Unsupervised clustering with k-means was applied on mean patch embedding per case and tested against EBV status and interim PET positivity (PET-2) by Fishers exact test, and 3-year progression-free survival (PFS) differences using log-rank test. In addition, a supervised EBV prediction was trained using attention-based multiple instance learning per stain and extractor. All metrics are 5-fold cross-validated.

Results: Supervised prediction for detection of EBV status worked best using H&E (5-fold out-of-fold [OOF] held-out cross-validation prediction AUC for all staining combined: 0.74; CD20: 0.70; CD30: 0.71; H&E: 0.77). Unsupervised clustering revealed distinct phenotypes (k = 2 for H&E/CD30, k = 3 for CD20). The CD30 phenotype clusters were associated with EBV (19% Cluster 0 (C0) vs. 11% C1; p = 0.01). CD20 phenotypes associated with interim PET (C0: 30%, C1: 25%, C2: 35%; p = 0.01). After the combination of similarly prognostic clusters a prognostic difference could be demonstrated (3-yr PFS C0&C2: 95.0% [95% CI: 93.0–96.4] vs. C1: 91.3% [95% CI: 87.2–94.1]; p = 0.02).

Conclusion: AI analysis of conventional histology slides reveal clinical phenotypes and show feasibility of detecting molecular features of Hodgkin-Reed-Sternberg-cells like EBV without directly testing for this feature. These findings will be validated in an additional cohort that will be presented at the meeting.

T048: A Reproducible Mutation- versus Copy-Number-Enriched Genomic Axis Underlies Molecular Subtypes of Classic Hodgkin Lymphoma

Cara Paulina Lange¹, Michael Yu Li², Andrea Garofalo³, Tanja Zamrik¹, Christian Reinhardt¹, Bastian Von Tresckow¹, Mohammad Esfahani⁴, Ash A. Alizadeh³, Christian Steidl², Tomohiro Aoki⁵, Stefan K. Alig¹

¹Department of Hematology and Stem Cell Transplantation, University Hospital Essen, Essen, Germany, ²Centre for Lymphoid Cancer, BC Cancer, University of British Columbia, Vancouver, Canada, ³Division of Oncology, Stanford University School of Medicine, Stanford, CA, USA, ⁴Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA, USA, ⁵Princess Margaret Cancer Centre, University of Toronto, Toronto, Canada

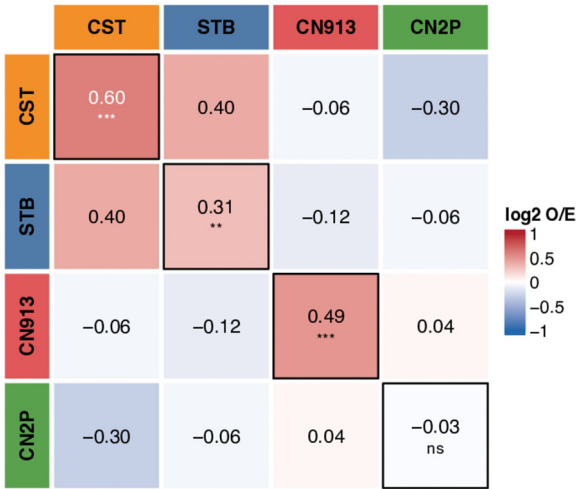


Figure 1: Cluster-level co-association of BC Cancer subtype-defining genomic features. Each cell shows mean pairwise log2(O/E) co-occurrence within (diagonal) or between (off-diagonal) subtypes. Red: co-enrichment; blue: mutual exclusivity.

Background: Several independent groups have recently proposed genomic subtype classifications of classic Hodgkin lymphoma (cHL), either by ctDNA profiling or analysis of microdissected tumor tissue: two subtypes by Alig et al. (Nature 2023, H1/H2), four by Aoki et al. (Cancer Discov 2026, CST/CN913/STB/CN2P), three by Heger et al. (JCO 2024), and two by Piroso et al. (Blood 2025, C1/C2). Whether these independently derived systems capture the same biology or identify orthogonal structure remains unknown.

Methods: We applied the BC Cancer (Aoki) subtype classifier to 293 cHL patients from the Stanford ctDNA targeted sequencing cohort (Alig et al., Nature 2023). Subtype concordance was assessed by cross-tabulation, cluster enrichments by Fisher's exact test, and prognostic associations by log-rank test. Co-association analysis of cluster-defining features by observed vs expected (O/E) frequencies was performed across all 4 classification systems.

Results: The BC Cancer classifier resolved the H1/H2 axis into four subtypes distributed as CST (39%), STB (23%), CN913 (15%), CN2P (5%), and unclassified (18%), with CST and STB (mutation-dominated) mapping predominantly within H1 (87% and 80% H1, respectively) and CN913

and CN2P (copy number aberration [CNA]-dominated) within H2 (73% and 63% H2; $p < 0.00001$). CN913 was enriched for older age (median 59 vs 29 years for CST/STB; $p = 0.002$) and EBV positivity (60% vs 15% for CST/STB; $p < 0.00001$). PFS differed significantly across subtypes ($p = 0.046$), with inferior outcomes in CN913/CN2P vs CST/STB. Co-association analysis of cluster-defining features showed strong within-cluster co-enrichment ($\log_2$ O/E CST = 0.60, CN913 = 0.49, STB = 0.31, CN2P = -0.03), with mutual exclusivity largely restricted to features crossing the mutation- versus CNA-dominant axis. Co-association analyses using defining features from the Heger and Piroso classifications also each independently reproduced the same CNA- versus mutation-dominated pattern.

Conclusion: A binary mutation- versus CNA-dominant axis represents the primary organizing feature of cHL tumor genome biology and appears highly reproducible across independent studies supporting at least two molecular subtypes. More granular models may provide additional resolution within this framework, with their additional clinical impact an area of active investigation. Harmonization efforts across studies are warranted to define a consensus classification for prospective clinical application.

P049: Detection of traces of EBNA2 in the Microenvironment of Pediatric Classical Hodgkin Lymphoma Reveals Its Immunomodulatory Role

Tamara Mangiatterra¹, Karen Lindl¹, Oscar Jimenez¹, Elena De Matteo¹, Paola Chabay¹

¹Instituto Multidisciplinario de Investigaciones en Patologías Pediátricas (IMIPP). CONICET-GCBA, Hospital de Niños Ricardo Gutiérrez

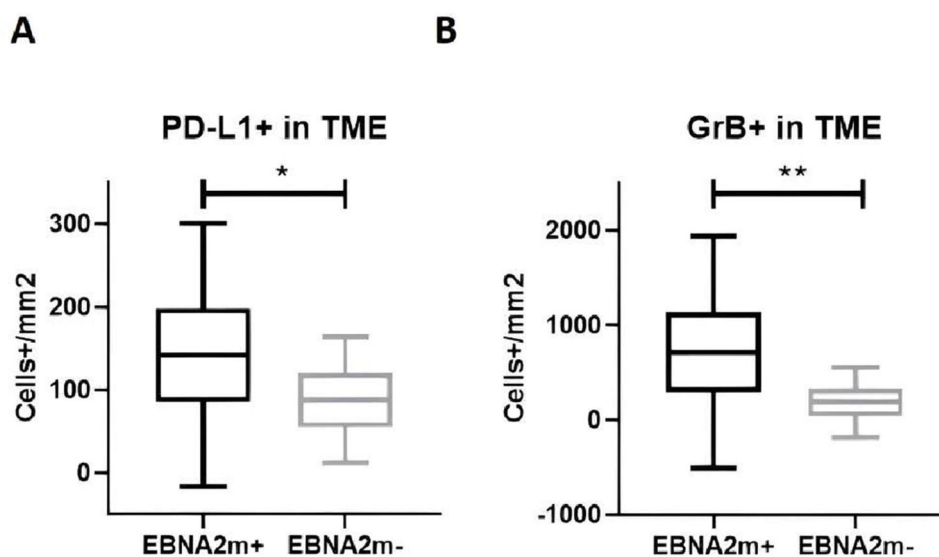


Figure 1: Marker expression. (A) PD-L1 expression in the tumor microenvironment according to EBNA2 transcript expression status. (B) Granzyme B (GrB) expression in the tumor microenvironment according to EBNA2 transcript expression status.

The detection of Epstein-Barr virus (EBV) traces using ultrasensitive techniques in B-cell lymphomas previously classified as EBV-negative by conventional methods suggests a broader role for the virus in lymphomagenesis. Its contribution in classical Hodgkin lymphoma (cHL) remains unexplored. This study aimed to characterize viral transcripts expression by sensitive methods.

A total of 48 pediatric cHL cases were analyzed. EBV status was evaluated with the conventional approach: EBER in situ hybridization (ISH). LMP1 and EBNA2 transcripts were assessed using highly sensitive dual ISH combined with CD30 immunohistochemistry (IHC) to distinguish tumor cells from cells of the tumor microenvironment (TME). IHC evaluated protein expression for LMP1, CD4, CD8, CD56, CD68, CD163, PD-1, PD-L1 (TME and tumor cells), IL-10, FOXP3, Granzyme B (GrB), TGF- β , and T-bet. Event-free survival was analyzed using the Kaplan-Meier method.

Among the 32 EBERs+ cases, 32 expressed LMP1 transcripts in both tumor cells (LMP1t+) and the TME (LMP1m+), none expressed EBNA2 transcripts in tumor cells (EBNA2t-), and 23 expressed EBNA2 transcripts in the microenvironment (EBNA2m+). In the 16 EBERs-, 10 cases displayed LMP1t+ cells, 11 cases LMP1m+ and 6 EBNA2m+. Remarkably, EBNA2m were exclusively observed in the TME. 5 cases did not express any of the analyzed transcripts.

PD-L1 expression in the TME was significantly higher in cases expressing EBNA2 transcripts compared to those without EBNA2 expression ($p = 0.0373$, Mann-Whitney test). Similarly, GrB expression was also significantly increased in EBNA2m+ cases ($p = 0.0012$, Mann-Whitney test) (Figure 1). The count of IL10+ cells in the groups defined by EBNA2 transcript expression showed a trend ($p = 0.0768$, Mann-Whitney test). Only cases expressing traces of LMP1 in both tumor cells and the TME exhibited a predominant M1 profile (CD68+cells/CD163+ cells > 1.5) ($p = 0.0339$, $p = 0.0096$, Fisher's exact test). No significant differences in event-free survival were observed according to viral transcript expression ($p > 0.05$).

EBNA2 expression in the TME, even in EBV- cases, might be associated with immune checkpoint regulation and cytotoxic responses, highlighting a previously underrecognized role of EBV and its viral traces in shaping the cHL microenvironment. Additionally, LMP1 expression in tumor cells and the TME could contribute to the M1-polarized profile previously described in pediatric EBV-associated cHL.

P050: Variant Histology in Pediatric NLPBL: Adverse Features Mitigated by R-CHOP, Including Feasible Early-stage De-Escalation

Nesreen Ali¹, Emad Moussa², Eman Khorshed³, Mohamed Zaghloul⁴, Amr Elnashar⁵, Amr Abdalla⁶

¹Pediatric Oncology and Hematology Department, National Cancer Institute (NCI), Cairo University and Children Cancer Hospital, Cairo, Egypt(CCHE-57357), ²Clinical Oncology Department, Menoufya University and Children Cancer Hospital Egypt (CCHE-57357), ³Pathology Department, National Cancer Institute (NCI), Cairo University and Children Cancer Hospital Egypt (CCHE-57357), ⁴Radiation Therapy Department, National Cancer Institute (NCI), Cairo University and Children Cancer Hospital Egypt (CCHE-57357), ⁵Clinical Research Department, Children Cancer Hospital Egypt (CCHE-57357), ⁶Pediatric Oncology and Hematology Department, National Cancer Institute (NCI), Cairo University, Egypt and Child Health Department, SultanQaboos University, Muscat, Oman

Background: Nodular lymphocyte-predominant B-cell lymphoma (NLPBL) is an uncommon subtype of pediatric Hodgkin-lymphoma comprising typical-histology (patterns A-B) and variant-histology (patterns C-F). Variant patterns have been linked to higher-risk features and increased relapse, but the optimal pediatric treatment approach, particularly the safety of de-escalation in early-stage disease, remains uncertain.

Methods: We retrospectively reviewed pediatric patients diagnosed with NLPBL at Children's Cancer Hospital Egypt. Histology was classified as typical or variant, with variant subtypes recorded as patterns C-F. Survival outcomes were analyzed according to frontline treatment, with focused evaluation of early-stage patients managed with observation after complete resection (stage IA) or reduced-cycle R-CHOP for unresected stage I-II disease.

Results: Among 87 patients, variant histology was identified in 41 (47.1%). Variant histology was associated with less favorable presentation, including advanced stage ($p = 0.06$), B symptoms ($p = 0.05$), and extranodal disease, particularly bone marrow and bone involvement ($p = 0.01$). Progression/relapse was more frequent in variant than typical histology (39.0% vs 15.2%, $p = 0.009$), and variant subtypes C and D were associated with inferior event-free survival (EFS; $p = 0.05$). Among patients with variant histology, 5-year EFS was 94.4% with R-CHOP versus 33.3% with ABVD. In the updated early-stage analysis, 7/12 completely resected stage IA patients managed with observation had variant histology, with relapse patterns comparable to typical histology. Among unresected stage I-II patients treated with 3–4 cycles of R-CHOP, variant histology was present in 20/39 (51.3%), with only 2 relapses. Within the R-CHOP-treated cohort, variant-histology did not significantly affect 5-year EFS, including in early-stage patients treated with fewer cycles.

Conclusion: Variant-histology identifies a biologically and clinically higher-risk subgroup of pediatric NLPBL. However, this adverse impact appears to be mitigated by R-CHOP, with excellent outcomes even in patients with variant histology. Our findings further suggest that risk-adapted de-escalation may be feasible in early-stage disease, including observation after complete resection and reduced-cycle R-CHOP for unresected stage I-II disease, without an apparent loss of efficacy. These findings support prospective multicenter validation of histology-guided, response-adapted strategies.

P051: Genetic tumor cell heterogeneity and genomic instability in classic Hodgkin lymphoma

Sophie Klotz¹, Bettina Budeus¹, Frederik Schramm¹, Lilian K. Beeck¹, Marc A. Weniger¹, Paul J. Bröckelmann^{2,3}, Ralf Küppers¹

¹Institute of Cell Biology (Cancer Research), Faculty of Medicine, University of Duisburg-Essen, Essen, Germany, ²University of Cologne, Faculty of Medicine and University Hospital of Cologne, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and German Hodgkin Study Group (GHSG), Cologne, Germany, ³MV-Zentrum Onkologie und Hämatologie Am Sachsenring GmbH, Cologne, Germany

Classic Hodgkin lymphoma (cHL) is one of the most prevalent types of lymphomas in the Western world and one of the most frequent cancers in young adults. Hodgkin and Reed-Sternberg (HRS) lymphoma cells are highly heterogeneous and typically show multiple chromosomal abnormalities. The rarity of HRS cells has hampered their analysis over the last decades, but understanding the tumor cell heterogeneity is essential to reveal mechanisms of therapy resistance. Therefore, we developed an advanced workflow to perform whole-exome sequencing (WES) of single HRS cells to reveal signs of intraclonal tumor evolution and the underlying mutagenic processes.

Frozen cHL lymph node suspensions were processed using an antibody-based staining method, and single HRS cells were transferred to a 96-well plate using a fluorescence-activated cell sorter. We used a single-cell whole-genome amplification kit to barcode the DNA prior to the whole-exome capturing. Bulk non-tumor cells were simultaneously collected to later on distinguish germline from somatic mutations. The single-cell WES workflow was tested with a mixture of cells from two HL cell lines. By comparing cell line-specific mutations, the index-sorted cells could be explicitly assigned to its particular cell line, showing the robustness of this pipeline in identifying distinct mutations in subsets of cells. We further validated the method using a primary cHL case, which had previously been characterized in a bulk WGS study. Most of the identified exonic mutations from the bulk analysis were also identified in at least a subset of single cells, and subsequent genealogical analysis revealed first insights into the mutational development of this HL case. Six additional HL cases are currently being processed.

A detailed characterization of mutation patterns at the single-cell level may provide profound insights into the genetic complexity and heterogeneity of the unique HRS cancer cells. This characterization is expected to reveal novel insights into lymphoma progression and the underlying mutagenic processes and is a pivotal step towards our long-term objective of elucidating the mechanisms of genetic instability in HRS cells, to identify markers of treatment resistance and develop new diagnostic and therapeutic approaches.

P052: Emerging role of SAMHD1 in anti-tumor immune responses and sensitivity to chemotherapy in classical Hodgkin lymphoma

Dora Trogrlic¹, Eleni Psaroudaki¹, Georgios Mermelekas¹, Ying Yang¹, Erofil Bougka¹, Christian Nordentoft¹, Nikolas Herold², Andreas Lundqvist¹, Elias Drakos¹, Georgios Rassidakis¹

¹Karolinska Institutet, Department of Oncology-Pathology, ²Karolinska Institutet, Department of Women's and Children's Health

Background: The tumor microenvironment (TME) plays a pivotal role in the pathogenesis of classical Hodgkin lymphoma (cHL). SAMHD1, a dNTP hydrolase, is involved in anti-tumor immune responses through DNA damage mechanisms and cGAS-STING pathway. SAMHD1 expression in the neoplastic Hodgkin and Reed-Sternberg cells (HRS) is an independent adverse prognostic factor in cHL, however, the mechanisms underlying its clinical significance are unknown. In this study the biologic impact of SAMHD1 on anti-tumor immune responses and sensitivity to chemotherapy in cHL was investigated.

Methods: The in vitro system included 6 cHL cell lines, in 3 of which (L1236, L428, L540) SAMHD1-deficient clones (KO) were generated using CRISPR-Cas9 gene editing. In addition, the effects of plasmid-mediated forced expression of SAMHD1 were analyzed in 2 cHL cell lines with low (L428) or undetectable (MDAV) endogenous SAMHD1. The cHL cell lines were treated with a STING agonist, STING inhibitor (C-176), or doxorubicin. Protein expression and activation were analyzed by Western blot. Immune responses were evaluated using RT-qPCR for gene expression of critical immunomodulators, and targeted proteomics with Olink Target 48 Cytokine panel on culture supernates.

Results: SAMHD1-KO and -WT cHL cells showed differential gene expression of critical modulators of antitumor immune responses. The effects of SAMHD1 deficiency were associated with changes in cGAS-STING pathway activation, including phosphorylation of TBK1, IRF3 and IRF7. SAMHD1 deficiency resulted in decreased secretion of IL6, CSF2, TNF, CCL2/7. STING stimulation led to significantly increased IFN β gene expression by HRS cells in SAMHD1-WT but not in SAMHD1-KO cHL cell lines. STING inhibition also resulted in differential changes in immunomodulatory cytokines. Forced expression of SAMHD1 led to upregulation of CXCL10 and IFN β gene expression in cultured HRS cells. These effects were linked to lower levels of CXCL9, IL10, TNF, IL17a and CXCL8 in MDA-V cells following SAMHD1 forced expression as shown by proteomic profiling. SAMHD1-WT and -KO cHL cells differentially responded to doxorubicin treatment with changes in apoptosis-regulating proteins.

Conclusions: SAMHD1 expression seems to modulate the anti-tumor immune responses partially through the cGAS-STING pathway in cHL. SAMHD1 expression also affects the response to doxorubicin treatment in vitro.

P053: Development of CD30 CAR T-cells co-expressing an anti-PDL1.CD28 chimeric switch receptor for the treatment of r/r cHL

Mikalai Katsin¹, Dmitri Dormeshkin², Alexandr Migas², Hanna Klych³, Alexander Meleshko³, Konoplya Natalya⁴, Tatsiana Doroshenko⁴

¹Vitebsk Regional Clinical Cancer Centre, ²Institute of Bioorganic Chemistry of the National Academy of Sciences of Belarus, ³Belarusian Research Center for Pediatric Oncology, Hematology and Immunology, ⁴N.N. Alexandrov National Cancer Center of Belarus

Introduction: CD30 is a validated therapeutic target in Hodgkin lymphoma (HL), particularly in relapsed and refractory cases. Chimeric antigen receptor (CAR) T-cell immunotherapy targeting CD30 demonstrates promising clinical activity. However, inhibitory signals mediated by the PD-1/PD-L1 pathway may limit the durability of response. In this study, we investigated the impact of co-expressing a chimeric switch receptor (CSR) targeting PD-L1 on the proliferative and cytotoxic activity of second-generation CD30-CAR T-cells.

Materials and Methods: To compare the in vitro proliferative and functional activity of four second-generation CD30-CAR T-cell constructs (4-1BBz), including a variant with an anti-PD-L1 CSR (KN035.CD28), during repeated restimulation of CD30+ HL tumor cell lines. The following CAR constructs were evaluated: hHRS3.S-BBz.EGFRt – short hinge region (IgG4), hHRS3 scFv; SGN30.S-BBz.EGFRt – an analogous construct with SGN30 scFv (the antigen-binding fragment is identical to brentuximab vedotin); hHRS3.L-BBz.EGFRt – long hinge region (CH2-CH3) with two point mutations L235E, N297Q, and an alpha-tag for CAR detection and selection using an anti-alpha-tag nanobody; hHRS3.S-BBz.KN035-CD28 – a CAR with a CSR that binds PD-L1 and utilizes CD28 signaling. T-cells from healthy donors were activated via CD3/CD28 and transduced with the corresponding lentiviruses. Expansion was performed over 15 days in the presence of IL-7, IL-15, and IL-21. To evaluate the durability of response, a rechallenge model was applied: CD30+ tumor cells HDLM-2 (CD30+/PD-L1+) and KM-H2 (CD30+/PD-L1-) were added every 3–4 days for a total of 5 rounds. Analysis included the quantification of CAR T-cells, tumor burden evaluation, and the calculation of AUC (area under the curve) for both proliferation and cytotoxicity.

Results: Among the evaluated constructs, CAR.CSR T-cells (hHRS3.S-BBz.KN035-CD28) induced the most pronounced expansion on HDLM-2, demonstrating a 17-fold increase by day 21. The remaining constructs reached peak expansion (5–10 fold) by day 10, followed by a subsequent decline. Under conditions of stimulation with the PD-L1-negative line (KM-H2), differences in activity between CAR.CSR and baseline CARs were less pronounced.

Conclusions: CD30-CAR T-cells co-expressing the CSR KN035.CD28 demonstrated a sustained proliferative advantage and enhanced control of PD-L1+ tumor cells in vitro.

P054: Elucidation of transcriptomic tumor cell heterogeneity and microenvironment in classic Hodgkin lymphoma

Frederik Schramm¹, Sophie Klotz¹, Bettina Budeus¹, Lilian K. Beeck¹, Marc A. Weniger¹, Paul J. Bröckelmann², Ralf Küppers¹

¹Institute for Cell Biology (Tumor Research), University Medicine Essen, ²Max Planck Institute for Biology of Ageing, University Hospital of Cologne

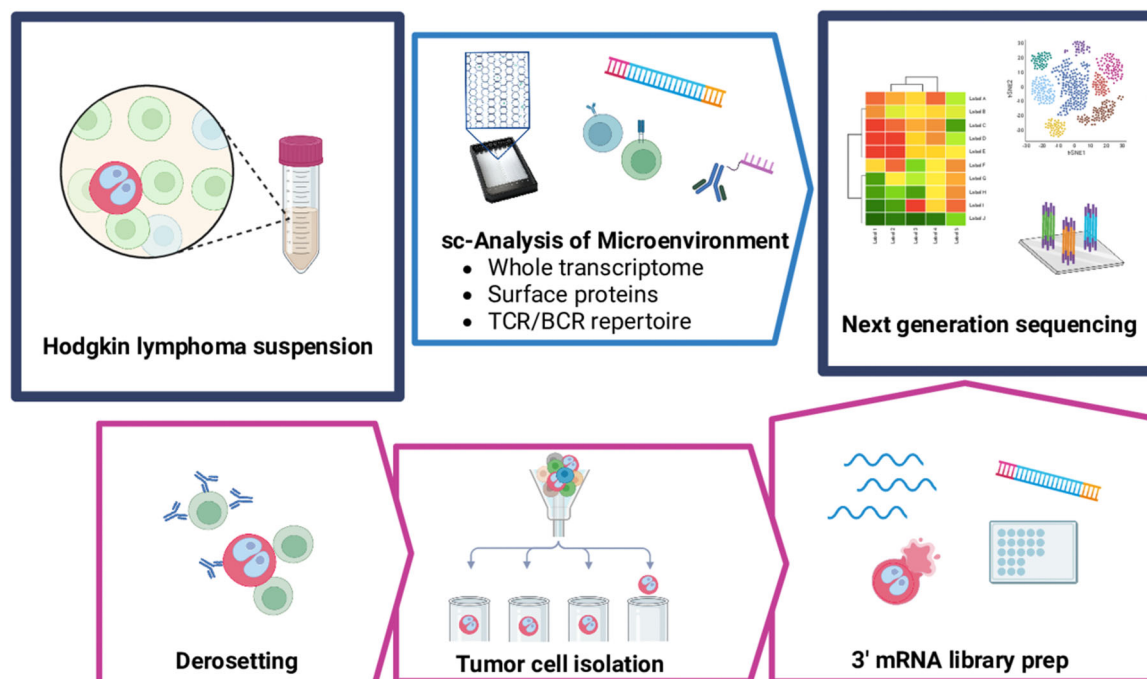


Figure 1: General workflow for processing primary cHL suspensions.

Classic Hodgkin lymphoma (cHL) is a B-cell-derived lymphoma that is unique among lymphoid malignancies due to its complex tumor microenvironment, which is dominated by dysregulated immune cells, and the presence of rare Hodgkin and Reed–Sternberg (HRS) tumor cells that comprise approximately 1% of the total tumor mass.

Despite major therapeutic advances, detailed molecular characterization of HRS cells remains technically challenging, limiting our understanding of cHL pathobiology.

To address this, we developed a workflow combining FACS index sorting of HRS cells with single-cell RNA sequencing. In parallel, we perform single-cell profiling of matched tumor microenvironment samples, enabling integrated analysis of whole transcriptomes, surface protein expression, and T-cell and B-cell receptor repertoires.

This approach allows us to dissect inter- and intratumoral heterogeneity in cHL at single-cell resolution across both malignant and non-malignant compartments.

Ultimately, our work aims to identify key molecular programs and interaction patterns in HRS cells and their microenvironment that contribute to therapy resistance and relapse, providing a foundation for improved treatment strategies and prognostic assessment in Hodgkin lymphoma.

P055: RHOA Mutation Analysis Identifies Potential nTFHL Among Cases With Classic Hodgkin Lymphoma Morphology

Rio Yamada¹, Midori Filiz Nishimura¹, Asami Nishikori¹, Yoshito Nishimura², Ritsuro Suzuki³, Yasuharu Sato¹

¹Department of Molecular Hematopathology, Okayama University Graduate School of Health Sciences, Okayama, Japan, ²Division of Hematology/Oncology, Mayo Clinic, Rochester, Minnesota, USA, ³Division of Hematology and Oncology, Department of Internal Medicine, Faculty of Medicine, Shimane University, Izumo, Japan

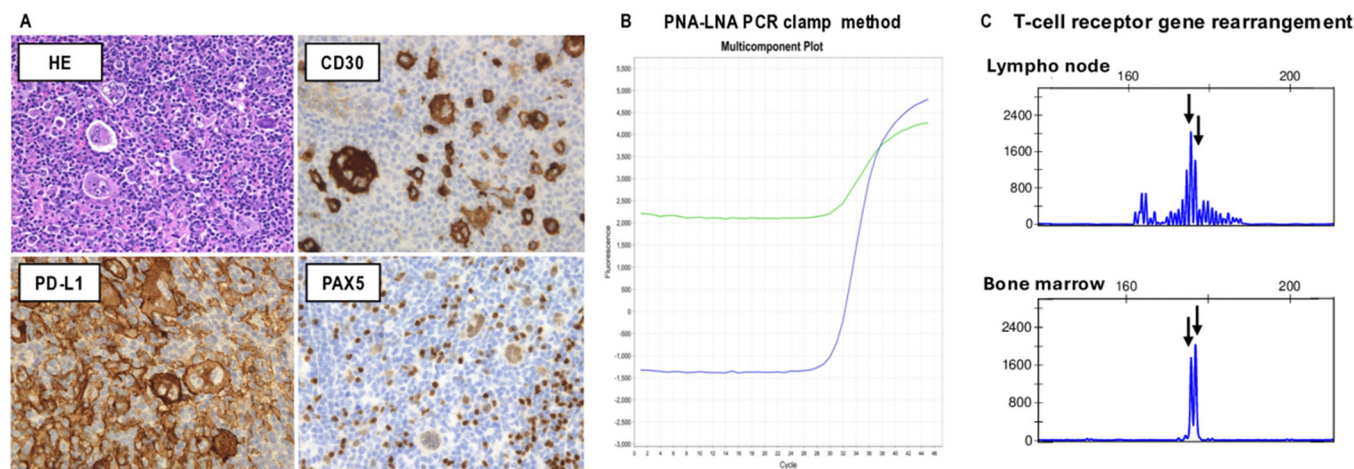


Figure 1: Representative case of nTFHL with CHL-like features. (A) CHL-like morphology and immunophenotype. (B) Specific amplification of the RHOA G17V mutant allele. Green indicates the internal control. (C) Oligoclonal TCR rearrangements with shared peaks.

Background: Nodal T-follicular helper cell lymphoma (nTFHL) may contain Hodgkin/Reed–Sternberg (HRS)-like cells and mimic classic Hodgkin lymphoma (CHL), but it is usually distinguishable from CHL by other histopathological features. We recently encountered a treatment-refractory case with highly convincing CHL morphology and immunophenotype, in which detection of the RHOA G17V mutation and shared T-cell receptor rearrangements in the lymph node and bone marrow redirected the diagnosis to nTFHL (Figure). This prompted us to investigate whether a subset of cases diagnosed as CHL based on morphology may represent “nTFHL with CHL features”.

Methods: We retrospectively analyzed 153 cases initially diagnosed as CHL based on excisional lymph node specimens in our consultation files (86 mixed-cellularity type and 67 nodular sclerosis type). RHOA G17V mutation was assessed using the PNA-LNA PCR clamp method, a highly sensitive assay suitable for low-tumor content samples. Clinicopathological features, histological findings, immunophenotype, EBV status, T-cell receptor gene rearrangement, treatment response, and clinical outcomes were compared according to RHOA mutation status.

Results: RHOA mutations were identified in 20/153 cases (13.1%), and all RHOA-mutated cases were detected exclusively among advanced-stage cases ($p < 0.001$). Compared with advanced-stage RHOA-wild-type cases, RHOA-mutated cases showed distinctive background features, including increased interfollicular vascularity and EBV-positive small- to medium-sized lymphoid cells (both $p < 0.001$). In the matched cohort, RHOA-mutated cases showed a poorer response to CHL-directed therapy and significantly shorter progression-free survival ($p < 0.01$), with a trend toward inferior overall survival ($p = 0.08$).

Conclusions: RHOA G17V mutations were detected in a substantial proportion of advanced-stage cases with CHL morphology, and these cases showed clinicopathological features suggestive of nTFHL. They may be better conceptualized as “nTFHL with CHL features” rather than conventional CHL. Given that morphology and immunophenotype alone make differentiation extremely challenging, RHOA mutation analysis should be considered in advanced-stage or treatment-refractory cases with CHL morphology, as its detection may have important diagnostic and therapeutic implications.

P056: Predictive significance of immunohistochemistry in patients with Hodgkin's lymphoma on the size of the tumor mass and IPS score

Snezana Sretenovic¹, Danijela Jovanovic¹, Predrag Djurdjevic¹, Nikola Mirkovic²

¹University in Kragujevac, Faculty of Medical Sciences, Department of Internal Medicine, Kragujevac, Serbia¹, University Clinical Center, Hematology Clinic, Kragujevac, Serbia², ²University in Kragujevac, Faculty of Medical Science Department of Surgery Kragujevac, Serbia³

Introduction: Hodgkin's lymphoma (HL) is a rare neoplasm of the lymphatic system, it is one of the most common cancers in the young adult population.

Methodology: Retrospective analysis of 58 patients treated by M. Hodgkin from December 31. 2018. until 31.12.2023. and monitored until December 31. 2025. Including the newly diagnosed HL and excluding relapsing disease. The diagnosis was established by pathohistological analysis of the biopsied lymph gland, immunohistochemistry was performed with the original (DAKO, Glostrup, Denmark). For the level of expression, the limit value for positivity $>30\%$. Bulky disease, the size of the tumor mass is greater than 70 mm. Statistical analysis SPS 23.0, significance $p < 0.05$.

The aim of the work: To examine the predictability of the immunohistochemistry record on the size of the tumor mass and the correlation with the IPS score.

Results: Analysis of the association of immunohistochemistry markers with the presence of bulky disease revealed a statistically significant association for CD30 ($\chi^2 = 4.603$; $p = 0.032$), PAX5 ($\chi^2 = 4.261$; $p = 0.039$) and CD3 ($\chi^2 = 5.695$; $p = 0.017$). The marker CD5 showed borderline statistical significance ($\chi^2 = 3.521$; $p = 0.061$), but without sufficient statistical confirmation, while the other markers CD20, MUM1, CD15, Ki67, BCL2 and BCL6 did not show a statistically significant association with the bulky disease ($p > 0.05$) at the time of diagnosis. Analysis of the relationship between immunohistochemistry markers and the diameter of the tumor mass revealed a statistically significant for CD5 ($\chi^2 = 5.839$; $p = 0.016$) and CD15 ($\chi^2 = 4.766$; $p = 0.029$). In patients with CD5-, the maximum diameter of the

tumor mass was 37 mm, and in CD5+ it was 98 mm. An inverse association was observed for CD15, with CD15- the maximum diameter was 98 mm, and CD15+ was 43.5 mm. The other markers have no statistically significant association with the diameter of the tumor mass ($p > 0.05$). Analysis of the relationship between immunohistochemistry markers and the IPS score a statistically significant association was observed only for CD3 ($\chi^2 = 4.016$; $p = 0.045$). All patients with positive CD3 expression had a low IPS score (100%). Other markers did not show association with IPS score ($p > 0.05$).

Conclusion: Immunohistochemistry markers in the studied show selective significance. CD30, PAX5 and CD3 showed a correlation with the size of the tumor mass and they can be a predictor of tumor burden. Only CD 3 shows a correlation with IPS score.

P057: Baseline PET Radiomics for Risk Stratification in Classic Hodgkin Lymphoma

Andrew Heider¹, Ajay Subramanian¹, Veit Sandfort², Natalie Park¹, Lei Xing¹, Richard Hoppe¹, Ash A. Alizadeh³, Joseph Schroers-Martin³, Ranjana Advani³, Michael Binkley¹

¹Department of Radiation Oncology, Stanford University, ²Department of Radiology, Stanford University, ³Department of Medicine, Division of Oncology, Stanford University

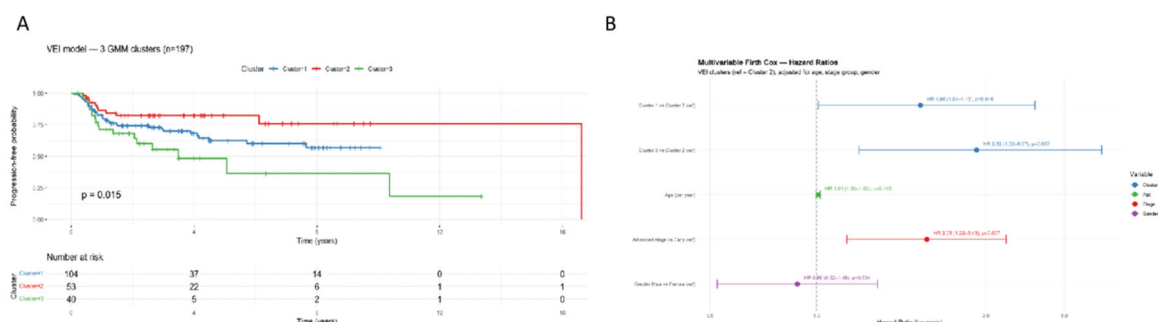


Figure 1: Freedom from progression analyses for PET-radiomic subgroups of patients with classic Hodgkin lymphoma.

Purpose: To identify distinct subgroups of patients with classic Hodgkin lymphoma (cHL) using unsupervised clustering of PET/CT-derived radiomic features, and to evaluate their prognostic associations with freedom from progression (FFP).

Methods: Baseline 18FDG PET/CT images were processed using an automated segmentation and PyRadiomics-based pipeline, extracting 1,316 features. Each feature was log transformed, z-score standardized, with a redundancy reduction correlation coefficient filter applied. Principal component analysis and a Gaussian mixture model (GMM) were used to assign radiomic clusters. Freedom from progression (FFP) was measured using Kaplan-Meier. A multivariable Firth-penalized Cox regression model was constructed using cluster membership after adjustments for age, stage, and sex.

Results: We identified 197 patients with cHL diagnosed at Stanford University between 2015–2024, with median age of 32 (range=6–79), 64.5% with early vs 35.5% with advanced stage, median IPS of 2, and median follow-up of 3.98 years. The GMM model partitioned into three radiomic clusters: RC1 (n = 104; 53%), RC2 (n = 53; 27%), and RC3 (n = 40; 20%). RC1 was defined by heterogeneous texture and low tumor volumes, RC2 by homogenous texture and low tumor volumes, and RC3 by heterogeneous texture and high tumor volumes. The 4-year FFP was 68.2%, 82.2%, and 48.4% for RC1, RC2, and RC3, respectively ($P = 0.015$). In a multivariable Cox model adjusted for age, stage, and sex, both RC1 (HR 1.96, 95% CI 1.01–4.13, $p = 0.046$) and RC3 (HR 2.82, 95% CI 1.32–6.37, $p = 0.007$) had higher risk of a PFS event relative to RC2. Posterior probabilities from the GMM clustering provided each patient with a continuous probability of belonging to each radiomic cluster. In time-dependent survival analyses and receiver-operator curves, a clinical-radiomic risk model incorporating these GMM posterior probabilities and 5-fold cross-validation trials (500 iterations) yielded high area under curve performance (AUC = 0.68 at 4 years), which outperformed total metabolic tumor volume alone (AUC = 0.61).

Conclusion: Unsupervised clustering of PET/CT-derived radiomic features can reproducibly identify three prognostically distinct cHL subgroups. These clusters capture significant FFP differences of these subgroups that remain independent of established clinical covariates including age, stage, and sex, suggesting that radiomic phenotyping may provide independent and complementary prognostic value.

P058: The TIGIT/CD155 Immune Checkpoint Axis in Classical Hodgkin Lymphoma: Clinical and Prognostic Implications

Ombretta Annibali^{1,2}, Teresa Marafioti^{3,4}, Valeria Tomarchio², Adheesh Ghosh³, Lara Antonelli², Muntasser Alsharabati⁴, Salvatore Iachino^{1,2}, Harriet Hunter⁴, Giulia Santoro^{1,2}, Sugerana Padmasri³, Antonella Bianchi⁵, Simona Spreafico³, Anna Crescenzi⁶, Luigi Rigacci^{1,2}

¹Hematology, stem cell transplantation, University Campus Bio Medico, ²Fondazione Policlinico Universitario Campus Bio medico, Roma, ³Department of Cancer Biology and Pathology, Cancer Institute, University College London, London, UK, ⁴Department of Cellular Pathology, University College London Hospitals NHS Foundation Trust, London, UK, ⁵Unit of Pathology, Fondazione Policlinico Universitario Campus Bio medico, Roma, ⁶Dept of Radiological, Oncological and Anatomic-Pathological Sciences, Sapienza University of Rome, Rome

Background: TIGIT (T-cell immunoreceptor with Ig and ITIM domains) is an inhibitory immune checkpoint receptor involved in tumor immune escape and T-cell exhaustion. Its main ligand, CD155, can be expressed by tumor cells and may contribute to suppression of the

anti-tumor immune response through activation of the TIGIT/CD155 axis. In classical Hodgkin lymphoma (cHL), the biological and prognostic significance of this pathway remains poorly defined. We retrospectively evaluated TIGIT expression by immunohistochemistry and its association with clinical characteristics, survival outcomes, and CD155 expression on Reed–Sternberg cells.

Methods: Eighty-six patients with cHL were retrospectively analyzed. TIGIT expression was assessed on diagnostic biopsy specimens by immunohistochemistry and dichotomized as negative (score 0) or positive (scores 1–3). Clinical data regarding treatment response and outcome were available for 66 patients, who constituted the cohort for clinicopathological and outcome analyses. Patients were additionally stratified according to age (<40 vs ≥40 years). Overall survival (OS) was defined as the time from diagnosis to death from any cause or last follow-up, while event-free survival (EFS) was defined as the time from diagnosis to relapse, progression, or death. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. Due to incomplete information regarding the timing of relapse or progression, survival analyses were evaluable in 62 patients. In a subset of 10 patients, CD155 expression on Reed–Sternberg cells was also evaluated.

Results: Among the 86 patients evaluated for TIGIT expression, 42 (48%) were TIGIT-positive and 44 (52%) were TIGIT-negative. Among the 66 patients with available clinical follow-up data, 35 (53%) were TIGIT-positive and 31 (47%) were TIGIT-negative.

Survival analysis was evaluable in 62 patients. With a median follow-up of 5.97 years, 7 deaths and 19 EFS events were observed. TIGIT expression was not significantly associated with stage, bulky disease, relapse, progression, or death. Likewise, no significant differences were observed in OS (log-rank $p = 0.419$) or EFS (log-rank $p = 0.292$) according to TIGIT status.

Patients aged ≥40 years accounted for 42 of the 66 cases, whereas 24 were younger than 40 years. TIGIT positivity was more frequently observed in older patients (61.9% vs 37.5%, $p = 0.075$), who also showed a higher prevalence of advanced-stage disease (61.9%).

P059: Secondary hemophagocytic lymphohistiocytosis after autologous HSCT: clinical vigilance in the absence of classical criteria

Elizaveta Kodrul¹, Stanislav Volchenkov², Larisa Filatova¹, Svetlana Elkhova², Ilya Zyuzgin²

¹FSBI «Petrov Research Institute of Oncology», ²FSBI «Petrov Research Institute of Oncology»

Background: Secondary hemophagocytic lymphohistiocytosis (sHLH) is a severe complication, predominantly associated with lymphomas, with <1% incidence post-HSCT. Neurological manifestations are rare and can mimic immune effector cell-associated neurotoxicity syndrome (ICANS).

Methods: A 35-year-old female with relapsed Hodgkin lymphoma achieved complete response after DHAP-Nivo and underwent autologous HSCT (auto-HSCT) with BeAM conditioning. The post-transplant course was complicated by sepsis and enterocolitis (days +4–+7). Neutrophil engraftment occurred on day +13, whereas platelet and erythroid lineages failed to recover. Initial sHLH workup showed normal LDH, triglycerides, and fibrinogen, ferritin 1500 ng/mL. CT showed no signs of localized infection or hepatosplenomegaly. The HLH-2004 score was 2 (low risk of sHLH).

On day +17, fever was 39°C, CRP and procalcitonin levels did not increase. CT scan revealed no foci of infection or other changes, myelogram showed a deficiency of megakaryocytic lineage, no phagocytes were detected. Blood PCR showed active HHV-6 infection, ganciclovir was prescribed. On day +18, the patient developed disorientation, along with impaired handwriting and memory. The ICE score was 7 (high risk of ICANS).

On day +18 disorientation, handwriting and memory impairment developed, with an ICE score of 7, high risk for ICANS. Blood tests revealed a ferritin level of 2500 ng/mL. MRI and lumbar puncture revealed no abnormalities. The HLH-2004 score was 3. From day +18 to day +24, neurological impairment did not progress, cytopenias and fever up to 39.3°C persisted. On day +25, HHV-6 was undetectable in the blood. On day 26, a bone marrow (BM) biopsy revealed hemophagocytosis and focal aplasia, increasing the HLH-2004 score to 4. Ruxolitinib was initiated 15 mg twice daily. During therapy the patient's dependence on transfusion support decreased, and the ICANS completely resolved.

Results: ICANS was the primary clinical manifestation of sHLH. Standard criteria and BM aspirate were uninformative; only BM trephine biopsy confirmed the diagnosis.

Conclusion: sHLH can present atypically as ICANS post auto-HSCT. BM biopsy is crucial when standard criteria are uninformative.

P060: Clinical relevance of serum TARC levels below 1000 pg/ml in Hodgkin lymphoma: a hidden biomarker?

Fanni Borics¹, Boglárka Dobó¹, Anita Gulyás¹, Dávid Tóthfalusi¹, László Imre Pinczés¹, Árpád Illés¹, Zsófia Miltényi¹

¹University of Debrecen Faculty of Medicine, Division of Haematology, Department of Internal Medicine

Background: Serum TARC (Thymus and Activation-Regulated Chemokine) is a specific biomarker for classical Hodgkin lymphoma (cHL), used to monitor tumor volume, clinical course and treatment response. Most clinical studies exclude patients with serum TARC levels below 1000 pg/mL at diagnosis. We aimed to analyse the clinical, histopathological and prognostic characteristics of this specific subgroup and compare them to cases with high (>1000 pg/mL) baseline serum TARC concentrations.

Methods: This retrospective study included 182 cHL patients diagnosed at our institute between 2010 and 2025 who had documented staging serum TARC results. The patterns of clinical stages, EORTC risk categories, and histological subtypes was analysed using Chi-square test. Overall survival (OS) and progression-free survival (PFS) were analysed using the Kaplan–Meier method, both in the total cohort and in subgroups categorized by age.

Results: Low TARC levels (<1000 pg/mL) were detected in 39 patients (21.4%), while 143 patients (78.6%) presented with high levels. The baseline TARC concentrations ranged from 34 to 476,000 pg/mL (median: 27,900 pg/mL). Highly significant correlations were observed between TARC distribution and clinical stages ($p < 0.001$), with low TARC being prominent in stage I and high TARC dominating in further (II–IV) stages. A significant correlation was also observed with EORTC risk categories ($p = 0.0139$), where the early favourable subgroup showed the highest prevalence of low TARC levels (43.4%). The distribution of histological subtypes significantly differed ($p < 0.0001$): the lymphocyte-rich subtype was predominant in the subgroup with low TARC levels, while a predominance of nodular sclerosis was observed at high serum levels. In the total

cohort, no significant differences were found in OS or PFS ($p = 0.75$ and $p = 0.547$). However, when analysed by age, patients under 60 years with low baseline TARC levels showed a significantly improved PFS compared to the high TARC group ($p = 0.048$). Conversely, no prognostic value was observed in patients over 60 years ($p = 0.939$).

Conclusion: Our findings confirm that the diagnostic value of serum TARC remains relevant below 1000 pg/mL, as it reflects tumor burden, risk stratification, and unique histopathological features. For patients under 60 years of age, low TARC levels at diagnosis can be an indicator of favourable prognosis. Therefore, integrating this commonly excluded subgroup into future studies is highly recommended.

P061: Familial Presentation of Classical Hodgkin Lymphoma in First-Degree Relatives

Boglárka Dobó^{1,2,3}, Dávid Tóthfalusi^{1,2,3}, Fanni Borics^{1,2,3}, László Imre Pinczés^{1,2,3}, Árpád Illés^{1,2,3}, Zsófia Miltényi^{1,2,3}

¹Division of Haematology, Department of Internal Medicine, Faculty of Medicine, University of Debrecen, 4032, Debrecen, Hungary, ²Doctoral School of Clinical Medicine, University of Debrecen, 4032, Debrecen, Hungary, ³Member of ERN-EuroBloodNet (European Reference Network on Rare Haematological Diseases)

Introduction: Hodgkin lymphoma (HL) is generally considered sporadic malignant lymphoproliferative disease, although familial aggregation has also been described. Several studies have demonstrated an elevated risk among first-degree relatives, suggesting a possible hereditary predisposition. Genetic susceptibility and shared environmental factors may both contribute to disease development.

Case presentation: A 38-year-old woman with a history of psoriasis was diagnosed with lymphocyte rich cHL in 2012. She received six cycles of ABVD followed by 36 Gy IFRT to the neck and mediastinum. Due to refractory disease, salvage DHAP chemotherapy and autologous stem cell transplantation (APSCT) were performed, resulting in complete metabolic remission (CMR) lasting more than 10 years. In 2024, she developed bilateral axillary lymphadenopathy and B symptoms. Histopathology confirmed diffuse large B-cell lymphoma (DLBCL). After 6 cycles of R-CHOP21 and consolidative ISRT, CMR was achieved. Shortly after the patient presented symmetrical lower-extremity paresis and secondary CNS involvement was confirmed by PET/CT, brain MRI and malignant B-cells were also identified in the cerebrospinal fluid. After R-MPV and IT therapy, imaging studies showed CMR. Urgent APSCT was performed. Unfortunately the patient died from multi organ failure due to an aggressive fungal infection.

Her daughter was diagnosed at the age of 20 after an incidental radiological finding following a household accident. Histology confirmed cHL nodular sclerosis subtype. Based on staging PET/CT, she was classified having advanced-stage (IV/BE) disease. Treatment was started with A+AVD and after 2 cycles the interim PET/CT showed CMR, then we followed with Nivolumab+AVD. Her treatment is ongoing and she is in good clinical condition.

Results: The occurrence of classical HL in a mother–daughter pair represents a rare example of familial aggregation. Despite differences in histological subtype and clinical course, the diagnosis of cHL in two first-degree relatives is notable given the predominantly sporadic nature of the disease. This observation is unlikely to be purely coincidental.

Conclusion: Although familial HL has been described, the development of subsequent DLBCL in one affected family member is particularly unusual and may indicate a broader inherited risk of lymphoid malignancies. Further genetic and molecular studies are needed to better understand the mechanisms underlying familial clustering.

P062: Correlating 18 FDG-PET/CT- and CT-derived Biomarkers to Neutrophil Extracellular Traps in Classical Hodgkin Lymphoma

Emma Pettersson¹, Alexander Korenyushkin², Ashish Chauhan³, Sambit Tarai³, Jeremia Collin¹, Rose-Marie Amini¹, Daniel Molin¹, Anna-Karin Olsson⁴, Håkan Ahlström^{2,3}, Joel Kullberg^{2,3}, Gunilla Enblad¹

¹Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden, ²Antaros Medical AB, Uppsala and Mölndal, Sweden, ³Department of Surgical Sciences, Radiology, Radiological Image Analysis, Uppsala University, Uppsala, Sweden, ⁴Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, Sweden

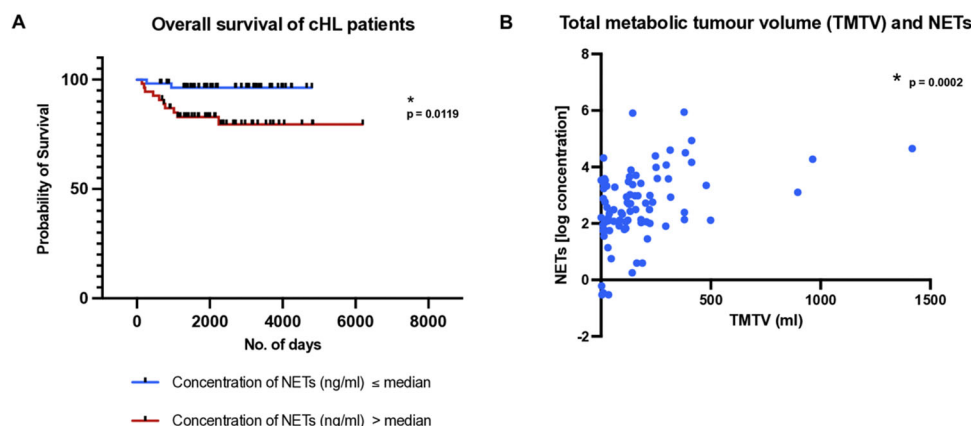


Figure 1: (A) Kaplan-Meier OS curves for cHL patients with plasma NET concentrations below versus above the median (log-rank test, $p = 0.0119$). (B) NET concentrations plotted against total metabolic tumour volume (simple linear regression, $p = 0.0002$).

Introduction: Accumulation of neutrophil extracellular traps (NETs), neutrophil-derived networks of decondensed chromatin and granule proteins, is associated to worse prognosis in many cancer types. To investigate their role in malignant lymphoma, we measured NETs in plasma in patients with classical Hodgkin lymphoma (cHL) and high-grade B-cell lymphomas (HGBCL) and found that NETs were associated with inflammation and worse patient outcome in univariate survival analyses. Here, the biology of NETs and inflammation in cHL was further explored using tumour and body composition data derived from 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18FDG-PET/CT) and CT scans.

Methods: NETs were measured in plasma taken at diagnosis in 113 cHL and 222 HGBCL patients from the Swedish U-CAN biobank with an ELISA targeting citrullinated histone complexes. Clinical data and routine blood counts at diagnosis were available for all included patients. Semi-automated tumour lesion segmentations of lesions with standardized uptake value (SUV) ≥ 4 were generated in 87 cHL baseline 18FDG-PET/CT scans, in order to extract data on total metabolic tumour volume (TMTV), maximum distance between tumour lesions (Dmax), maximum SUV (SUVmax) and lesion count. Furthermore, Body and Organ Analysis (BOA) was used on the corresponding CT scans to generate data on muscle mass and total (TAT) and visceral (VAT) adipose tissue volume.

Results: TMTV, Dmax and lesion count correlated positively to the plasma NET levels. Higher TMTV and SUVmax were associated with worse progression-free survival, with similar although non-significant trends for overall survival. Dmax and lesion count did not significantly correlate to patient outcome. No associations were observed between plasma NET levels and muscle mass, TAT or VAT. Other inflammatory blood counts investigated in the study also showed correlations to the 18FDG-PET/CT imaging biomarkers, but not to the muscle mass, TAT or VAT of the patients.

Conclusions: In cHL, NETs showed an association with 18FDG-PET/CT imaging biomarkers representing increased tumour burden and dissemination, but not with CT-based body composition parameters. These findings indicate that increased NET levels may reflect biological processes linked to tumour burden and tumour-induced inflammation, rather than chronic inflammation and alterations in the metabolic status of the patients. Additional patients will be included in the study.

P063: Genetic Clustering Reveals Biologic Similarities Across subgroups of Hodgkin Lymphoma, Primary Mediastinal Large B-Cell Lymphoma and Large B-Cell Lymphoma patients

Jon Felix Rischewski^{1,2}, Franziska Briest³, Julia Mattlener^{1,2,4}, Daniel Noerenberg³, Julia Katharina Schleifenbaum^{1,2,5}, Jessica Schneider^{1,2}, Sophie Heidenreich^{1,2,4}, Jan-Michel Heger^{1,2,5}, Frederik Damm^{3,6}, Sven Borchmann^{1,2,4,5}

¹Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD), University of Cologne, Faculty of Medicine and University Hospital of Cologne, Cologne, Germany, ²Cancer Center Cologne Essen (CCCE), Cologne and Essen, Germany, ³Department of Hematology, Oncology, and Cancer Immunology, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin Institute of Health, Berlin, Germany, ⁴German Hodgkin Study Group (GHSg), Cologne, Germany, ⁵Cologne Lymphoma Working Group (CLWG), Cologne, Germany, ⁶German Cancer Consortium, Partner Site, Berlin, Germany

Background: Primary mediastinal large B-cell lymphoma (PMBL) occupies a unique position in the spectrum of aggressive B-cell lymphomas, sharing molecular and clinical features with both Hodgkin lymphoma (HL) and diffuse large B-cell lymphoma (DLBCL) (Rosenwald et al., 2003; Savage et al., 2003; Savage, 2022; Duns et al., 2021). Here we use a data-driven approach integrating all three entities in a unified analytical framework to understand genetic similarities between subgroups of all three diseases.

Methods: Genetic alterations (SNPs, small InDels, CNVs) were assessed by circulating tumor DNA sequencing of HL patients at baseline and relapsed/refractory DLBCL patients. Genetic alterations of PMBL patients were analyzed by tissue DNA sequencing. Non-negative Matrix Factorization (NMF) clustering was used as the primary analytical framework.

Results: NMF clustering suggests that genetically coherent subgroups can be formed that are independent of disease entity. One cluster is defined by high weights for genes involved in JAK/STAT signaling and immune evasion, most prominently SOCS1, STAT6, B2M, TNFAIP3, NFKBIE, GNA13, ITPKB, CIITA, CD58, CD83, XPO1, and histone linker genes (HIST1H1B/C/E), and is strongly enriched for PMBL and HL cases. This signature aligns with constitutive NF- κ B and JAK/STAT activation, impaired MHC class I antigen presentation, and a pronounced immune privilege phenotype shared by PMBL and HL (Mottok et al., 2019). A second cluster is characterized by TP53, EZH2, FAT4, CREBBP, DDX3X, EP300, MYC, P2RY8, DTX1, and CD79A/B, a mutation-driven landscape more consistent with GCB-type DLBCL biology (Alizadeh et al., 2000; Li et al., 2018) although including some samples of all three disease entities.

Conclusion: Unsupervised genomic clustering across PMBL, HL, and DLBCL reveals biologically coherent subgroups transcending established diagnostic boundaries.

P064: Time-of-Day Immunotherapy Administration and Outcomes in Classic Hodgkin Lymphoma

Joseph Schroers-Martin¹, Anthony Yu¹, Austin Yeung¹, Chandley Silin², May Powell², Michael Binkley¹, Richard Hoppe¹, Ranjana Advani¹

¹Stanford University, ²Stanford Hospital & Clinics

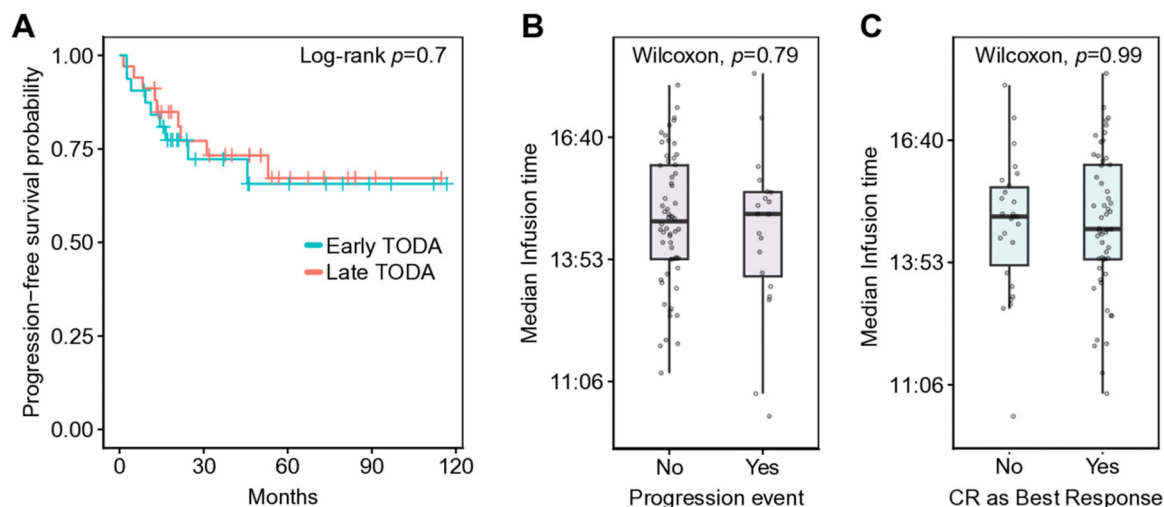


Figure 1: (A) KM curve demonstrates no difference for patients with majority early versus late time-of-day administration (TODA) of CPI infusions. Box plots demonstrate no difference in median TODA for patients with (B) progression or (C) CR as best response.

Introduction: Evidence in solid tumors suggests an association between earlier time of day administration of checkpoint inhibitor immunotherapy (TODA, CPI) and improved clinical outcomes, potentially driven by circadian immune variation. We hypothesized that a chronologic effect might be seen in classic Hodgkin lymphoma (cHL), where CPI are utilized in the frontline (1L) and relapsed/refractory (R/R) settings.

Methods: We included adult cHL patients who received CPI regimens at our institution with available infusion times and 1+ year of follow-up. N = 5 were excluded due to CPI discontinuation after first infusion due to immune-related adverse event. We categorized patients as early or late TODA if the majority of infusions occurred before or after the cohort median infusion time, and also evaluated common literature TODA thresholds of 13:00, 14:00, 16:00. Progression-free survival (PFS) was assessed via log-rank test, cross-group outcomes via Fisher's exact, and median infusion times via Wilcoxon rank-sum.

Results: Eighty patients were treated from 2016–2025 in the 1L (n = 23) or R/R (n = 57) settings, receiving total 568 infusions (median 4/pt) on clinical trial protocols (n = 47) or per standard of care (n = 33). Median age was 38 years (range 18 to >90), 48.8% female, and median follow-up was 29 months. 25% of patients had progression after CPI (n = 20). Most events occurred in R/R patients (n = 16) or 1L anthracycline-ineligible patients receiving BV-nivolumab (n = 3), and more frequently with age >60 years (p = 0.02).

The median infusion TODA was 14:48 (IQR 13:12–16:17). PFS was similar for patients with early versus late TODA, defined by either cohort median (Figure 1A) or literature thresholds. No significant difference was seen in median infusion TODA for patients with or without subsequent progression (Figure 1B) or complete radiographic response (Figure 1C). Progression was rare after CPI/chemotherapy for both 1L patients (1/18, 5.6%) and R/R patients who underwent ASCT (1/14, 7.1%).

Conclusions: In contrast to data in solid tumors, no clear chronologic effect on outcomes was observed in this single institution retrospective study. Given favorable outcomes in Hodgkin lymphoma as compared to solid tumors, particularly with combination CPI-chemotherapy, further investigation could focus on large multicenter cohorts in the R/R setting where event rates are higher.

P065: Redefining Hodgkin lymphoma pathogenesis: the central and indispensable role of CD4 T cells

Arjan Diepstra¹, Yajie Lei¹, Sophie Teesink¹, Wouter Plattel², Lydia Visser¹

¹Dept. of Pathology and Medical Biology, University Medical Center Groningen, the Netherlands, ²Dept. of Hematology, University Medical Center Groningen, the Netherlands

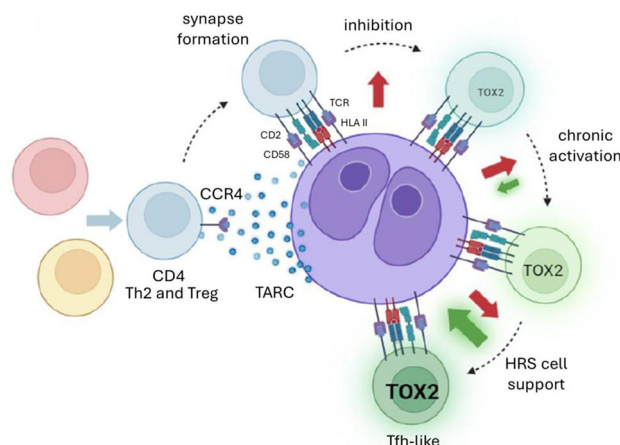


Figure 1: The central component of the pathogenic framework, supported by multiple studies (including PMIDs 37748137, 36345263, 32589698, and 35111387).

Background: Classic Hodgkin lymphoma (cHL) remains a biological paradox. A key conceptual puzzle is how the malignant Hodgkin Reed–Sternberg (HRS) cells manage to survive and thrive within a massive tumor microenvironment (TME) dominated by immune cells. Although mechanisms of immune evasion have been extensively explored, the active supportive functions of the TME are less widely recognized. CD4 T cells are particularly intriguing in this context, as they are consistently abundant and form intimate, often rosette-like contacts with HRS cells. Here, we propose a unifying pathogenetic framework that links these interactions to the origin, evolution, and diagnostic hallmarks of cHL.

Methods: We developed an integrative conceptual framework centered on the interaction between CD4 T cells and HRS cells, based on evidence from in vitro coculture systems, gene expression analyses, immunohistochemistry and established immunology principles.

Results: Our framework highlights that HRS cells produce exceptionally high levels of the chemokine TARC (CCL17), which begins to rise already years before diagnosis and selectively recruits Th2 and regulatory T cells (see figure). The recruited CD4 T cells establish immunological synapses with HRS cells through HLA class II and CD58 mediated interactions. However, the T cells do not become fully activated and the HRS cells deliberately orchestrate a chronic state of intermediate T-cell activation, marked by low-level expression of immune checkpoint molecules and the transcription factor TOX2. Remarkably, this phenotype resembles early commitment toward the T follicular helper (Tfh) lineage which can explain strong support of HRS cells at diagnosis. It also links the cHL immune landscape to the germinal center (GC) niche from which HRS cells arise. Within this niche, GC B cells depend on strong Tfh cell derived survival signals to escape from apoptosis. Disruption of this tightly controlled system may enable the accumulation of genetic aberrations and facilitate the earliest steps of lymphoma development within GCs.

Conclusions: We propose that the core biology of cHL is built on functional units composed of malignant B cells and cooperating CD4 T cells. Within this unit, GC B cells acquire the capacity to recruit and modulate CD4 T cells through TARC production and controlled chronic activation, thereby securing Tfh-like support signals that promote their survival, growth and malignant transformation.

P066: The Role of CD59 in Mediating T Cell Rosette Formation in Classic Hodgkin Lymphoma

Yajie Lei¹, Rodrigo Martinez Alcala¹, Annika Seitz¹, Lydia Visser¹, Arjan Diepstra¹

¹University medical center Groningen

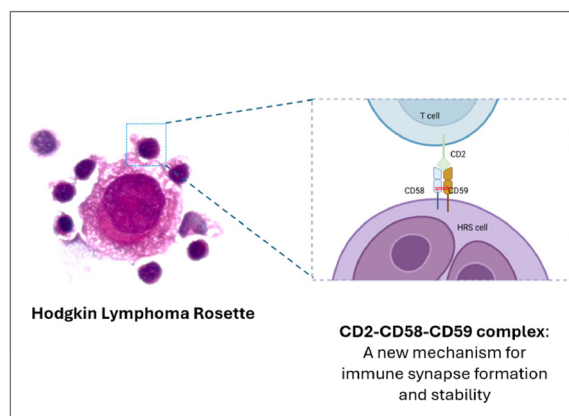


Figure 1: CD2-CD59 interaction is involved in the generation of rosettes in HL and enhances immunological synapse formation in conjunction with CD2 and CD58. The CD2-CD58-CD59 interaction is a new immunoregulatory mechanism that contributes to HL pathogenesis.

The tumor cells in classic Hodgkin lymphoma (HL) are surrounded by CD4⁺T-cell rosettes that provide support and form a physical shield against anti-tumor immune responses. To study the mechanisms behind rosette formation, we previously developed an in vitro co-culture model and found that CD2-CD58 interactions increase rosetting and activation of CD4⁺T cells. In the current study, we explore the role of CD59, an alternative CD2 ligand, in rosetting. In 45/62 diagnostic cases, tumor cells showed increased expression of CD59. HL cell lines L428 (CD58⁺/CD59⁺), L1236 (CD58⁺/CD59⁻) and KMH2 (CD58⁻/CD59⁺) and peripheral blood mononuclear cells (PBMCs) from healthy donors were co-cultured. After 30 minutes, L428 showed the highest percentage of rosette formation, followed by L1236 and KMH2, respectively. Accordingly, the production of IL-2 after 24 hours, as a marker of T cell activation, showed the same pattern. CD59 knockout in L428 reduced the rosette formation, strongly indicating that CD59 expression is involved. During rosette formation, CD58 firstly redistributed along the HRS cell membrane towards the T cell interaction site, and CD59 followed CD58 to the same sites within 30 minutes. Proximity ligation assays showed that the CD58-CD59 interaction was only present at the interface between tumor cells and T cells. There were more CD2-CD58 signals in L428 than in L1236, while CD2-CD59 signals were present in L428 and missing in KMH2. In conclusion, CD59 expression is upregulated by tumor cells and helps to enhance the interaction between CD58 and CD2 during the formation of rosettes in HL.

P067: Fragmentomics analysis to enhance ctDNA based risk stratification in Hodgkin Lymphoma

Jessica Schneider¹, Julia Mattlener¹, Sophie Heidenreich¹, Julia Katharina Schleifenbaum¹, Max Freihammer¹, Daniel Schütte¹, Peter Borchmann¹, Phillip Gödel¹, Hyatt Balke-Want¹, Christian Reinhardt², Bastian Von Tresckow², Roland Schwarz³, Jan-Michel Heger¹, Sven Borchmann¹

¹Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD), University of Cologne, Faculty of Medicine and University Hospital of Cologne, Cologne, Germany, ²Department of Hematology and Stem Cell Transplantation, West German Cancer Center and German Cancer consortium (DKTK partner site Essen), University Hospital Essen, University of Duisburg-Essen, Essen, Germany, ³Institute for Computational Cancer Biology (ICCB), Center for Integrated Oncology, University of Cologne, Faculty of Medicine and University Hospital of Cologne, Germany

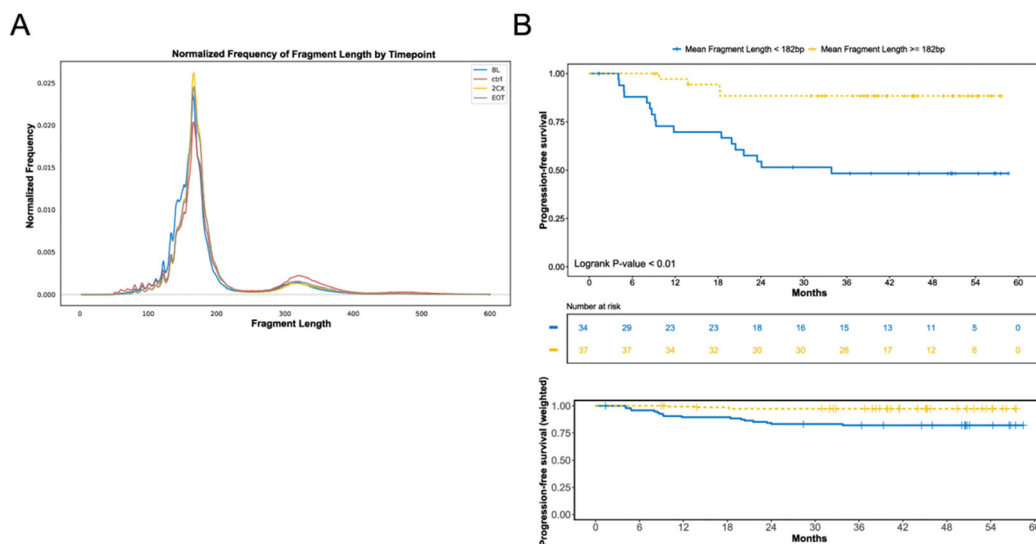


Figure 1: (A) Size profile of HL samples before treatment start (blue; BL), after two cycles of therapy (yellow, 2CX) as well as healthy controls (red, ctrl). (B) Kaplan-Meier curve of start of therapy samples stratified by mean fragment length.

Background: Current clinical challenges in Hodgkin lymphoma (HL) include long-term treatment-related toxicities and relapsed/refractory disease. Up to now, risk stratification tools mainly rely on clinical characteristics and lack sensitivity. Recent studies, including ours, demonstrated that circulating tumor (ct)DNA sequencing offers the potential to overcome this limitation.

Aims: We aim to increase the sensitivity to distinguish tumor (ctDNA) from non-tumor derived cell-free (cf)DNA and thus refine detection of minimal residual disease (MRD) (Sobesky, Med, 2021; Heger, J Clin Oncol, 2024; Heger, Blood, 2026) by incorporating fragmentomics analysis.

Methods: We developed a software tool to extract advanced fragmentomics data at the read level and incorporate mutational information. The tool was applied to 154 plasma samples from 71 patients with previously untreated HL (sampled from the HD21 trial) and 10 healthy controls.

Results: We found significant differences in cell-free DNA fragment length distribution between pre-treatment HL samples and healthy controls (mean 180 vs. 200 bp, Mann-Whitney U test, $p < 0.01$). Interestingly, fragment length increased with more treatment applied, ultimately approximating healthy controls (healthy control=200 bp; pre-treatment=180 bp; mid-treatment=185 bp; end-of-treatment=187 bp). Not only is this shift noticeable for the mean fragment length but it is also independently present for the peak corresponding to mono-nucleosomal length as well as the second peak (corresponding to di-nucleosomal length) when comparing HL samples (Figure 1 (A), pre-treatment (blue; BL), mid-treatment (yellow; 2CX), and end-of-treatment (grey; EOT)) to healthy controls (red; ctrl).

We found that shorter mean fragment length (<182 bp) in pre-treatment HL samples was associated with shorter progression free survival (PFS) (Logrank P-value < 0.01).

Further results will be presented at the meeting.

Conclusion: Fragmentomics analysis in our HL cohort showed shorter mean pre-treatment fragment length compared to healthy controls, with shorter mean length associated with inferior PFS. These findings suggest a potential use of fragment size and other fragmentomic features for dynamic risk stratification in patients with HL.

P068: Plasma Proteomic Profiling of Classical Hodgkin Lymphoma

Ragnhild Risebro¹, Jeremia Collin¹, Johan Mattsson Ulfstedt¹, Emma Pettersson¹, Mats Hellström¹, Ingrid Glimelius¹, Mattias Berglund¹, Gunilla Enblad¹, Eva Freyhult², Daniel Molin¹

¹Department of Immunology, Genetics, and Pathology, Uppsala University, Uppsala, Sweden, ²Department of Cell and Molecular Biology, National Bioinformatics Infrastructure Sweden, Science for Life Laboratory, Uppsala University, Uppsala, Sweden

Background: The proteomic landscape of classical Hodgkin lymphoma (cHL) remains incompletely explored. Plasma proteomics may provide insight into disease biology, diagnosis, and prognosis. Using Olink protein panels, we performed large-scale analysis of protein expression in plasma from cHL patients and healthy controls (HC). Additionally, cHL is often accompanied by systemic inflammation, including elevated erythrocyte sedimentation rate (ESR) and B-symptoms, though not all patients present with these features. Inflammatory response does not uniformly correlate with tumor stage, with discordant cases occurring in both directions. Hence, the inflammatory proteomic profile in cHL was also investigated.

Aims: This study aims to characterize the plasma proteomic profile of cHL in comparison with HC and identify protein patterns associated with the presence or absence of an inflammatory response.

Methods: The plasma proteome (1443 proteins) from 115 cHL patients and 122 HC was compared using age- and sex-adjusted linear regression with multiple testing correction. Inflammatory ($n = 77$) and non-inflammatory ($n = 38$) subtypes were defined by elevated ESR. Inflammatory group differences were assessed using estimated marginal means and partial least squares discriminant analysis. Selected findings will be validated by ELISA.

Results: The results revealed 675 significantly differentially expressed proteins in cHL plasma. Beyond established markers such as TARC, PD1, PDL1, and CD30, we identified VWF and ATP5IF1 as markedly elevated across the cohort, while the suggested tumor suppressor protein CRTAC1 was reduced compared to HC. The inflammatory subtype was characterized by increased expression of many immune mediators, among them proteins associated with an antibacterial response, including LBP, CD14, DEFA1_DEFA1B, and PLA2G2A. In contrast, the non-inflammatory subtype showed higher expression of immune suppressive proteins VTCN1, CD83, FASLG, and PLA2G7. ELISA results will be ready before the conference.

Conclusions: Large-scale proteomic analysis revealed pronounced alterations in the plasma proteome of cHL compared to HC. This study confirms known cHL markers, while also identifying novel findings. Furthermore, the two inflammatory states show distinct differences in plasma proteome expression. The inflammatory subtype is characterized by elevation of antibacterial-associated proteins, while the non-inflammatory subtype displays a more immunosuppressive profile.

P069: Analysis of circulating tumor DNA shows Epstein-Barr virus associated differences of mutagenic processes in classical Hodgkin lymphoma

Kristyna Kupcova¹, Lubica Gaherova², Adriana Velasova¹, Maria Maco², Iva Hamova³, Petr Nehasil⁴, Petra Zemankova⁴, Pavla Stepankova⁵, Alexandra Kredatusova⁶, Jana Markova², Blanka Vackova⁷, Jan Koren⁷, Alice Sykorova⁵, Vit Prochazka⁶, Tomas Kozak², Heidi Mocikova², Ondrej Havranek³

¹BIOCEV, First Faculty of Medicine, Charles University, Prague, Czech Republic, ²Department of Haematology, Fakultni nemocnice Kralovske Vinohrady and Third Faculty of Medicine, Charles University, Prague, Czech Republic, ³BIOCEV and First Dept. of Internal Medicine- Hematology, First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic, ⁴Institute of Medical Biochemistry and Laboratory Diagnostics, First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic, ⁵5th Department of Internal Medicine, University Hospital and Faculty of Medicine - Hematology, Hradec Kralove, Czech Republic, ⁶Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacky University and University Hospital, Olomouc, Czech Republic, ⁷First Dept. of Internal Medicine- Hematology, General University Hospital in Prague and First Faculty of Medicine, Charles University, Prague, Czech Republic

Background: About 30% of classical Hodgkin lymphomas (cHL) are associated with EBV (Epstein-Barr virus) infection. However, it is not fully understood how EBV positivity affects genetic profile of cHL and associated characteristics of circulating tumor DNA (ctDNA).

Methods: We prospectively analyzed pre-treatment plasma samples of 140 patients with cHL using Cancer Personalized Profiling by deep Sequencing (CAPP-Seq) and Clinical Lymphoma Exploration and Research Sequencing (CLEARs) panel (521 genes). COSMIC (Catalogue of Somatic Mutations in Cancer) mutational signatures were detected by SigProfiler. EBV status was determined by immunohistochemistry (LMP1), ISH (EBER), or qPCR (peripheral EBV DNA).

Results: Among 140 analyzed cHL patients, the median age at diagnosis was 39 years (range 19–77); the most frequent histological subtype was nodular sclerosis (64.7%; mixed cellularity - 28.7%; lymphocyte rich - 6.6%); most patients had advanced GHSG (German Hodgkin Study Group) clinical stage (70.1%; intermediate stage - 16.7%, early stage - 12.7%); 24% of patients were EBV positive. Advanced GHSG stage was associated with higher levels of pre-treatment ctDNA in comparison to patients with intermediate/early stages (18.4 vs. 8.1 ng/mL, respectively; $P < 0.001$). EBV positivity was associated with lower tumor mutational burden (median TMB 6.07 vs. 10.0 mut/Mb; $P = 0.03$) and a trend towards higher ctDNA concentration (mean 2.3 vs. 1.7 ng/mL; $P = 0.13$). Importantly, EBV+ tumors were largely missing alterations in several critical genes most frequently (20% of cases) altered in EBV- cases, namely in TNFAIP3 and NFKBIE (negative regulators of NF κ B signaling) and in ITPKB (a negative regulator of PI3K/AKT signaling). Other cHL driver genes were altered in EBV+ and EBV- cHL tumors at similar frequencies (e.g., SOCS1, HLA-B, GNA13, or KMT2C). Based on identified mutagenic processes, EBV- cHL tumors showed higher contribution of activation induced cytidine deaminase (AID) and had evidence of mismatch repair deficiency (MMRD, which was missing in EBV+ tumors).

Conclusion: EBV positivity and related expression of viral proteins (e.g. LMP1) seems to trigger similar cellular signaling as alterations of several key driver genes in EBV- cHL. Consequently, EBV+ tumors need lower number of additional mutations and EBV- cHL is associated with other mutagenic processes, as are AID activity and MMRD.

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P070: Kinetics of PD-1 Blockade on Circulating CD8+ T Cells After Exposure to low-dose Nivolumab

Anu Korula¹, Phaneendra Datari¹, Arunkumar Arunachalam¹, Vikram Mathews¹

¹Department of Haematology, Christian Medical College Vellore

Introduction: Low-dose (40 mg) nivolumab results in near-complete saturation of PD-1 receptors on circulating T cells, suggesting that current dosing schedules may exceed the biological requirements for effective target engagement in classical Hodgkin lymphoma (cHL). Here we evaluate the durability of PD-1 receptor occupancy (RO) following treatment cessation in patients enrolled in an ongoing trial of low-dose nivolumab in advanced-stage cHL.

Methods: Peripheral blood samples were collected at baseline, immediately following nivolumab infusion, and at 2-week intervals following the final nivolumab dose up to 12 weeks. PD-1 RO on circulating T cells was assessed using a standardized flow cytometry-based assay.

Results: Between August 2024 and January 2026, 44 patients were enrolled onto the nivolumab arm, of whom 34 completed all four planned doses and had at least one follow-up sample available for analysis. At baseline, the PD-1 expression on circulating CD8+T cells was 44.2% (range 10.5–85.8%). One hour after nivolumab infusion, median PD-1 RO was 99.7% (IQR 97.3–99.95%). Five patients (18.5%) demonstrated <90% RO including one patient with occupancy of only 44.3%.

Following the final nivolumab dose, RO remained high at week 2, with a median occupancy of 99.8% (IQR 97.3–99.9%); however, 4/34 patients (11.8%) demonstrated RO < 90%. At 12 weeks following the final infusion, median RO remained 99.9% (IQR 95.5–99.9%), with 4/28 evaluable patients (14.3%) demonstrating occupancy <90%. Thus, near-complete PD-1 RO was maintained in most patients for up to 12 weeks following the last dose of nivolumab.

Among 29 patients who completed 6 cycles of therapy, one had progressive disease at end-of-treatment and three relapsed within one year. No clear association was observed between RO and remission status. Three of four patients with subsequent progression or relapse maintained near-complete RO throughout the 12 week period of testing, while several patients with occupancy <90% remained in remission.

Conclusions: PD-1 RO remained near-complete for up to 12 weeks post-nivolumab, indicating prolonged target engagement after low-dose nivolumab. Current 2-weekly dosing intervals may therefore exceed the biological requirements for sustained target engagement. The lack of an apparent association between RO persistence and clinical outcome suggests that receptor saturation alone may be an insufficient biomarker of therapeutic efficacy.

Children and adolescents

T071: The Genomic Landscape of Pediatric High-Risk Hodgkin Lymphoma: A Liquid Biopsy Study of COG AHOD1331

Shuyu Shi¹, Lianna J. Marks², Hrishikesh K. Srinagesh³, Lena Osswald³, Stefan K. Alig⁴, Ragini Adams², Maya Strohsband³, Xiaoman Kang³, Mari N. Olsen³, Chih Long Liu³, Lindsay A. Renfro⁵, Lisa Giulino-Roth⁶, Kara M. Kelly⁷, Tyler J. Bradshaw⁸, Maximilian Diehn⁹, Steve Yoon-Ho Cho^{10,11}, Sharon M. Castellino¹², Ash A. Alizadeh³

¹Department of Bioengineering, Stanford University, Stanford, CA, USA, ²Department of Pediatrics, Stanford University, Stanford, CA, USA, ³Department of Medicine, Stanford University, Stanford, CA, USA, ⁴Department of Hematology and Stem Cell Transplantation, University Hospital Essen, Essen, Germany, ⁵Division of Biostatistics,

University of Southern California and Children's Oncology Group, Los Angeles, CA, USA, ⁶Department of Pediatrics, NYU Grossman School of Medicine, New York, NY, USA, ⁷Roswell Park Comprehensive Cancer Center/Department of Pediatrics, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY, USA, ⁸Department of Radiology, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, ⁹Department of Radiation Oncology, Stanford University, Stanford, CA, USA, ¹⁰Department of Radiology, University of Wisconsin School of Medicine, Madison, WI, USA, ¹¹University of Wisconsin Carbone Comprehensive Cancer Center, Madison, WI, USA, ¹²Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta/Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA

Noninvasive genomic profiling of pediatric cHL in AHOD1331 using ctDNA

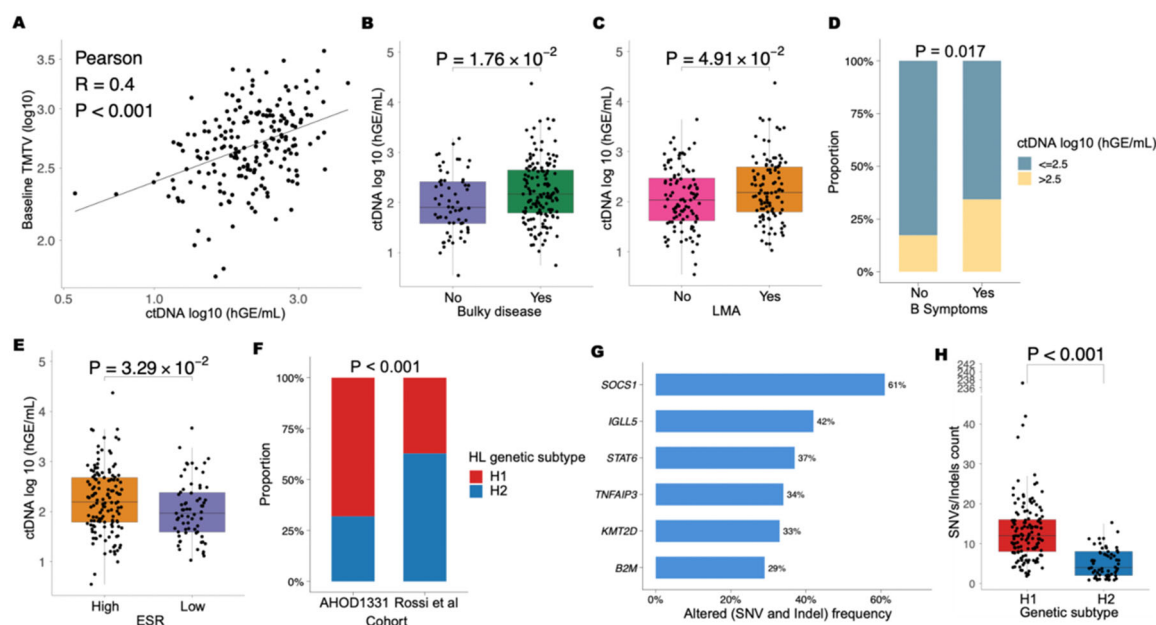


Figure 1: Pretreatment ctDNA levels significantly associated with (A) TMTV (B) bulk (C) LMA (D) B-symptoms (E) ESR. (F) Prevalence of genetic subtype H1 higher in peds vs adult. (G) Most recurrently altered genes. (H) Higher SNV/Indel counts observed in H1 vs H2.

Background: Pediatric classic Hodgkin lymphoma (cHL) has excellent survival, yet risk stratification relies on baseline clinical and imaging features that incompletely capture disease biology. We hypothesized that circulating tumor DNA (ctDNA) level and derived genomic subtypes, defined at baseline before therapy, are associated with disease burden, and could inform risk.

Methods: We studied patients ≥ 2 -<22 years with newly diagnosed high-risk cHL enrolled in COG study AHOD1331 with available blood specimens. Baseline plasma was profiled using CAPP-Seq to detect tumor-derived somatic mutations and quantify ctDNA levels. Baseline ctDNA was dichotomized into high vs low levels using a previously defined threshold (2.5log10 hGE/mL) and classified into genomic subtypes (H1 and H2) using an established algorithm (Alig et al, Nature 2024). Univariate associations between genomic subtype, somatic mutation features, and clinical characteristics including age, stage, and centrally reviewed PET-derived total metabolic tumor volume [TMTV] were evaluated.

Results: 323 patients (55%) from the eligible trial cohort had evaluable samples, with median age of 15.7 years (range 3.4–22), 54% male, and stage distribution representative of the overall trial (20.1% bulky IIB, 21.4% IIIB, 28.8% IVA, 29.7% IVB; $p = 0.86$). All patients (100%) had detectable ctDNA at baseline, varying across a broad range (4–23622 hGE/mL, median 129 hGE/mL). Higher pretreatment ctDNA levels were significantly associated with higher TMTV ($P < 0.001$, Figure 1A), bulky disease ($P = 0.018$, Figure 1B), large mediastinal adenopathy (LMA; $P < 0.05$, Figure 1C), B-symptoms ($P = 0.017$, Figure 1D), and erythrocyte sedimentation rate (ESR; $P < 0.05$, Figure 1E).

Children had significant enrichment of H1 subtype (68.1% in AHOD1331) when compared to adults older than 60 (37.2% in Rossi et al ICML2025, $p < 0.001$, Figure 1F). H1 tumors harbored significantly higher somatic SNV/Indel counts than H2 counterparts ($p < 0.001$, Figure 1H). Key genetic alterations had expected recurrence frequencies (Figure 1G).

Conclusion: In the largest genomic study of pediatric cHL to date, we establish the universal detection of baseline ctDNA and enrichment of H1 subtype. We confirm significant associations with key clinical indicators of tumor burden, including baseline TMTV, known to be significantly associated with EFS in this trial. Ongoing analyses of ctDNA at interim and end of therapy are being used to develop a dynamic radiogenomic risk prediction model.

T072: Body-Size Normalisation of Metabolic Tumour Volume in Paediatric Hodgkin Lymphoma: Does MTV/BSA Improve Prognostic Stratification and Reclassify Smaller Children?

Claire Gowdy¹, Caron Strahlendorf¹, Andrea C. Lo¹, Yvonne Mbithi¹, Carlos Uribe², Arman Rahmim³, Fereshteh Yousefirizi⁴

¹BC Children's Hospital, ²BC Cancer, ³University of British Columbia, ⁴BC Cancer Research Institute

Table 1. Prognostic performance of baseline metabolic tumour burden metrics and body surface area (BSA)-normalised counterparts for predicting progression-free survival (PFS) in paediatric Hodgkin lymphoma.

Feature	AUC	Cut-off	Sens.	Spec.	HR (1 SD)	p
Raw MTV (mL)	0.710	501.5 mL	90%	56%	1.57	0.043*
MTV / BSA (mL/m ²)	0.673	297 mL/m ²	89%	58%	1.31	0.301
Raw TLG	0.746	947	100%	49%	1.75	0.014*
TLG / BSA	0.710	496	100%	44%	1.54	0.081
BSA alone (m ²)	0.707	1.69 m ²	100%	44%	1.37	0.164

* $p < 0.05$. HR per 1 SD. Green = significant; Orange = BSA-normalised counterpart. $n = 45$ for MTV/BSA; $n = 49-55$ for raw features.

Table 1: Prognostic performance of baseline metabolic tumour burden metrics and body surface area (BSA)-normalised counterparts for predicting progression-free survival (PFS) in paediatric Hodgkin lymphoma.

Background: In paediatric Hodgkin lymphoma (HL), total metabolic tumour volume (MTV) is an established prognostic biomarker, yet published cut-offs apply a single absolute threshold regardless of body size. A 400 mL tumour represents greater relative burden in a 7-year-old (BSA 1.0 m²) than a 17-year-old (BSA 2.0 m²). We investigated whether normalising MTV by body surface area (MTV/BSA) improves prognostic performance and reclassifies smaller children into higher risk groups.

Methods: Sixty-one paediatric HL patients (BC Children's Hospital, 2014–2023; median age 15.6 y, range 7.2–19.5) were included. MTV and TLG were extracted from baseline FDG-PET/CT using an IBSI-compliant pipeline. BSA was available in 55/61 patients. Normalised metrics (MTV/BSA, TLG/BSA) were compared with raw values using ROC analysis, Youden-index cut-offs, Cox regression (HR per 1 SD), and Kaplan–Meier analysis. Reclassification analysis identified patients changing risk categories when MTV/BSA replaced raw MTV. Endpoint: PFS (13/61 events [21%]; median follow-up 4.7 years).

Results: BSA correlated weakly but significantly with raw MTV (Spearman $r = 0.33$; $p = 0.026$). Despite this, MTV/BSA did not improve prognostic performance (AUC 0.673 vs 0.710; HR 1.31; $p = 0.301$; see Table 1). TLG was the strongest predictor (AUC 0.746; HR 1.75; $p = 0.014$) and was not improved by normalisation (TLG/BSA: AUC 0.710; $p = 0.081$). BSA alone showed moderate prognostic value (AUC 0.707; $p = 0.164$); progressors had higher median BSA than non-progressors (1.89 vs 1.73 m²). Reclassification analysis ($n = 45$) showed 3/45 patients (7%) changed risk group as derived statistically: 1 upstaged (MTV 405 mL, BSA 1.30 m², age 16.6 y; no progression) and 2 downstaged (BSA ≥ 2.44 m²; no progression). No progressing patient was reclassified.

Conclusion: In this adolescent-predominant cohort (age 7–19 y), BSA normalisation of MTV did not improve prognostic discrimination and produced clinically minimal reclassification (3/45 patients; no progressor reclassified). Raw TLG outperformed all normalised metrics. These findings suggest that for the typical paediatric HL age range, absolute volumetric burden is an adequate prognostic surrogate without body-size correction. However, a reclassification signal was observed in one patient with small habitus (BSA 1.30 m²), supporting prospective evaluation in young children (≤ 10 years) with wider BSA variation.

P073: Outcomes of Pediatric Hodgkin Lymphoma Patients treated with ABVD Regimen. A retrospective Cohort Study

Hany Abdel Rahman¹, Emad Moussa², Mohamed Sedky³, Nesreen Ali¹, Walaa El Sayed¹, Maram Farouk⁴, Sally Talaat¹, Hanaa Rashad⁴, Eman Khorsheed⁵, Mohamed Saad Zaghloul⁶, Esraa Roshdy⁷, Madeha El Wakeel⁸

¹Department of Pediatric Oncology, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt, ²Department of Clinical Oncology, Monoufeyah University, and Children Cancer Hospital Egypt, ³Department of Pediatrics, National Research Center, and Children Cancer Hospital Egypt, ⁴Department of Pediatric Oncology, Children Cancer Hospital Egypt, ⁵Department of Pathology, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt, ⁶Department of Radiation Oncology, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt, ⁷Department of Nuclear medicine and Radiation Oncology, South Egypt Cancer Institute, Assiut university, and Children Cancer Hospital Egypt, ⁸Department of Radio-diagnosis, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt

Background: Hodgkin lymphoma (HL) a highly curable malignancy has a peak incidence in adolescent and young adults. Chemotherapy regimen ABVD and involved field radiotherapy (IFRT) is the gold-standard treatment for early and advanced stages of HL in adults.

Aim of the study

To analyze data of patients who received first line chemotherapy ABVD and IFRT at the Children Cancer Hospital Egypt 57357 (CCHE) over 12 years period.

Methodology: A retrospective analysis including all patients, <18 years, diagnosed and treated as classic HL during the period from 2007–2019. Patients were stratified as low (stage IA/IB/IIA with ESR < 30 and without bulky disease), intermediate (stage IEA/IEB/IIA/IIIA with ESR ≥ 30 or with bulky disease), and high risk (stage IIBE/IIIAE/IIIB/IV) disease. Chemotherapy consisted of 4 cycles for low, and 6 for intermediate and high risk patients, followed by IFRT total dose 1,980 Gy. The median follow up period was 105 months (range 6–217 months).

Results: This study included 1378 patients. Their median age was 9.3 years. The majority (70%) were from 5–15 years. There was a strong male predominance accounting for 72%. The most common pathologic subtype was nodular sclerosis (54%), followed by mixed cellularity (38%). Stage 2A was the most common (31%). Low risk patients were the most common (46%), followed by high risk (31%). Two hundred thirteen patients (15.4%) had relapse (187, 13.5%) or refractory (26, 0.18%) disease. Following salvage chemotherapy, 123 (8.9%) patients received a hematopoietic stem cell transplant (HSCT), mainly (98%) autologous. The 5 years overall survival (OS) for the entire cohort was 95.3% (95% CI 94.2%–96.4%), while the 5 years progression free survival (PFS) probability was 86.7% (95% CI 84.9%–88.5%). The 5 years PFS for low risk group was 94.2%, compared to 86.8% for intermediate risk and 75.6% for high risk patients ($P < 0.001$). Second malignant neoplasm (SMN) was detected in 31 patients (0.22) mainly cancer thyroid (58%). One hundred patients (7.2%) died, mainly from disease progression including 28 post HSCT and 6 post SMN.

Summary and conclusion: ABVD regimen at our institution has an excellent outcome. late effects of therapy, include an elevated risk for SMN, cardio toxicity, pulmonary toxicity, and endocrine dysfunction. Recently, new treatment strategies have been developed to balance the intensity of therapy needed to maintain disease-free survival while simultaneously preserving overall survival.

P074: Outcomes of Second-Line EuroNet Salvage Regimens in Pediatric Patients with Relapsed and Primary Refractory Hodgkin Lymphoma

Emad Moussa¹, Sara Badawy², Asmaa Hamouda³, Asmaa Attia³, Sally Talaat³, Hany Abdelrahman¹, Nesreen Ali³, Mohamed Sedqy¹, Nashwa Ezz El Din³, Walaa El Sayed³, Maram Farouk³, Mona Fakhry³, Ebtihal Shoukry³, Yassin Taher³, Amr El Nashaar², Mohamed Saad Zaghloul⁴, Eman Naguib⁵, Esraa Roushdy⁶, Madeha El Wakeel⁷, Reham Abdelaziz³, Alaa El Haddad¹

¹senior consultant PHO-Children's cancer hospital Egypt, ²CRA Children's Cancer hospital Egypt, ³consultant PHO Children's Cancer Hospital Egypt, ⁴Senior Consultant radiation therapy Children's Cancer hospital, ⁵Senior consultant Pathology Children's Cancer hospital, ⁶consultant Nuclear Medicine Children's Cancer hospital, ⁷consultant Radiology, Children's Cancer hospital

Background: Since EuroNet-PHL-C1 protocols are standard but real-world data on salvage outcomes in resource-limited settings are scanty. The majority of patients with Hodgkin's lymphoma (HL) are cured with first-line therapy; however, approximately 15%–25% of patients relapse or become refractory. The importance of chemosensitivity, stage at relapse, time to relapse, and the type of response after salvage chemotherapy and before HDT/ASCT in predicting outcome has been stated in several studies.

Aim: We aim in this study to evaluate the response rates and survival outcomes (PFS/OS) of pediatric patients treated with EuroNet-PHL salvage regimens, and to test the efficacy of IGEV and IEP/ABVD regimens in a large cohort of pediatric Hodgkin lymphoma patients.

Methodology: A retrospective review was conducted on 79 cases of patients between 2019 and 2023 having a relapsed or primary refractory cHL treated at the Children Cancer Hospital of Egypt. Patients were given the EuroNet-PHL recommended salvage regimens such as IGEV or IEP/ABVD regimens. PET-CT using Lugano 2014 criteria, assessed the response after two cycles of chemotherapy.

Result: The 3-year OS was 73.4%. However, PFS at 3 years was merely 26.5% for the whole cohort. For High-Risk patients, the 3-year PFS was 11.4% (95% CI: 5.0–25.9%), for Standard-Risk patients 3-year PFS was 45.3% (95% CI: 26.5–77.5%) while for Low-Risk 3-year PFS was 74.3% (95% CI: 51.7–100%). ($p < 0.0001$). Surprisingly, all the 6 patients who were low-risk and received radiation therapy relapsed later and underwent ASCT.

Conclusion: The survival outcomes in our cohort were much lower than in international trials, most probably due to non-availability of new agents as PDL1 inhibitors, and delays in stem cell transplantation.

P075: Response Adapted Therapy of Pediatric Classic Hodgkin Lymphoma According to Modified EURO-NET Protocol-Single Center Experience

Hany Abdel Rahman¹, Nesreen Ali¹, Mona Fakhry², Maram Farouk², Ebtihal Shoukry², Nashwa Mahmoud¹, Asmaa Attia¹, Walaa El Sayed¹, Mohamed Sedqy³, Yassin Taher², Riham Abdel Aziz¹, Asmaa Hamoda¹, Sally Talaat¹, Eman Khorshed⁴, Mohamed Saad Zaghloul⁵, Esraa Roushdy⁶, Madeha El Wakeel⁷, Sarah Badawy⁸, Mohamed Kamal⁸, Emad Moussa⁹, Alaa El Haddad¹

¹Department of Pediatric Oncology, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt, ²Department of Pediatric Oncology, Children Cancer Hospital Egypt, ³Department of Pediatrics, National Research Center, and Children Cancer Hospital Egypt, ⁴Department of Pathology, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt, ⁵Department of Radiation Oncology, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt, ⁶Department of Nuclear medicine and Radiation Oncology, South Egypt Cancer Institute, Assiut university, and Children Cancer Hospital Egypt, ⁷Department of Radio-diagnosis, National Cancer Institute, Cairo University, and Children Cancer Hospital Egypt, ⁸Department of Clinical Research Children Cancer Hospital Egypt, ⁹Department of Clinical Oncology, Monoufeyah University, and Children Cancer Hospital Egypt

Background: Hodgkin lymphoma (HL) represents about 5–7% of all malignancies in children, with a 5-year probability of overall survival (pOS) exceeding 90%. Radiotherapy containing regimen bear an increasing risk for late effects particularly secondary malignancies and cardiovascular disease. The omission of radiotherapy in patients with an adequate 18FDG-PET CT metabolic response after two intensive induction chemotherapy cycles has become the current treatment approach in the EuroNet-PHL consortium.

Aim: To report the results of HL patients treated according to the EuroNet protocol at the Children Cancer Hospital Egypt (CCHE 57357).

Methodology: This retrospective study included all patients diagnosed with classic HL, and treated as per EuroNet protocol during the period from 2/2019 till end of 12/2023. Patients demographic data (age, sex), disease characteristics; histologic subtypes, initial ESR, stage, B symptoms, treatment groups (TG), response to induction chemotherapy either adequate or inadequate according to interim 18FDG-PET CT, radiotherapy dose and duration, outcomes including overall (OS), event free (EFS) survival were collected and analyzed.

Results: Seven hundred and nineteen patients were included in the study. The most common age group was from 5–15 years (68.8%). There was a clear male predominance (69.1%). Nodular sclerosis was the most common pathologic subtype (60.3%). Stage II-A was the most commonly seen (24.3%). TG 3 according to EuroNet risk stratification was predominant (40.0%). Seventy percent of the patients had an adequate metabolic and radiologic response, while 26.2% received upfront radiotherapy. Relapse rate was 13.4% and progression on chemotherapy was seen in 0.28%.

The 5-year OS was 96.1% (95% CI: 93.7%–98.5%), while the EFS was 82.7% (95% CI: 78.4%–85.8%). For patients with adequate response, the 5-year EFS was 86.9% (95% CI: 83.2%–90.6%), compared to 73.2% (95% CI: 64.2%–82.2%) for those with inadequate response.

Conclusion: EuroNet risk adapted response adapted protocol for pediatric classic HL seems a good strategy. The rationale is to reserve radiotherapy, with its potential serious late effects to patients with high risk disease.

In addition to interim 18FDG-PET CT results, serum disease response biomarkers (CD163, TARK, ctDNA) may be able in the future to refine risk stratification, with the potential of adding targeted and/or immunotherapy as upfront treatment for high risk patients.

P076: Ataxia Telangiectasia Associated Pediatric Hodgkin Lymphoma: High Response Rates but Substantial non-Relapse Mortality

Nesreen Ali¹, Hany Abdelrahman¹, Emad Moussa², Nesreen Radwan³, Eman Khorshed⁴, Sara Badawy⁵, Walaa Elsayed¹

¹Pediatric Oncology and Hematology Department, National Cancer Institute (NCI), Cairo University and Children Cancer Hospital, Cairo, Egypt (CCHE-57357), ²Clinical Oncology Department, Menoufya University and Children Cancer Hospital Egypt, Cairo, Egypt (CCHE-57357), ³Department of Pediatrics, Pediatric Allergy, Immunology, & Rheumatology Unit, Ain Shams University, Egypt and Children Cancer Hospital Egypt (CCHE-57357), ⁴Pathology Department, National Cancer Institute (NCI), Cairo University and Children Cancer Hospital Egypt (CCHE-57357), ⁵Clinical Research Department, Children Cancer Hospital, Egypt (CCHE-57357)

Background: Ataxia-telangiectasia (AT) is a rare inherited disorder characterized by immunodeficiency, defective DNA damage response, chromosomal instability, and marked radiosensitivity, predisposing affected children to lymphoma while increasing treatment-related toxicity. Evidence guiding optimal management of Hodgkin lymphoma (HL) in children with AT remains limited.

Methods: We retrospectively reviewed children with AT diagnosed with HL at Children's Cancer Hospital Egypt between July 2007 and July 2024. Data included clinical presentation, disease characteristics, frontline treatment, dose modifications, number of cycles, interim response, and survival.

Results: Fourteen patients were identified; median age at diagnosis was 9 years (range, 6–17), and 11/14 were male. Advanced presentation was frequent, with stage IV disease in 7/14 (50.0%) and B symptoms in 6/14 (42.9%). Risk stratification showed 7/14 high-risk, 5/14 intermediate-risk, and 2/14 low-risk disease. Histology was predominantly classical HL, with mixed cellularity in 8/14 (57.1%) and nodular sclerosis in 5/14 (35.7%); 1 case showed features intermediate between diffuse large B-cell lymphoma and classical HL. Frontline treatment was heterogeneous and toxicity-adapted: 4/14 patients received AVPC with 50% dose reduction, 3/14 AVPC with 25% reduction, 1/14 full-dose AVPC, and 4/14 ABVD. One additional patient received 2 cycles of dose-reduced ABVD without doxorubicin, then shifted to dose-reduced COPDAC. The patient with intermediate features received rituximab alone because of very poor general condition. Eleven patients achieved complete metabolic response after 2 cycles, 1 had progressive disease, and 2 died before response evaluation. Despite the high early response rate, all patients ultimately died, predominantly from non-relapse causes, mainly chest infection, respiratory failure, and septic shock. Median survival was 6 months.

Conclusion: AT-associated pediatric HL appears highly chemosensitive, but outcomes are dominated by extreme non-relapse mortality, mainly related to infectious, pulmonary, and treatment-related complications. These findings underscore the need for AT-adapted strategies that preserve efficacy while minimizing toxicity, with intensive prophylaxis, pulmonary support, and immune optimization.

P077: Real-World Outcomes of IGEV Salvage Therapy in Relapsed or Refractory Pediatric Hodgkin Lymphoma: Challenges from a Resource-Limited Setting

Walaa Elsayed^{1,2}, Maram Salama³, Hany Abdelrahman^{1,2}, Emad Moussa^{4,5}, Yousef Medany¹, Mohamed Saad Zaghloul^{6,7}, Madeha El Wakeel^{8,9}, Eman Khorshed^{10,11}, Esraa Roshdy^{12,13}, Nesreen Ali^{1,2}

¹Pediatric oncology department, National Cancer Institute, Cairo University, Egypt, ²Pediatric oncology department, Children's Cancer Hospital Egypt 57357, ³Pediatric Oncology department, Children's Cancer Hospital Egypt 57357, ⁴Clinical Oncology Department, Menoufya University, Egypt, ⁵Pediatric oncology department, Children's Cancer Hospital Egypt 57357, ⁶Radiotherapy department, National Cancer Institute, Cairo University, Egypt, ⁷Radiotherapy department, Children's Cancer Hospital Egypt 57357, ⁸Radio diagnosis department, National Cancer Institute, Cairo University, Egypt, ⁹Radio diagnosis department, Children's Cancer Hospital Egypt 57357, ¹⁰Pathology department, National Cancer Institute, Cairo University, Egypt, ¹¹Pathology department, Children's Cancer Hospital Egypt 57357, ¹²Radiotherapy and Nuclear medicine department, South Egypt Cancer institute, Assiut university, Egypt, ¹³Nuclear medicine department, Children's Cancer Hospital Egypt 57357

Background: Outcomes for relapsed or refractory (R/R) pediatric classical Hodgkin lymphoma (HL) remain suboptimal in low- and middle-income countries (LMICs), where access to timely autologous stem cell transplantation (ASCT), immune checkpoint inhibitors, and targeted therapies is often restricted, limiting salvage treatment options. While the ifosfamide, gemcitabine, vinorelbine, and prednisone (IGEV) regimen is recommended as first-line salvage therapy, real-world data from resource-constrained settings remain scarce. We evaluated the efficacy, toxicity, and stem cell mobilization potential of IGEV, with a focus on treatment delays and their impact on outcomes.

Methods: We conducted a retrospective study of children and adolescents (≤ 18 years) with R/R classical HL treated with IGEV at Children's Cancer Hospital Egypt between August 2021 and December 2022. The response was assessed using FDG PET-CT per EuroNet criteria. Outcomes included overall response rate (ORR), toxicity, stem cell mobilization, event-free survival (EFS), and overall survival (OS).

Results: Forty patients were included (median age 12 years); 37.5% had primary refractory disease, 22.5% early relapse, and 40% late relapse. After two cycles of IGEV, ORR was 70% (CR 42.5%, PR 27.5%). Treatment was well tolerated, with grade 3–4 febrile neutropenia in 22.5% and no treatment-related mortality. Among responders, a substantial proportion experienced disease progression while awaiting stem cell collection or ASCT, with a median time to progression of 5.5 months during delays. Only 7 patients proceeded directly to ASCT after successful CD34+ mobilization. At 2 years, OS was 86% while EFS was 33.7%. Inferior EFS was significantly associated with positive interim PET-CT and with primary refractory or early relapsed disease.

Conclusions: IGEV demonstrates meaningful efficacy and acceptable toxicity as salvage therapy for pediatric R/R HL in LMIC settings. However, survival outcomes are substantially compromised by delays in ASCT, with progression occurring in a significant proportion of responding patients during the waiting period. These findings highlight a critical gap between response and consolidation in resource-limited settings and underscore the urgent need to improve transplant access and expand availability of novel targeted therapies for high-risk patients.

Keywords: Hodgkin lymphoma; Pediatric; Relapsed/refractory; IGEV; Low- and middle-income countries.

P078: Baseline and Delta PET/CT Radiomics for Prognostic Stratification in Paediatric Hodgkin Lymphoma

Claire Gowdy¹, Caron Strahlendorf¹, Andrea C. Lo², Yvonne Mbithi¹, Carlos Uribe², Arman Rahmim³, Fereshteh Yousefirizi⁴

¹BC Children's Hospital, ²BC Cancer, ³University of British Columbia, ⁴BC Cancer Research Institute

Background: Reliable prognostic biomarkers are needed to improve risk stratification and treatment adaptation in paediatric Hodgkin lymphoma (HL). While conventional PET metrics such as SUVmax and total metabolic tumor volume (TMTV) are clinically established, the added value of longitudinal radiomic heterogeneity features remains incompletely understood. This study investigated the prognostic significance of baseline and delta PET/CT radiomic features for progression-free survival (PFS) in paediatric HL.

Methods: A retrospective cohort of 61 paediatric HL patients undergoing FDG PET/CT imaging was analyzed. Clinical, PET, CT, and radiomic features were extracted from baseline and paired longitudinal scans. Baseline metrics included SUVmax, TMTV, total lesion glycolysis (TLG), DMaxBulk, entropy-based texture features, and neighborhood gray-tone difference matrix (NGTDM) features. Longitudinal delta features were computed between sequential scans. Cox proportional hazards analysis, Kaplan–Meier survival analysis (log-rank test), ROC analysis, and subgroup analyses for early- and advanced-stage disease were performed. Optimal prognostic cutoffs were determined using the Youden index.

Results: On univariate analysis (UVA), baseline TMTV and DMaxBulk demonstrated significant associations with PFS ($p = 0.016$ and $p = 0.001$, respectively), whereas baseline SUVmax was not predictive ($p = 0.757$). CT NGTDM Complexity showed strong prognostic value ($p = 0.001$), while baseline PET and CT entropy demonstrated borderline significance. ROC analysis with Youden-index optimization identified prognostic cutoffs for MTV, DMaxBulk, TLG, SUVmax, body surface area, and chest ratio, with corresponding Kaplan–Meier stratification analyses confirming significant survival separation for selected biomarkers. On univariate analysis, longitudinal analysis revealed that delta TMTV remained significantly associated with outcome ($p = 0.016$), whereas changes in SUVmax were not predictive ($p = 0.631$). Delta PET NGTDM Strength demonstrated significant prognostic value ($p = 0.001$), supporting the importance of temporal heterogeneity assessment. Subgroup analyses showed that standard early response assessment retained prognostic significance in early-stage patients ($p = 0.025$), while several radiomic biomarkers demonstrated stronger predictive performance in advanced-stage disease. Multivariable modeling suggests incremental prognostic value when combining radiomic biomarkers, clinical variables, and treatment.

P079: Survival benefit of brentuximab vedotin in classical Hodgkin lymphoma: a multicenter real-world study

Wenhui Zhang¹, Yuanyuan Wang², Shaoxuan Hu¹, Ming Jiang³, Shujuan Wen², Weiping Liu¹

¹Peking University Cancer Hospital, ²The Affiliated Tumor Hospital of Xinjiang Medical University, ³West China Hospital, Sichuan University

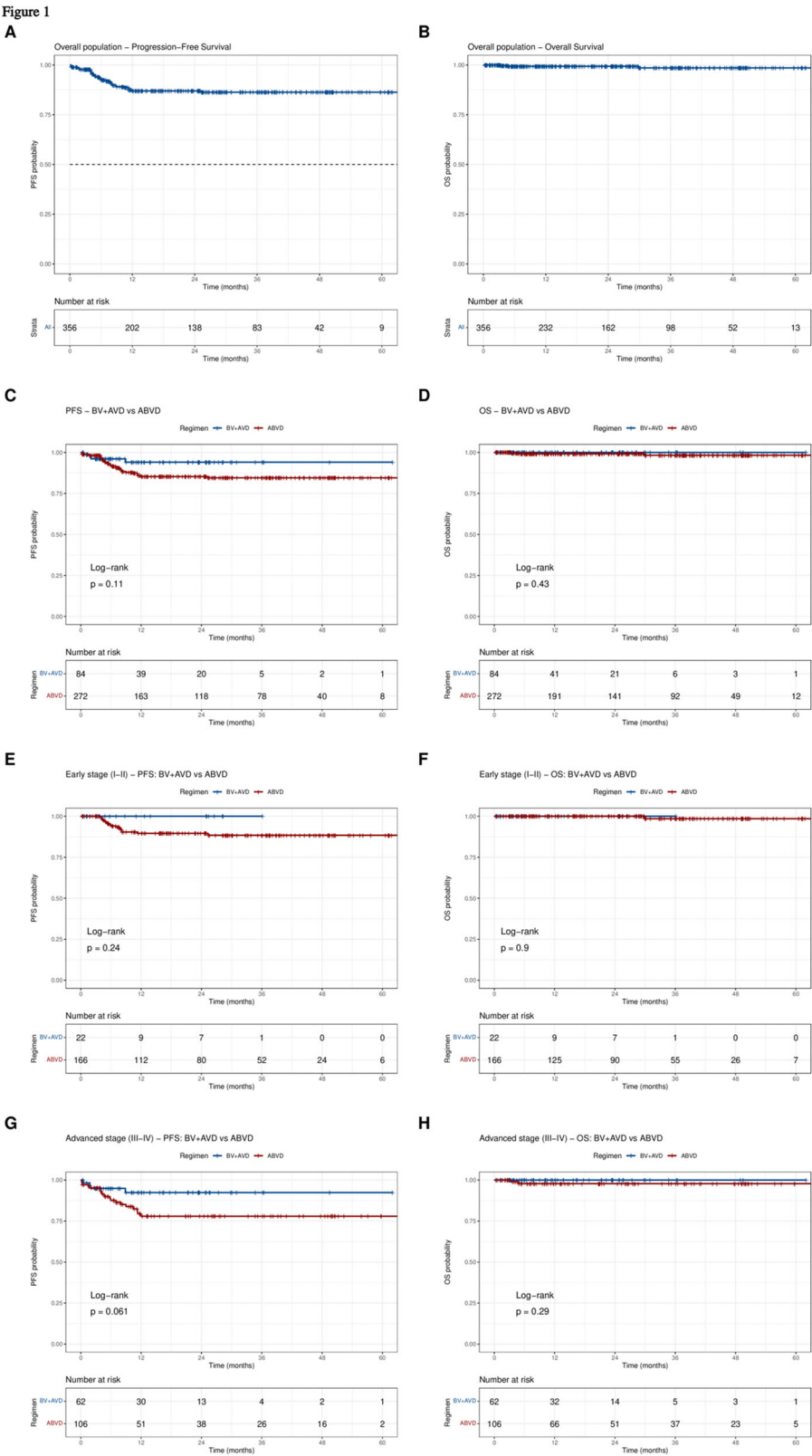


Figure 2

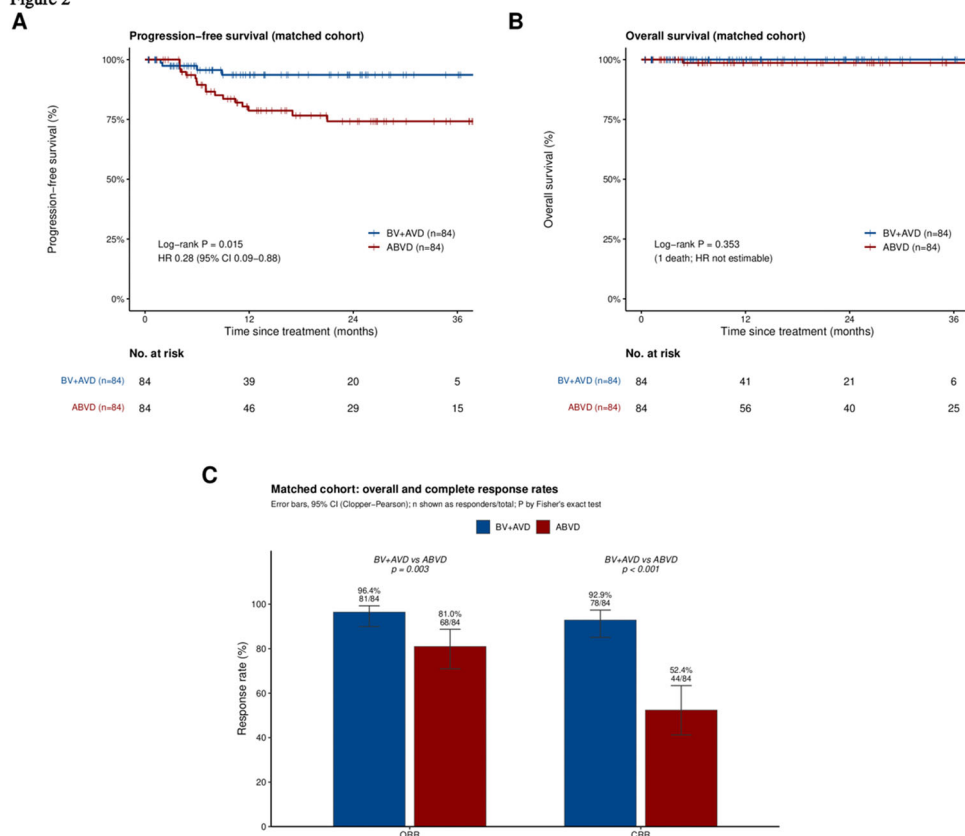


Figure 1: Kaplan–Meier survival curves for the overall population and by disease stage. **Figure 2:** Efficacy outcomes in the propensity score-matched cohort (n = 84 per group).

Background: Classical Hodgkin lymphoma (cHL) is highly curable, yet a meaningful proportion of patients still relapse after frontline chemotherapy, making deeper and more durable first-line responses a key goal. Adding the CD30-directed antibody-drug conjugate brentuximab vedotin (BV) to AVD (Doxorubicin, Vinblastine, Dacarbazine) has increasingly been used in clinical practice due to improved survival outcome. However, pivotal comparative evidence derives largely from selected, advanced-stage trial populations, whereas real-world, multicenter data across the full spectrum of disease stages are needed to confirm the benefit of BV+AVD over ABVD (Doxorubicin, Bleomycin, Vinblastine, Dacarbazine) and to inform first-line regimen selection. Applying rigorous propensity-score matching to balance baseline risk, we directly compared first-line BV+AVD with ABVD in a real-world cohort.

Methods: Patients with cHL receiving first-line BV+AVD or ABVD were retrospectively analyzed. Response rates were compared by Fisher's exact test. PFS and OS were estimated by Kaplan–Meier curve. To reduce confounding, 1:1 propensity-score matching was used to analyze the survival benefit of different treatment regimens.

Results: A total of 356 patients were enrolled, of whom 84 received the BV+AVD regimen and 272 received ABVD regimen. Compared with the ABVD regimen, the BV+AVD regimen achieved higher ORR (96.4% vs 83.8%; $P = 0.002$) and CRR (92.9% vs 66.2%; $P < 0.001$).

The 2-year PFS was 86.3% in the whole cohort. The 2-year PFS were 93.6% (95% CI 87.6–100) for BV+AVD versus 78.7% (69.6–89.0) and 74.2% (64.0–86.0) for ABVD (log-rank $P = 0.015$). BV+AVD was associated with significantly improved PFS (HR 0.28, 95% CI 0.09–0.88; $P = 0.029$). After matching, the BV+AVD regimen significantly improved PFS (2-year PFS 93.6% vs 78.7% and 74.2%; log-rank $P = 0.015$; HR 0.28, 95% CI 0.09–0.88).

Conclusion: In this multicenter real-world matched analysis, the BV+AVD regimen provided superior PFS and response rates, supporting it as an effective frontline option in routine practice and extending comparative evidence beyond selected trial populations. Longer follow-up is warranted to assess overall survival.

P080: Feasibility of tumor microenvironment analysis in pediatric and adolescent classical Hodgkin lymphoma by automated cyclic immunofluorescence staining

Mira Albracht¹, Fatih Yalcin¹, Julia Richter¹, Sarah Reinke¹, Matthias Braun², Marius Rohde², Alexander Claviez³, Britta Maecker-Kolhoff³, Birgit Burkhardt⁴, Arndt Borkhardt⁵, Tobias Feuchtinger⁶, Anja Tröger⁷, Martin Ebinger⁸, Gabriele Escherich⁹, Dominik Schneider¹⁰, Jan-Henning Klusmann¹¹, Anne Thorwarth¹², Dieter Körholz², Christine Mauz-Körholz², Wolfram Klapper¹

¹Department of Pathology, Hematopathology Section, University Hospital Schleswig-Holstein, Campus Kiel, Germany, ²Department of Pediatric Hematology, Oncology and Immunodeficiency, University Hospital Justus-Liebig University Giessen, Germany, ³Department of Pediatric Hematology, Oncology, Medical University Hannover, Germany, ⁴Department of Pediatric Hematology and Oncology and NHL-BFM study center, University Hospital Muenster, Germany, ⁵Department of Pediatric Hematology and Oncology, University Hospital Duesseldorf, Germany, ⁶Department of Pediatric Hematology and Oncology, University Hospital Freiburg, Germany, ⁷Department of Pediatric Hematology and Oncology, University Hospital Regensburg, Germany, ⁸Department of Pediatric Hematology and Oncology, University Hospital Tuebingen, Germany, ⁹Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, ¹⁰Department of Pediatric Hematology and Oncology, Dortmund, Germany, ¹¹Department of Pediatric Hematology and Oncology, University Hospital Frankfurt, Germany, ¹²Department of Pediatric Hematology and Oncology, Charite, Berlin, Germany

Background: The tumor microenvironment (TME) plays a central role in classical Hodgkin lymphoma (cHL) biology. While the TME has been extensively studied in adult cHL, spatial and single-cell data of pediatric and adolescent patients remain limited. In this study, we implemented cyclic immunofluorescence to characterize the cellular composition of the TME in pediatric and adolescent cHL.

Methods: Diagnostic biopsy material from pediatric and adolescent patients treated within the EuroNet-PHL-C1 trial was analyzed (Mauz-Körholz et al., 2023). Early response after two cycles of OEPA was defined as adequate response (AR) with partial morphological remission or greater and PET negativity and inadequate response (IR) when criteria for AR were not met (Mauz-Körholz et al., 2023). Overall, n = 39 specimens were assembled in a tissue microarray (TMA). Multiplex phenotyping was performed on TMAs using the MACSimaTM imaging platform and a 28-antibody panel (including CD30, CD3, CD4, CD8a, CD20, CD11c, CD163, CD68, CD56, CD66b, CD45RA, CD45RO, LAG3, TIM3, PD1, PDL1, HLA-DR, HLA-ABC). Single-cell segmentation and phenotyping were performed using StarDist and Nimbus, followed by downstream quantification in QuPath.

Results: By standard protocols of multiplex immunophenotyping, Hodgkin-Reed-Sternberg cells (HRSCs) were insufficiently detected and frequently oversegmented (one HRSC erroneously considered as multiple cells due to multinuclearity). We established and optimized a workflow allowing us to reliably identify and localize HRSCs as a prerequisite for spatial analysis in cHL. Moreover, we developed an analysis pipeline that allows us to assign phenotypes to the densely packed cells of the cHL microenvironment, including reliable macrophage detection. Overall, our assay assigned a phenotype to 78.5% of all cells in the tissue. As expected, HRSCs comprised a minority of cells (1.1%) and CD4 + T-cells (44.7%) dominated the TME. The content of B-cells was variable, and NK-cells were rarely detected. M1 macrophages were more abundant than M2 macrophages.

Conclusion: We demonstrate feasibility of multiplex immunophenotyping of the TME in cHL using the MACSimaTM imaging platform. We managed to overcome limitations in detecting HRSCs and implemented a data analysis pipeline for the TME of cHL. Data acquisition is currently ongoing and a correlation of TME features and treatment response (AR vs. IR) will be presented at the meeting.

P081: Allogeneic stem cell transplantation for multiply recurrent EBV-driven classic Hodgkin lymphoma arising in the setting of suspected activated PI3-kinase delta syndrome (APDS) associated with a novel variant: a case report spanning 13 years

Joseph Debettencourt¹, Rebecca Hale², Jaclyn Schienda¹, Amy Keating¹, Marian Harris¹, Leslie Lehmann¹, Angela Feraco¹

¹Dana-Farber/Boston Children's Cancer and Blood Disorders Center, ²Boston Children's Hospital

Initial Presentation: Original diagnosis at age 8 was stage IIB EBV+ nodular sclerosis classic Hodgkin lymphoma (cHL). The male patient was treated with escalated BEACOPDac and involved field radiotherapy.

First Recurrence: EBV+ cHL re-emerged at age 15. The patient was treated with single agent pembrolizumab every 3 weeks with frank disease progression. Upon arrival to our center, the patient had stage IVB disease and sepsis-like episodes concerning for secondary hemophagocytic lymphohistiocytosis (HLH). Disseminated dermatophyte infection remitted only with systemic terbinafine.

Investigating host immunity: Testing for primary immunodeficiency revealed a heterozygous variant of uncertain significance in PIK3CD (c.1013 G > A; p.Arg338Gln; CADD score 26.6), concerning for a pathologic variant.

Treatment approach: Autologous (auto) versus allogeneic (allo) stem cell transplant were considered. Given that Activated PI3K Delta Syndrome (APDS) was suspected but not definitively diagnosed, potential morbidity of allo, and poor HLA matches in the United States bone marrow repository, auto was recommended. At age 16, after achieving a complete metabolic response to brentuximab vedotin (BV) and bendamustine treatment, the patient had auto with BEAM conditioning.

Post-auto course: Approximately 60 days after auto, the patient presented with florid disseminated EBV and secondary HLH (massive splenomegaly, refractory thrombocytopenia, unremitting fever) requiring rituximab and high-dose intravenous immunoglobulin to quell. Received post-auto consolidation with BV per the AETHERA trial. Abnormal marrow signal was detected ~7 months after auto and confirmed by biopsy. Measurable nodal disease emerged shortly thereafter. Clinical trials were considered but the patient was ineligible due to progressive cytopenias. Treated with BV and nivolumab followed by BV and bendamustine per AHOD1721 to provide a >12-week interval between final dose of anti-PD1 checkpoint inhibition and intake for allo.

Allo and subsequent course: Allo performed at age 19 with busulfan and fludarabine conditioning and post-allo cyclophosphamide. To ensure an EBV-exposed donor, a cryopreserved 9/10 HLA-matched peripheral blood stem cell product was used. Course complicated by significant colitis and prolonged hospitalization. Today, the patient appears free of cHL 21 months after allo SCT with excellent performance status. Immune evaluation may benefit the youngest with cHL, particularly upon relapse.

Early stages

T082: Radiation-free initial treatment of early-stage favorable classic Hodgkin Lymphoma (RAFTING) trial: three-year follow-up

Andrea Gallamini¹, Kateryna Filonenko², Marco Picardi³, Stephane Chauvie⁴, Andrea Riccardo Filippi⁵, Maria Cristina Piroso⁶, Luca Guerra⁷, Federico Fallanca⁸, Marta Bednarek⁹, Michał Kurlapski¹⁰, Eva Domingo-Doménech¹¹, Andrea Visentin¹², Caterina Patti¹³, Ramón García Sanz¹⁴, Javier Nunez¹⁵, Javier Lopez¹⁶, Agnieszka Giza¹⁷, Adam Wyszomirski¹⁸, Alessandro Rambaldi¹⁹, Davide Rossi⁶, Anna Sureda¹¹, Jan Maciej Zaucha²

¹Research and Clinical Innovation Department, Lacassagne Cancer Center, Nice, France, ²Department of Hematology and Transplantology, University Medical Center in Gdansk, Gdansk, Poland, ³Department of Clinical Medicine and Surgery, AOU Federico II, Naples, Italy, ⁴Medical Physics Division, Santa Croce e Carle General Hospital, Cuneo, Italy, ⁵Radiation Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori and Department of Oncology, University of Milan, Milan, Italy, ⁶Laboratory of Experimental Hematology, Institute of Oncology Research, ⁷School of Medicine and Surgery, University of Milano Bicocca, Milan, Italy, Nuclear Medicine Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, ⁸IRCCS San Raffaele Scientific Institute, Nuclear Medicine, Milan, Italy, ⁹nd Division of Radiology, Medical University of Gdansk, ¹⁰Department of Hematology and Transplantology, Medical University of Gdansk and University Clinical Center, Gdansk, ¹¹Clinical Hematology Department, Institut Català d'Oncologia - L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain, ¹²Hematology Unit, Department of Medicine (DIMED), at the University of Padua in Padua, Italy, ¹³U.O.C. di Oncoematologia, Ospedali Riuniti Villa Sofia - Cervello (Presidio V. Cervello), Palermo, Italy, ¹⁴Hematology Division at Hospital Universitario de Salamanca in Salamanca, Spain, ¹⁵Hematology Service at Hospital Universitario Marqués de Valdecilla (HUMV) Santander, Spain, ¹⁶Hematology and Chemotherapy Department at Hospital Universitario Ramón y Cajal Madrid, IRYCIS, Universidad Alcalá de Henares, Spain, ¹⁷Department of Haematology, Jagiellonian University Medical College, Krakow, Poland, ¹⁸Department of Adult Neurology, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland, ¹⁹Fondazione per la Ricerca Ospedale Papa Giovanni XXIII, Bergamo, Italy

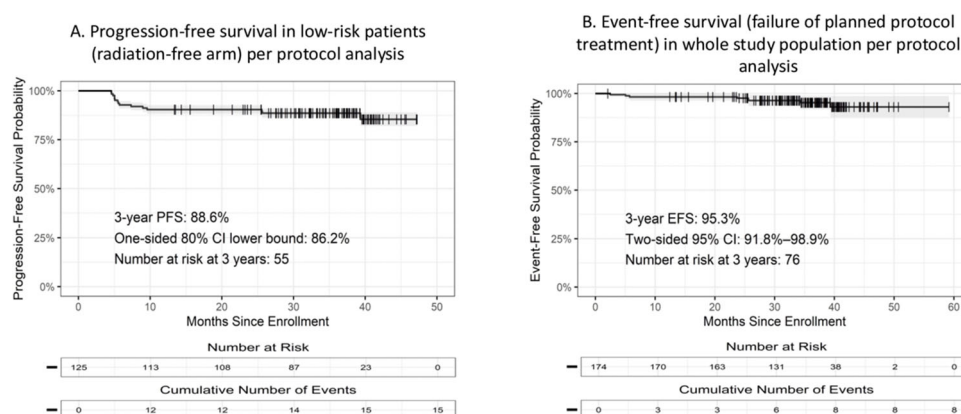


Figure 1: Progression-free survival in low-risk patients (radiation-free arm) (A) and Event-free survival (failure of planned protocol treatment) in whole study population (B) per protocol analysis.

Background: The RAdiotherapy-Free Treatment for the INitial Therapy of Good-prognosis early-stage (RAFTING) classic Hodgkin Lymphoma (cHL) is a phase 2, multicenter, prospective study to assess feasibility and effectiveness of a risk-adapted therapy for early favorable cHL (efHL). The protocol is an example of a fully personalized medicine approach in a single-patient basis.

Methods: Untreated stage I–IIA efHL patients (p.), aged 18–70 years, without bulky, B-symptoms, or extranodal site, were stratified to high (HR), Low (LR) and very-low risk (VLR). HR p. had either or both risk factors (RF): total metabolic tumor volume (TMTV) $\geq$ 84 ml and/or a positive interim PET (PET-2). Very-Low risk (VLR) or Low-Risk (LR) p. were further identified by the absence/presence of $\square$ one modified EORTC RF, in which bulky was replaced by a large nodal mass (LNM), with a largest diameter 5–10 cm. VLR and LR p. received 2 and 4 ABVD cycles respectively and HR p. 4 ABVD, INRT (20/30 Gy) + Nivolumab (N) 240 mg q2w, for $\leq$ 24 doses. VLR/LR p. with ABVD limited relapse (LIR) in initially involved $\pm$ up to 3 new nodal sites were rescued by INRT (36 Gy) and N $\times$ 24 q2w. Extended Relapse (ER) was considered a therapy failure requiring an off-study salvage. The primary study endpoint is a 3-Y PFS $\geq$ 85% in RT-free p., key 2nd endpoint: 3-Y event-free survival (EFS)-failure to planned treatment or death. All the PET/CT scans were centrally reviewed and TMTV measured with a 41% SUV threshold.

Results: Between 03/21 to 10/23, 174/180 (97%) stratified p. are evaluable in a per-protocol analysis as follows: 36 p. belonged to VLR, 89 to LR, and 49 to a HR group. Main RF in LR group were: LNM (49), age $>$ 50 (30), ESR $>$ 50 mm/h (28), and $>$ 4 nodal areas (25). Among HR pts, 35 had a high TMTV, 9 – positive PET-2, and 5 – both. 13 RT-free p. relapsed: 10 p. with LIR and 3 ER. 12 relapses occurred within the first 6 months. Ten p. were rescued per protocol and only 1 relapsed later after N. After a median follow-up of 35(5–60) months, 112 RT-free p. (90% of RT-free p., 64% of all p.) remained disease/RT-free. Two deaths (non-relapsed) and 3 secondary malignancies occurred. The 3-year PFS is 88.6%, with a one-sided 80% lower confidence bound of 86.2%, still above the predefined non-inferiority threshold of 85%. The 3-year EFS was 95.3% (95% CI, 91.8–98.9%).

Conclusion: The long-term results of the RAFTING trial confirm that a patient risk-adapted approach could cure $>$ 95% of the efHL with 64% being RT-free p.

T083: Integrating E-HIPI and Interim PET to Refine Risk Stratification in Early-Stage Classic Hodgkin Lymphoma

Alessandro Cellini¹, Martina De Ferrari¹, Giovanni Manfredi Assanto², Alessandra Romano³, Gabriella Santuccio³, Candida Vitale^{4,5}, Maria Chiara Montalbano^{4,5}, Francesco Angotzi¹, Andrea Serafin¹, Nicolo' Danesin¹, Arianna Bevilacqua¹, Mattia D'Antiga¹, Giovanni Leone¹, Marta Coscia⁶, Francesco Di Raimondo³, Ilaria Del Giudice², Francesco Piazza¹, Livio Trentin¹, Andrea Visentin¹

¹Hematology Unit, Department of Medicine, University of Padova, Padova, Italy, ²Hematology, Department of Translational and Precision Medicine, Sapienza University, Rome, Italy, ³Hematology and BMT Unit, A.O.U. "G. Rodolico-San Marco", Catania, Italy, ⁴Department of Molecular Biotechnology and Health Sciences, University of Torino, ⁵Division of Hematology, A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy, ⁶Hematology Unit, Department of Medicine and Surgery, University of Insubria, Varese, Italy

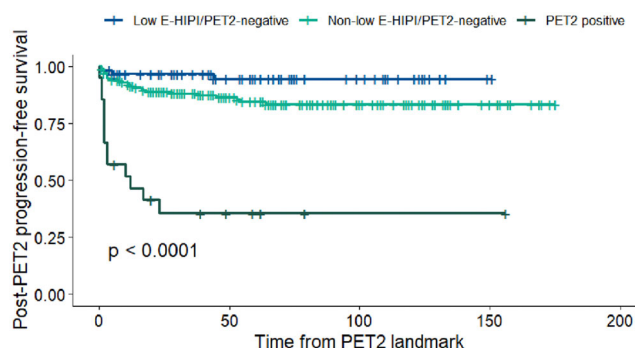


Figure 1: Landmark analysis of Progression-free survival within dynamic risk groups.

Background: The E-HIPI is a baseline prognostic index developed to predict 2-year progression-free survival (PFS) in early-stage classic Hodgkin lymphoma (cHL). Since contemporary treatment is also guided by interim PET, we assessed whether PET after 2 cycles of chemotherapy (PET2) refines E-HIPI-based risk stratification.

Methods: We retrospectively analysed patients with early-stage cHL treated in 2007–2025 at 4 Italian centres with ABVD- or BEACOPP-based PET-guided approaches. E-HIPI was calculated using published coefficients for sex, maximum tumour diameter, albumin and hemoglobin, applying the original plausibility exclusions. PET2 was classified by Deauville score (DS), with DS 4–5 being considered as positive. Post-PET2 PFS was evaluated by landmark analysis among patients alive and progression-free at interim assessment. E-HIPI was analysed as continuous score and as low risk (<25th percentile) versus non-low risk. A dynamic classification was defined as: low E-HIPI/PET2-negative, non-low E-HIPI/PET2-negative, and PET2-positive.

Results: Overall, 264 patients were included; 130 (49%) were female and median age was 31 years. Stage II disease was present in 244 (92%), bulky disease in 84 (32%) and B-symptoms in 64 (24%). After a median follow-up of 62 months, 38 (14%) patients experienced progression or relapse and 8 (3%) died. E-HIPI showed moderate discrimination for 2-year PFS (C-index 0.654, 95% CI 0.55–0.75). PET2 was available in all patients; 242 (92%) were PET2-negative and 22 (8%) PET2-positive. Two-year post-PET2 PFS was 91% after negative PET2 and 35.6% after positive PET2 (HR [8.8, 95% CI 4.4–17.5; $p < 0.001$]). The combined model identified an ultra-low-risk group with low E-HIPI and negative PET2, with 2-year post-PET2 PFS of 96.8%, compared with 89.0% in non-low E-HIPI/PET2-negative patients and 35.6% in PET2-positive patients. Compared with all other patients, the low E-HIPI/PET2-negative group had reduced risk of progression or relapse (HR 0.2, 95% CI 0.05–0.97; $p = 0.04$).

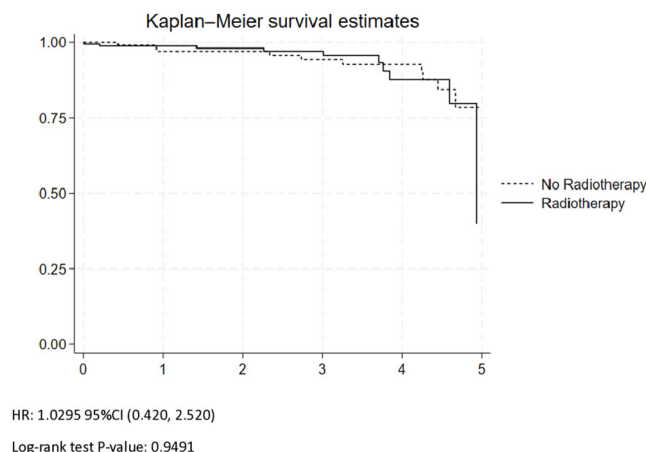
Conclusions: In this multicentre PET-guided early-stage cHL cohort, PET2 refined baseline E-HIPI risk stratification. Low E-HIPI combined with negative PET2 identified an ultra-low-risk subgroup with excellent disease control, supporting integrated baseline and early-response models for treatment de-escalation studies. PET2-positive patients may require alternative strategies or novel combinations.

P084: Role of consolidative radiotherapy in preventing relapses and subsequently salvage ASCT in early-stage classic Hodgkin lymphoma

Reyad Dada¹, John Apostolidis², Refaei Belal Ibrahim¹, Asma Ahmed Salem¹, Mostafa Ibrahim Mahmoud¹, Hafiz Asif Iqbal¹, Tarik Boubakra¹, Hamza Ghatasheh³, Khalid Halahleh³

¹King Faisal Specialist Hospital and Research Centre, Jeddah, Kingdom of Saudi Arabia, ²Department of Hematology & Stem Cell Transplantation, King Fahd Specialist, ³King Hussein Cancer Center, Amman, Jordan

Figure 1: 5-year survival

**Figure 1:** 5-year survival.

Introduction: The role of consolidative radiotherapy (RT) in upfront management of patients with early-stage classic Hodgkin lymphoma (cHL) is subject of debates. Particularly, its impact on preventing relapses and subsequent necessity of salvage autologous stem cell transplantation (ASCT).

Patients and methods: We analyzed in this multicenter retrospective study data of patients with early stage cHL. The study evaluates whether the omission of RT increases risk of relapse and consequently need of ASCT. Relapse rates and frequency of ASCT were compared between patients who got combined modality treatment (CMT) versus chemotherapy alone.

Total of 490 patients (median age 27, mean follow-up 57 months) were included with 57.8% patients receiving CMT. After end of treatment, complete metabolic remission (CMR) was documented in 90.4% in CMT versus 90.8% in chemotherapy alone arm. 33.3% of patients with positive EOT-PET gained CMR after RT.

Relapse rates in chemotherapy alone and CMT cohort were 10.6% and 8.5% ($p = 0.92$), respectively. Of the 42 patients who had r/r disease during observation time 45.2% and 54.7% were in chemotherapy alone and CMT group, respectively. Among these patients, ASCT was carried out in 42.1% in chemotherapy alone and 65.2% in CMT (HR 0.65, 95% CI 0.35–1.18; $p = 0.14$). Considering both cohorts, overall 8/207 (3.9%) versus 15/283 (5.3%) had ASCT, respectively ($p = 0.19$). Post-ASCT complete metabolic remission rate was similar (80% in CMT vs 75% in chemotherapy alone; $p = 0.78$). Five-years overall survival rate was not different (HR: 1.03; $p = 0.95$). During the observational period, one patient in the chemotherapy alone group failed ASCT in comparison with three patients in the CMT group corresponding to ASCT failure rate of 12.5% and 20%, respectively. One patient in CMT cohort had allogeneic stem cell transplantation due to relapse post ASCT.

Conclusions: Our real-world data suggests that routine consolidative RT can be omitted in patients with early-stage cHL who achieve a negative EOT-PET, without increasing of the likelihood of requiring ASCT. Conversely, RT demonstrates meaningful efficacy in significant proportion of patients with positive EOT-PET. Therefore, we suggest to reserve consolidative RT for responding patients with early-stage cHL with positive EOT-PET, where it confers clear therapeutic benefit.

P085: Definition of a risk collective for high cardiac radiation doses - A post-hoc analysis of the HD17 study by the German Hodgkin Study Group reference radiation oncology panel

Michael Oertel¹, Christopher Kittel¹, David Rene Steike¹, Michael Fuchs², Christian Baues³, Dirk Vordermark⁴, Rita Engenhart-Cabilic⁵, Klaus Herfarth⁶, Heinz Schmidberger⁷, Peter Lukas⁸, Peter Borchmann², Hans Theodor Eich¹

¹Department of Radiation Oncology, University Hospital Muenster, Muenster, Germany, ²Department of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne, Dusseldorf, University Hospital of Cologne, Cologne, Germany, ³Department of Radiation Oncology, University Hospital of Ruhr-Universität Bochum, Marien Hospital Herne, Herne, Germany, ⁴Department of Radiation Oncology, University Hospital Halle (Saale), Halle (Saale), Germany, ⁵Department of Radiotherapy and Radiation Oncology, University Hospital Giessen-Marburg, Marburg, Germany, ⁶Department of Radiation Oncology, Heidelberg University Hospital, Heidelberg, Germany, ⁷Department of Radiotherapy and Radiation Oncology, University Hospital Mainz, Mainz, Germany, ⁸Department of Radiooncology, Medical University Innsbruck, Innsbruck, Austria

Background: Radiotherapy (RT) is an essential part of modern treatment strategies for Hodgkin lymphoma (HL). However, efficacy has to be careful weighted against putative toxicity. Identifying those patients with high cardiac radiation exposure prior to RT may be a valuable strategy to guide optimization or even omit RT in favor of a chemotherapy-only treatment. We analyzed patients with a high RT dose to the heart within the patient collective of the HD17 study, as a modern study for intermediate-stage HL.

Methods: Overall, 176 patients (134 with involved-node RT) were analyzed by the reference radiation oncology panel as part of the study's quality assurance. The present analysis focusses on patients exceeding dose recommendations given by the International Lymphoma Radiation Oncology Group. Dosimetric and toxicity data were taken from the radiation plans and documentation by the study central.

Results: From the 176 patients evaluated, 139 had a mediastinal involvement, 43 of whom had a mean heart exposure >15 Gy, defined as a threshold for RT plan optimization (mean: 19.8 Gy). Of these 43 patients, the majority had stage II disease (91%), no B-symptoms (86%) and was <50 years of age (86%). Disease spread to both the upper (95%) and lower (98%) mediastinum in most cases. Except for the mediastinum, the

most prevalent regions were supraclavicular right/left (63%/77%) and infraclavicular right/left (61%/72%). Concerning GHSG risk factors, mediastinal bulk, extranodal spread, involvement of >3 lymph node areas and elevated ESR were seen in 47%, 16%, 61% and 35%, respectively. In comparison to patients with lower heart doses, bulky disease and extranodal spread were seen more frequently in patients with increased heart dose ($p = 0.043$ and $p = 0.035$, respectively). This was in contrast to an elevated ESR ($p = 0.058$), >3 areas ($p = 0.552$), stage II HL ($p = 0.722$) as well as involvement of the left axilla, lower or upper mediastinum ($p = 1.0$).

Conclusion: Pre-chemotherapy risk factors may be suitable predictors for RT dose exposure and can help to identify patients at higher risk for long-term toxicity. Further analysis on the influence of partial mediastinal involvement as well as modern RT techniques will broaden the perspective.

P086: TRIAL IN PROGRESS: PRIORITY (PET guided dose Reduction for Involved site Radiotherapy In early sStage unfavourable Hodgkin lymphoma: a randomized, phase III, non-inferiority study)

Umberto Ricardi¹, Fabio Matrone², Barbara Botto³, Mario Levis¹, Patrizia Ciammella⁴, Andrea Evangelista⁵, Ilenia Iamundo De Cumis⁶, Stephane Chauvie⁷, Francesca Ricci⁸, Piero Maria Stefani⁹, Luigi Rigacci¹⁰

¹Department of Oncology University of Torino, ²Department of Radiation Oncology, Centro di Riferimento Oncologico (CRO) IRCCS Aviano, ³SC Ematologia AOU Città della Salute e della Scienza Torino, ⁴Radioterapia Oncologica Azienda USL-IRCCS Reggio Emilia, ⁵SSD Epidemiologia Clinica e Valutativa AOU Città della Salute e della Scienza Torino, ⁶Radioterapia oncologica, Dipartimento Cura delle malattie Oncologiche, Ospedale Oncologico A. Businco, ARNAS G. Brotzu, ⁷Medical Physics Division, Santa Croce e Carle Hospital, Cuneo, ⁸Department of Oncology and Hematology, IRCCS Humanitas Research Hospital Rozzano Milano, ⁹UOC Hematology ULSS 2 Ospedale Ca' Foncello Treviso, ¹⁰Fondazione Policlinico Campus Bio-Medico e Università Campus Bio-Medico Roma

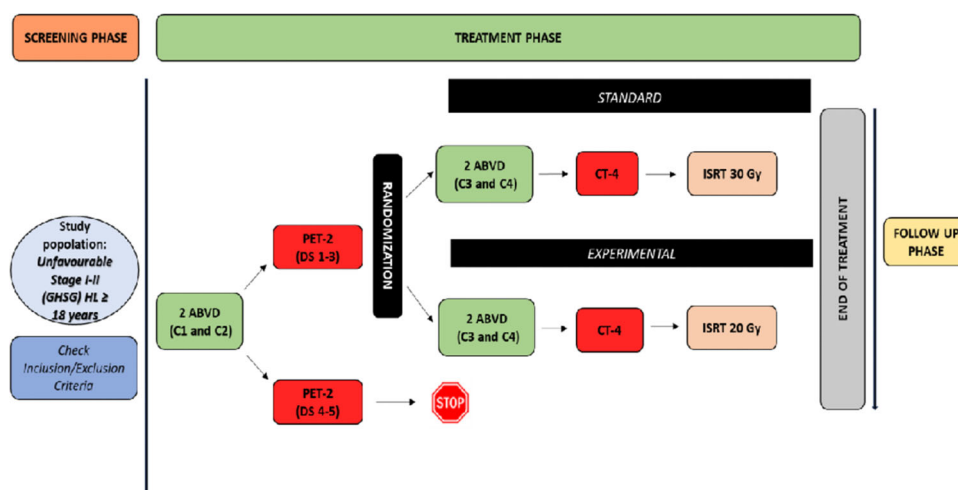


Figure 1: Priority protocol.

Introduction: Treatment of early-stage Hodgkin lymphoma (HL) is extremely successful, with more than 90% cure rate. The mainstay of treatment for early stage Hodgkin's disease includes an approach combining chemotherapy and radiotherapy. The introduction of 18 F-FDG PET for metabolic response assessment has certainly provided the opportunity for a more individualized approach, both in terms of treatment intensification and de-escalation. Therefore, since H10 trial showed that consolidation radiotherapy cannot be safely omitted even in PET-2 negative patients, it becomes now important to re-consider radiation dose de-escalation from the standard 30 Gy to the 20 Gy level in patients achieving a metabolic complete response (mCR) at early PET.

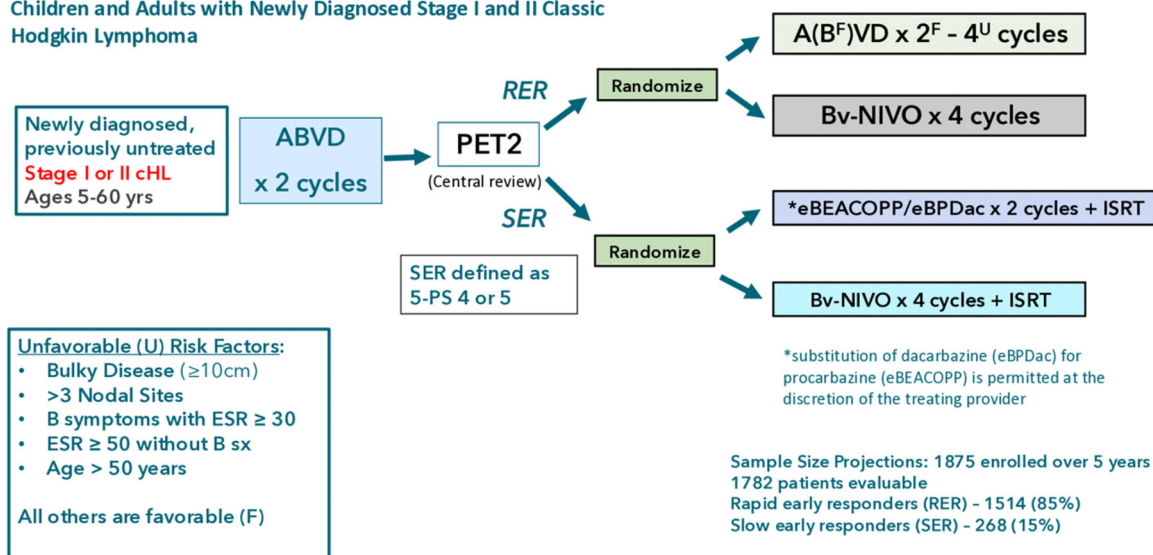
Methods: NCT07256158 PRIORITY is a phase III Italian multicentric, randomized, non-inferiority, interventional study. Patients aged ≥ 18 years with unfavourable early stage HL according to GHSG criteria will be treated with 2 cycles of ABVD. Patients in mCR according to 2014 Lugano criteria (DS score 1–3) after 2 cycles ABVD will receive two other ABVD cycles (total 4 cycles) and randomized to standard arm of ISRT 30 Gy vs experimental arm with ISRT 20 Gy. Patients in partial response/progressive disease (DS 4–5) will be withdrawn from trial and will receive further treatment at the discretion of the investigators. The primary endpoint is 3-year Progression-Free Survival (PFS) of the randomized population. Secondary endpoints are: Overall Survival (OS) for the randomized population and for the whole population, PFS for the whole population, incidence of adverse events, RT dose received by organs at risk. Exploratory endpoints are planned: performance of risk-adapted automatic RT re-planning in comparison with manual plans used for clinical treatment, prognostic value of baseline metabolic tumour volume (MTV) and/or tumour lesion glycolysis impact on PFS/OS, association between baseline radiomics and clinical characteristics and/or global clinical outcome. Assuming a 3-year PFS in the standard arm (30 Gy) of 92%, with a non-inferiority margin of 7% for the experimental arm (20 Gy), with 80% power (one-sided alpha 5%), and considering eligibility criteria (Deauville score 1–3 after two ABVD cycles), 518 patients must be enrolled to reach the target. Trial has been recently approved by EC and recruitment is ready to start (June 2026) in 38 Italian centers affiliated to FIL (Fondazione Italiana Linfomi).

P087: AHOD2131: A Randomized Phase 3 Response-Adapted Trial Comparing Standard Therapy with Immuno-oncology Therapy for Children & Adults with Newly Diagnosed Stage I & II Classic Hodgkin Lymphoma

Jennifer Seelisch¹, Boyu Hu², Lindsay A. Renfro³, Adam Duvall⁴, Yue Wu⁵, Steve Yoon-Ho Cho⁶, Bradford Scott Hoppe⁷, Sarah Milgrom⁸, Raymond Mailhot Vega⁹, Andrea C. Lo¹⁰, David Hodgson¹¹, Lisa Guilino Roth¹², Natalie Grover¹³, Ann Steward Lacasce¹⁴, Justine M. Kahn¹⁵, Susan Parsons¹⁶, Pamela Sue Hinds¹⁷, Pamela Blair Allen¹⁸, Andrew M. Evens¹⁹, Heiko Schoder²⁰, Sharon M. Castellino²¹, Kara M. Kelly²²

¹Children's Hospital London Health Sciences Centre, Western University, London, ON, Canada, ²Huntsman Cancer Institute/University of Utah, Salt Lake City, Utah, USA, ³University of Southern California and Children's Oncology Group, Los Angeles, CA, USA, ⁴University of Chicago Comprehensive Cancer Center, Chicago, IL, USA, ⁵COG Data Center, University of Florida, Gainesville, FL, USA, ⁶University of Wisconsin Hospital and Clinics, Madison, WI, USA, ⁷Mayo Clinic Radiation Oncology, Jacksonville, FL, USA, ⁸Children's Hospital Colorado, Aurora, CO, USA, ⁹University of Florida, Jacksonville, FL, USA, ¹⁰BC Cancer, Vancouver, BC, Canada, ¹¹University of Toronto, Toronto, Ontario, Canada, ¹²NYU Langone Health, New York, NY, USA, ¹³UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA, ¹⁴Dana-Farber/Harvard Cancer Center, Boston, MA, USA, ¹⁵NYP/Columbia University Medical Irving Center/Herbert Irving Comprehensive Cancer Center, New York, NY, USA, ¹⁶Tufts Medical Center, Boston, MA, USA, ¹⁷Children's National Medical Center, Washington, DC, USA, ¹⁸Emory University Hospital/Winship Cancer Institute, Atlanta, GA, USA, ¹⁹Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA, ²⁰Memorial Sloan Kettering Cancer Center, New York, NY, USA, ²¹Emory University School of Medicine, Children's Healthcare of Atlanta, Atlanta, GA, USA, ²²Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

AHOD2131: A Randomized Phase 3 Response-Adapted Trial Comparing Standard Therapy with Immuno-Oncology Therapy for Children and Adults with Newly Diagnosed Stage I and II Classic Hodgkin Lymphoma



Background: Chemotherapy (CT) in combination with radiotherapy (RT) is the current frontline standard for early-stage (ES) classic Hodgkin lymphoma (HL), with cure rates of >90%. Recently, novel treatments have aimed to maintain high cure rates while minimizing acute and long-term toxicities associated with CT and RT. Incorporation of novel immunotherapy (IO) agents into frontline settings offer new potential therapy options that may reduce exposure to CT and RT while improving progression-free survival (PFS) and maintaining overall survival (OS).

Methods: AHOD2131 (NCT05675410) was collaboratively developed between pediatric and adult oncology members of the National Cancer Institute's National Clinical Trial Network (NCTN), aiming to harmonize frontline IO-based treatment approaches for ES HL. Study champions from each North American cooperative group (NACGs) (Children's Oncology Group [COG], SWOG, ECOG-ACRIN, Alliance, NRG) and experts in imaging, radiation oncology, HL biology and patient-reported outcomes (PROs) were included in the development.

AHOD2131 is a randomized, phase 3 trial for patients ages 5 to 60 years with newly diagnosed stage I/II HL, investigating the addition of brentuximab vedotin (Bv) with nivolumab compared to standard CT+/- RT. The primary objective is to compare PFS of patients treated through a response-adapted, superiority design with either standard or IO (i.e. BV/Nivo) therapies. There are 11 secondary and exploratory study aims. 12-year OS is a key secondary aim. AHOD2131 was activated in April 2023 with a target enrollment of 1875 patients over 5 years.

Patients are initially stratified as favorable or unfavorable risk. All patients receive 2 cycles of ABVD followed by interim PET2 (central review). Patients who are PET2 positive (slow early response [SER]) undergo separate randomizations compared to those who are PET2 negative (rapid early response [RER]). SERs receive involved site RT after completion of further systemic therapy while those with RER receive systemic therapy only (Figure).

Results: As of 28 April 2026, 395 sites have activated, and 838 participants have enrolled. To date, 49% are <18 years old and 65% are ES unfavorable risk.

Conclusion: This COG-led pan-NCTN trial will be the largest study for ES HL in the history of NACGs. AHOD2131 strengthens the effort between NACGs to conduct collaborative clinical trials and aims to harmonize an improved standard of care for ES HL across the age continuum.

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P088: Individualizing Consolidative Radiotherapy in Intermediate-Stage Hodgkin Lymphoma: A PET-Residual Re-Planning Analysis of Patients from the GHSG HD17 Trial

David Rene Steike¹, Michael Oertel¹, Patrick Hölken¹, Sebastian Lohmann¹, Nick Schulze², Johannes Rosenbrock³, Michael Fuchs², Dirk Vordermark⁴, Rita Engenhardt-Cabilic⁵, Klaus Herfarth⁶, Heinz Schmidberger⁷, Peter Lukas⁸, Christian Baues⁹, Bouthaina Dabaja¹⁰, Peter Borchmann², Hans Theodor Eich¹

¹University Hospital of Muenster, Department of Radiotherapy – Radiooncology, Muenster, Germany, ²Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf, Faculty of Medicine and University Hospital Cologne, University of Cologne, Germany, ³Department of Radiation Oncology and Cyberknife Center, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany, ⁴Department of Radiotherapy, Faculty of Medicine, Martin Luther University Halle-Wittenberg, Halle (Saale), Germany, ⁵Department of Radiotherapy, University Medical Center Giessen-Marburg, Marburg, Germany, ⁶Department of Radiation Oncology, Heidelberg University Hospital, Heidelberg, Germany, ⁷Department of Radiation Oncology, University Medical Center Mainz, Mainz, Germany, ⁸Department of Radiation Oncology, University of Innsbruck, Innsbruck, Austria, ⁹Department of Radiation Oncology, Marienhospital Herne, Ruhr University Bochum, Bochum, Germany, ¹⁰The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

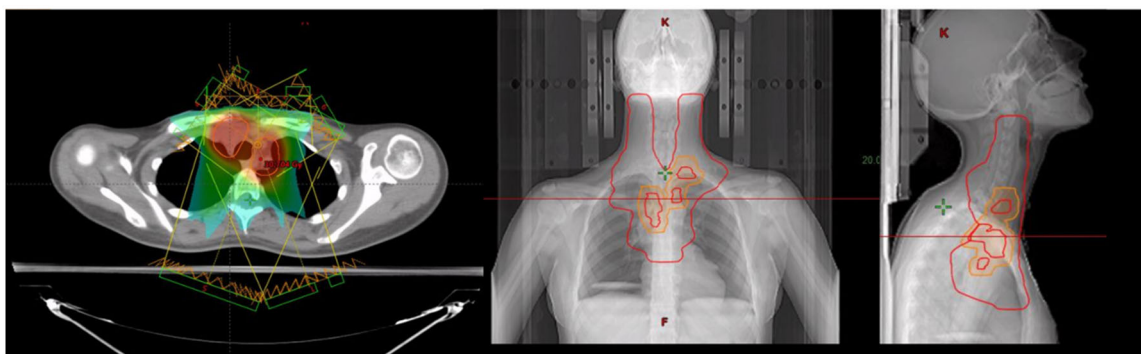


Figure 1: Example of focal PET-residual radiotherapy re-planning. PET-positive residual sites were delineated and expanded with a small safety margin, adapted to adjacent anatomy, as shown in axial CT and coronal/sagittal projection views.

Background: In intermediate-stage Hodgkin lymphoma, consolidative radiotherapy (RT) is increasingly challenged by chemotherapy-only strategies. In the GHSG HD17 trial, patients with PET-positive residuals after chemotherapy received involved-node radiotherapy (INRT) with 30 Gy. However, further limitation of RT field to focal RT to PET+ residuals has not been tested, yet. We therefore performed an exploratory post-hoc re-planning analysis comparing standard INRT with focal PET-residual RT.

Methods: Overall, 21 patients (16 female, 5 male) from the GHSG HD17 trial were evaluated. For each patient, the original INRT plan was compared with a focal PET-based re-plan using the PET/CT after four cycles of chemotherapy (2x eBEACOPP followed by 2x ABVD). Focal target volumes included PET-positive residual sites with a small anatomy-adapted margin of approximately 0.8–1.2 cm. Dose-volume histogram endpoints were assessed for target volume and organs at risk, including heart, lungs, esophagus, thyroid, spinal canal, liver and, where applicable, female breast. Paired comparisons used a two-sided Wilcoxon signed-rank test. Relapse patterns were reviewed in relation to the original and focal fields.

Results: Focal PET-based re-planning reduced mean PTV from 1194.0 cm³ to 87.0 cm³, corresponding to a 92.7% reduction ($p < 0.001$). Organ-at-risk exposure was significantly reduced, including mean heart dose from 9.6 Gy to 1.5 Gy, esophageal dose from 20.9 Gy to 4.0 Gy, thyroid dose from 22.7 Gy to 2.9 Gy, spinal canal maximum dose from 29.1 Gy to 11.3 Gy, and mean total lung dose from 9.4 Gy to 2.3 Gy (all $p < 0.001$). Total lung V20 decreased from 46.1% to 11.2% ($p < 0.001$). In female patients, total breast mean dose decreased from 4.1 Gy to 0.6 Gy ($p = 0.016$). Two patients later relapsed: one in-field relapse two months after therapy completion, which would have been covered by the focal PTV, and one abdominal relapse outside the thoracic irradiation field after one year.

Conclusion: In patients from the GHSG HD17 trial, focal PET-based radiotherapy re-planning reduced target volume by 90% and relevant organ-at-risk dose. There was no recurrence adjacent to the involved regions which would have been covered by INRT but missed by focal RT-only. PET-residual fields therefore merit prospective evaluation as a potential RT de-escalation strategy, with mature relapse-pattern data required before clinical implementation.

P089: Real-world implementation of a modified PET-adapted HD17 approach in early-stage Hodgkin lymphoma: a single-centre audit

Athanasia Sinti Papadaki¹, Rory Morrice¹, Kirit Ardeshtna¹, Kate Cwynarski¹, Satyen Gohil¹, Irfan Kayani², Suganya Sivabalasingham³, Jonathan Lambert¹, Christopher McNamara¹, Sajir Mohamedbhai¹, Michael Northend¹, Hassan Al-Sader¹, Asma Batool¹, Ingo Ringshausen¹, Ali Rismani¹, Andres Virchis¹, William Townsend¹, Maria Marzolini¹

¹Department of Haematology, University College London Hospitals NHS Foundation Trust, London, United Kingdom, ²Institute of Nuclear Medicine, University College London Hospitals NHS Foundation Trust, London, United Kingdom, ³Department of Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom

Background: Intermediate risk classical Hodgkin lymphoma (HL) has excellent outcomes, but radiotherapy (RT) contributes to late toxicity. The GHSG HD17 trial demonstrated that RT can be omitted in PET4-negative patients after escalated BEACOPP×2 and ABVD×2. We evaluated real-world feasibility, safety and early outcomes of a PET-adapted HD17 approach at University College London Hospital using an interim PET2 (iPET2) in a subgroup of patients and substituting procarbazine with dacarbazine.

Methods: We retrospectively evaluated patients with early-stage HL treated with an HD17-based approach between August 2022 and September 2025. Patients received escalated BEACOPP×2 followed by iPET2, performed according to multidisciplinary team decision, with aim to avoid RT. Deauville scores 1–3 were considered negative (neg), in contrast to the HD17 trial definition of Deauville scores 1–2 as negative, and 4–5 positive (pos). End-of-treatment (EoT) PET4 response, RT use, toxicity, relapse and survival were reviewed to 1 April 2026.

Results: 40 patients were included; median age was 23.5 years. 39 had intermediate-stage disease and 1 had early favourable disease but was treated with this approach to avoid RT for mediastinal disease. iPET2 was performed in 28/40 patients (70%); 23/28 (82%) were PET2-neg and de-escalated to ABVD×2, all achieving PET4 complete metabolic response (CMR). 5 were PET2-pos; 2 received additional escalated BEACOPP×4 (HD18 approach), both were EOT PET-pos and 1 required salvage chemotherapy to CMR. 3 PET2-pos patients de-escalated to ABVD×2; 2 achieved PET4 CMR, 1 was PET4-pos and received RT to CMR. 12 patients did not undergo iPET2; all followed standard HD17 approach, with 1 PET4-positive patient requiring RT to CMR. Overall, PET4 CMR was achieved in 36/40 patients (90%) including 26/28 patients (93%) who underwent iPET2. PET4 positivity was confined to mediastinal disease and occurred mainly in the iPET2-pos group. Post-EoT RT was delivered to 1/28 patients (4%) undergoing iPET2 and 2/40 patients (5%) in total cohort. Grade 3–4 toxicity occurred in 20/40 patients, predominantly during escalated BEACOPP×2. With median follow-up of 17 months, 39/40 patients were in CMR, 1 relapsed and overall survival was 100%.

Conclusion: PET-adapted HD17 management achieved high EoT PET negativity with minimal RT use: no iPET2-neg patients were PET4-pos, while 96% avoided RT and 93% achieved PET4 CMR. iPET2 may identify high risk patients in whom HD18 approach can be a RT sparing alternative.

P090: Omission of Radiotherapy is Associated with Inferior Progression-Free Survival in Bulky and Interim-PET-Positive Early-Stage Hodgkin Lymphoma: A Propensity-Matched Multicenter Real-World Analysis

Alexandra Dreyfuss^{1,2}, Nikita Dave³, Alison Moskowitz⁴, Joachim Yahalom¹, Maria Alfaro⁵, Nicole Birrer⁶, Boyu Hu⁶, Rachel Koch⁷, Zachary Frosch⁷, Meryl Colton⁸, Carrie Ho⁸, Behzad Amoozgar⁹, Tatyana Feldman⁹, Abhiraj Saxena¹⁰, Joanna Rhodes¹⁰, Ashley Dunton¹¹, Nirav Shah¹¹, Amelia Mantione¹², Harper Hubbeling¹³, Michael Lariviere¹³, John Plastaras¹³, Beatrice Desai¹, Brandon Imber¹, Reid Muenzen¹⁴, Stefan Barta³, Jordan Carter³, Elise Chong³, Michael Cook³, Daniel Landsburg³, Sunita Nasta³, Stephen Schuster³, Colin Thomas³, Emily Tomasulo³, Jakub Svoboda³

¹Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, ²Department of Radiation Oncology, Sylvester Cancer Center, University of Miami, Miami, FL, ³Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, ⁴Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, ⁵Department of Biostatistics, Epidemiology and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, ⁶Division of Hematology and Hematologic Malignancies, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, ⁷Department of Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, PA, ⁸Hematology, Blood & Marrow Transplant, and Cellular Therapy Program, Department of Hematology/Oncology, University of California San Francisco, San Francisco, CA, ⁹John Theurer Cancer Center, Hackensack Meridian Health Hackensack University Medical Center, Hackensack, NJ, ¹⁰Division of Blood Disorders, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, ¹¹Medical College of Wisconsin Cancer Center, Brookfield, WI, ¹²Drexel University College of Medicine, Philadelphia, PA, ¹³Department of Radiation Oncology, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, ¹⁴Department of Hematology/Oncology, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

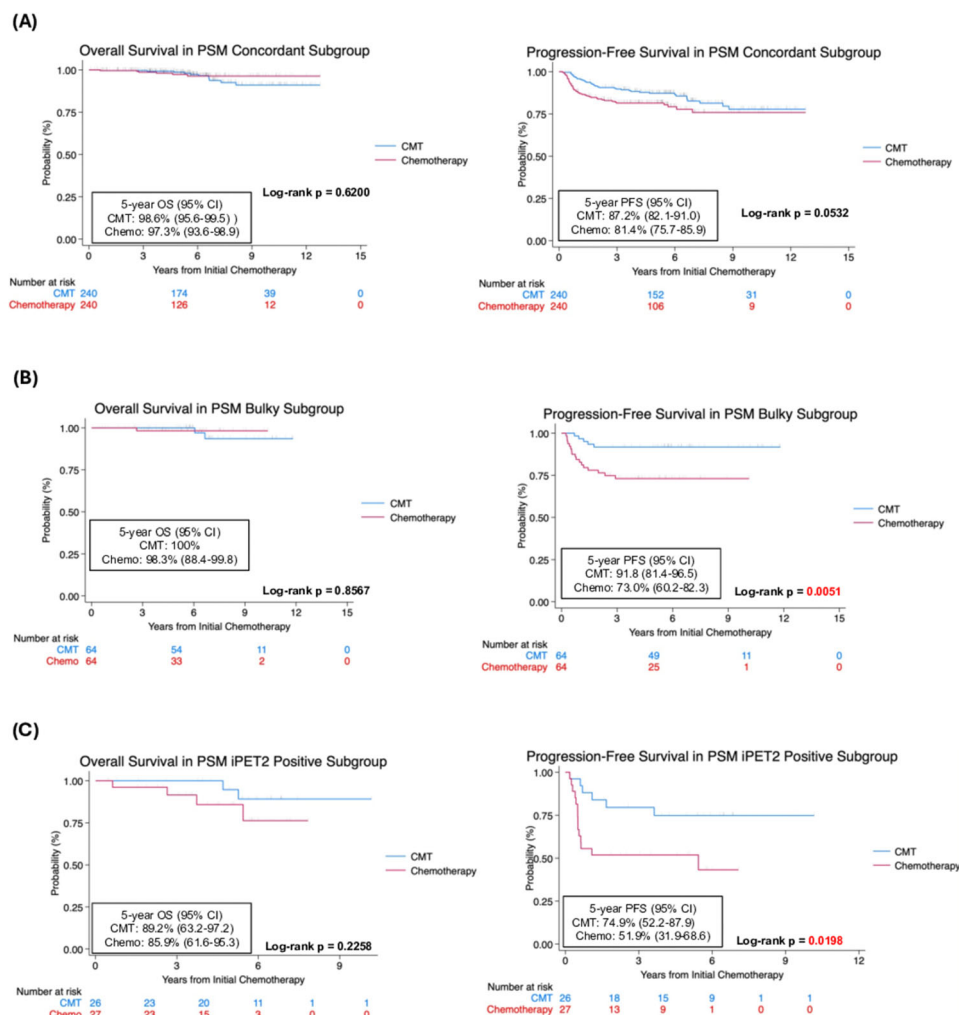


Figure 1: (A) OS and PFS in PSM concordant subgroup; (B) OS and PFS in PSM bulky subgroup; (C) OS and PFS in PSM iPET2 positive subgroup. RT at the outset.

Background: The role of consolidative radiotherapy (RT) in early-stage classic Hodgkin lymphoma (cHL) remains debated, particularly in the era of PET-adapted therapy. We evaluated real-world treatment patterns, outcomes, and toxicity of combined modality therapy (CMT; chemotherapy and RT) v chemotherapy alone.

Methods: We identified 810 consecutive patients with stage I-II cHL treated at eight academic centers between 2012 and 2020. Treatment was analyzed by intention-to-treat. Propensity score matching (PSM) by age, stage, sex, and prognosis (favorable v unfavorable per NCCN) yielded 480 patients for comparison of CMT (N = 240) vs chemotherapy alone (N = 240). Progression-free survival (PFS) and overall survival (OS) were estimated by the Kaplan-Meier method. Subgroups were assessed by disease bulk and interim PET (iPET2) Deauville score (DS).

Results: Median age of the entire cohort was 33 (range 18–84); 436 (54%) were female. By intention-to-treat, 300 (37%) received CMT and 510 (63%) chemotherapy alone, with 90% receiving A(B)VD-based regimens. At median follow-up of 5.4 years, 5-year PFS and OS for the full cohort were 82% and 98%, respectively. In the PSM cohort, 5-year OS did not differ between CMT and chemotherapy alone (99% v 97%; $p = 0.620$), but trended towards improved PFS with CMT (87% v 81%; $p = 0.053$; Figure 1A). CMT improved PFS in bulky disease (92% v 73%; Hazard Ratio [HR] 3.8, 95% CI 1.4–10.2; $p = 0.005$) and iPET2 DS ≥ 4 (75% v 52%; HR 3.0, 95% CI 1.1–7.8; $p = 0.020$; Figure 1B-C). Patients receiving CMT were less likely to relapse at sites of prior disease (7% v 18%; $p < 0.001$). iPET2 DS4-5 was associated with inferior 5-year PFS (46%) v DS1-2 (92%) and DS3 (79%; $p < 0.001$). Among iPET-positive patients, those who received unplanned consolidative RT were less likely to require salvage therapy than those treated with chemotherapy escalation alone (29% v 45%; $p = 0.037$). CMT was associated with higher rates of hyperlipidemia, hypothyroidism, and second malignancy, though 69% of second malignancies occurred outside the RT field. Pulmonary fibrosis was more common with $6 \leq 4$ cycles of bleomycin (4% v 0.4%; $p = 0.008$) and when it occurred resulted in worse 5-year OS (50% v 99%; $p < 0.001$).

Conclusion: In this large cohort, CMT and chemotherapy alone yielded comparable OS, but CMT conferred a PFS advantage in bulky or iPET2-positive (DS ≥ 4) disease. These findings support a risk-adapted approach in which consolidative RT is preferentially considered for high-risk subgroup.

P091: Characteristic of patients with a positive end of treatment PET or experiencing early relapse despite interim PET negativity: analysis from the EORTC-LYSA-FIL H10 trial

Luigi Rigacci¹, Wouter Plattel², Marc André³, Luigi Marcheselli¹, Berthe Aleman², Umberto Ricardi¹, Caterina Christinelli³, Manuel Gotti¹, Alessandro Re¹, Martin Hutchings², Véronique Edeline³, Monica Bellei¹, Francesco Merli¹, Aspasia Stamatoulas³, Sanne Tonino², Vincent Ribrag³, Barbara Botto¹, Massimo Federico¹

¹FIL, ²EORTC, ³Lysa

Introduction: Assessment with early positron emission tomography (ePET) is an important predictor of outcome in both limited and advanced stages. The EORTC-LYSA-FIL 20051 H10 trial included patients with untreated favourable and unfavourable localized stage HL patients. The H10 trial was designed to establish whether in ePET negative patients (after two cycles of ABVD) radiotherapy could be safely omitted. The aim of this analysis is to evaluate the clinical characteristics and outcome of the subset of patients who were ePET negative but had either a positive end-of-treatment (EoT) PET or experienced early relapse, regardless of treatment arm.

Methods: We evaluated all patients who had a negative ePET in both the standard and experimental arms. Considering the accrual period of the study population, October 2006 and July 2009, the evaluation of the response at EoT was done according to the 1999 Cheson criteria. Very few patients had been evaluated with an EoTPET. We compared the characteristics of patients with negative ePET that maintained in remission with patients with negative ePET but who had early treatment failure. Early treatment failure was defined as either a positive EoT PET or progressive disease or start of new treatment within 6 months of EoT.

Results: Of 1925 eligible patients 1402 had a negative ePET. Of these, 1064 (76%) achieved a CR/CRu and 59 (4.2%) had early treatment failure. The remaining 279 patients with a partial response did not progress or start second line treatment. By comparing the characteristics of those who maintained in remission versus early relapses we identified significant differences and a multivariate logistic regression analysis showed that stage II with an OR of 2.67 (95% CI 1.54–4.63) and bulky disease defined by MT ratio with an OR 2.24 (95% CI 1.51–3.33) are associated with worse outcome. The overall survival analysis showed that considering patients with an ePET negative early relapse had a significantly worse OS (86%) versus patients maintaining in remission (97%, $p < .001$). Survival was not significantly different among patients with an early relapse and a positive interim PET (86% vs 89%).

Conclusions: While a negative ePET is associated with a favorable prognosis in early stage HL, a small subgroup of patients experience early relapse with stage II disease and MT ratio >0.35 as independent risk factors for early relapse. In concordance with data on patients in advanced stage HL, early relapse among ePET.

Living beyond lymphoma

T092: Patients with a history of Hodgkin lymphoma have lower quality of life than matched comparators regardless of time elapsed since diagnosis

Sissel Johanne Godtfredsen¹, Joachim Baech¹, Mikkel Porsborg Andersen^{2,3,4}, Harman Yonis⁵, Paw Jensen^{6,7}, Peter Kamper⁸, Jacob H. Christensen⁹, Rasmus Bo-Dahl Sørensen¹⁰, Martin Hutchings^{11,12}, Christian Torp-Pedersen^{4,13}, Peter Sogaard^{1,7}, Henrik Boggild^{13,7,14}, Kristian H. Kragholm^{1,7}, Tarek C. El-Galaly^{8,15,16,17}

¹Department of Cardiology, Aalborg University Hospital, ²The Prehospital Center, Region Zealand, Naestved, Denmark, ³Department of Health Science and Technology, Aalborg University, Aalborg, Denmark, ⁴Copenhagen University Hospital, Steno Diabetes Center Copenhagen, Herlev, Denmark, ⁵The Department of Cardiovascular Surgery, Aalborg, Denmark, ⁶Department of Hematology, Clinical Cancer Research Center, Aalborg University Hospital, Aalborg, Denmark, ⁷Department of Clinical Medicine, Aalborg University, Aalborg, Denmark, ⁸Department of Hematology, Aarhus University Hospital, Denmark, ⁹Department of Hematology, Odense University Hospital, Odense, Denmark, ¹⁰Department of Hematology, Zealand University Hospital, Roskilde, Denmark, ¹¹Department of Hematology, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark, ¹²Department of Clinical Medicine, University of Copenhagen, Denmark, ¹³Department of Public Health, University of Copenhagen, Denmark, ¹⁴Research Data and Biostatistics, Aalborg University Hospital, Aalborg, Denmark, ¹⁵Department of Molecular Medicine, Aarhus University Hospital, Denmark, ¹⁶Department of Clinical Epidemiology, Aarhus University Hospital, Denmark, ¹⁷Department of Medicine Solna, Clinical Epidemiology Division, Karolinska Institutet, Stockholm, Sweden

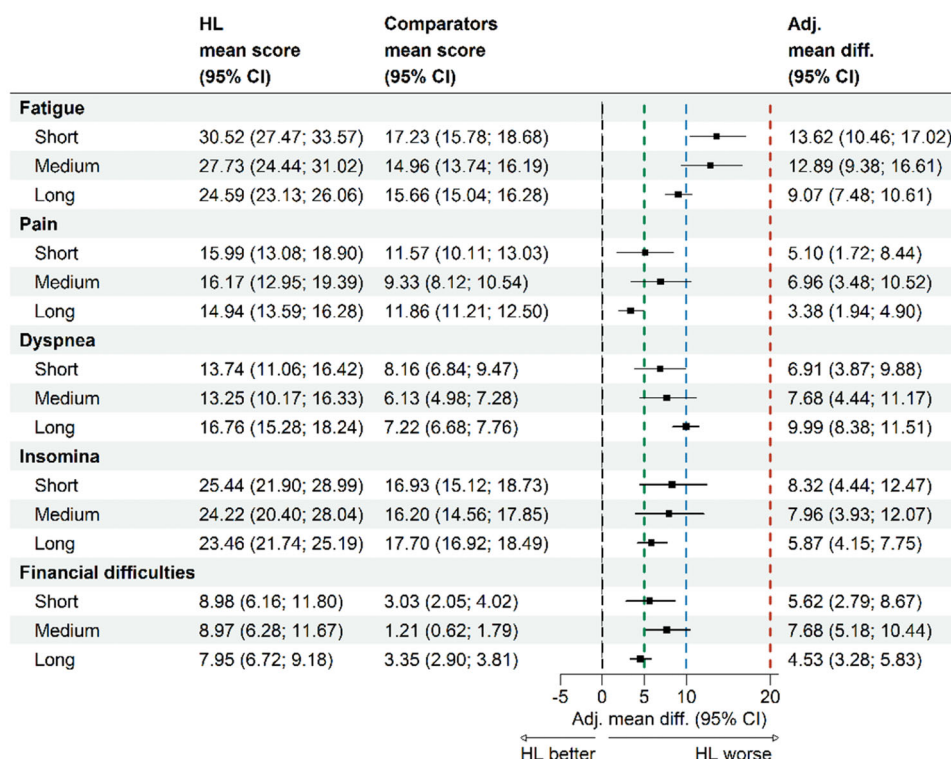


Table 1: EORTC QLQ-C30 selected symptom score means (scale: 0–100, higher= worse symptoms) and adjusted mean differences for the HL group stratified by time since diagnosis (short, medium, long). The colored lines marks minimal clinically relevant differences.

Background: Modern treatment strategies have led to excellent survival rates for Hodgkin lymphoma (HL); however, the long-term burden of the disease remains a concern. This study examines health-related quality of life (QoL) in individuals with HL compared to a matched general population cohort, with a specific focus on time since HL diagnosis.

Methods: A cross-sectional digital survey was conducted, inviting all patients with a history of HL in Denmark and up to 10 age- and sex-matched general population comparators per patient. QoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Core-30 questionnaire (QLQ-C30). Adjusted mean differences (MD) between groups were calculated using linear regression, adjusted for age and sex, and stratified by time since HL diagnosis: 0–5 years (short follow-up [FU]), >5–10 years (medium FU), and >10 years (long FU). Minimal clinically important difference (MCID) thresholds were defined as small (MD >5–10 points), moderate (MD >10–20 points), and large (MD >20 points).

Results: The final study population included 1,519 individuals with a history of HL (37% of 4,156 invited) and 5,110 comparators (12% of 41,558 invited). By time since diagnosis, 245 individuals were in the short group (with 703 comparators), 234 in the medium group (with 718 comparators), and 1,040 in the long group (with 3,689 comparators). Median time since HL diagnosis was 16 years (IQR: 8–28). QoL was clinically meaningfully lower than in patients with a history of HL compared to comparators across all time strata (QLQ-C30 summary score for short FU: 84 [95% CI: 82–86] vs. 91 [95% CI: 91–92]; medium: 85 [95% CI: 83–87] vs. 93 [95% CI: 92–93]; long: 86 [95% CI: 85–87] vs. 92 [95% CI: 91–92]). Patients with previous HL reported clinically meaningfully higher levels of fatigue, dyspnea, pain, insomnia, and financial difficulties than comparators (Table 1). Notably, fatigue levels appeared to improve with increasing time since diagnosis, whereas dyspnea appeared to worsen over time.

Conclusion: A history of HL was associated with a persistent QoL gap compared to age- and sex-matched general population comparators. The enduring nature of these deficits suggests the need for specialized survivorship initiatives.

T093: The MyHodgkin MyHealth App: patient-derived data for tracking Hodgkin Lymphoma survivorship

Nicole Wong Doo^{1,2}, Angeline A. Josiah¹, Georgia Klemm¹, Lara Meli³, Alisha Ganesh¹, Ibrahim Tohidi-Esfahani^{1,2}, Janlyn Falconer¹, Ryan Low⁴, Patrick Lawrence⁵, Pietro R. Di Ciccio^{6,7}, Eve Propper³, Nicole Weekes⁸, Elizabeth Harris⁸, Nathan Chapman⁹, Sharon Winton⁸, Judith Trotman^{1,2}

¹Concord Repatriation General Hospital, Sydney, Australia, ²University of Sydney, Sydney, Australia, ³Consumer Investigator, ⁴University College Hospital London, ⁵Princess Alexandra Hospital, Brisbane, Australia, ⁶Department of Haematology, The Canberra Hospital, Garran, ACT, Australia, ⁷College of Health and Medicine, ⁸Lymphoma Australia, ⁹Pixelscope Pty Ltd

Background: Very long term follow up (LTFU) after HL therapy remains essential to track long-term sequelae. Ideal features of a LTFU tool include longitudinal design, reach to diverse populations, capture of patient-reported outcomes (PROs), sustainability and patient acceptability. The MyHodgkin MyHealth (MHMH) App (ANZCTRN12624001013550) was developed in partnership with HL consumers to meet these needs.

Methods: MHMH participants download the App to review study information and self-consent in-app. Access to the Pilot is limited within Australia. The.NET MAUI cross-platform App feeds separate encrypted Amazon Web Server databases keeping identifiable information separate from responses to questionnaires. Baseline survey results are presented here; longitudinal follow-up and PRO modules will go live in Q3-4 2026.

Results: MHMH launched in March 2025. As of 12 June 2026, 300 participants are enrolled, 231 have entered survey data. Of these, 77.5% baseline surveys are complete. Age at diagnosis was median 37.5 y (range 14.7–83.8 y). Residence was metropolitan (68.9%), regional/rural (27.8%), remote (1%). Median time from diagnosis to enrolment was 42.5 mths (range 2.1 m–53 y). First line treatment was reported in 225/231: chemo alone (64.4%), chemo/radiotherapy (25.8%), chemo/immunotherapy (4.4%), chemo/immuno/radiotherapy (1.3%), radiotherapy (2.2%). First-line chemo regimen was reported in 199: 117 (58.8%), received ABVD, 40 (20.1%) escBEACOPP, other in 17, and 20 unsure. In 23/193 respondents there were 32 second cancer events: non-melanoma skin cancer (10), non-Hodgkin lymphoma (5) and lung (3), breast (3) and thyroid (2) cancers. There was an association between radiotherapy and developing a second cancer (OR 2.45, 95% CI 1.01–5.94, $p = 0.03$). In 192 respondents, 26 self-reported a new or worsening lung condition since completing HL therapy, with a trend toward an association with radiotherapy (OR 2.24, 95%CI 0.96–5.19, $p = 0.07$) but not bleomycin (OR 0.8, 95%CI 0.32–1.98, $p = 0.64$). Regarding neuropathy, 120/192 (65.5%) self-reported experiencing neuropathic symptoms after treatment.

Conclusion: MHMH demonstrates proof of concept of a mobile App platform developed in close partnership with HL consumers, putting HL research into the hands of survivors. Recruitment is ongoing and future plans include integration of MHMH as a PRO and LTFU tool in clinical trials is planned and scale-up to global research populations.

P094: Evidence of Statistical Cure for Hodgkin Lymphoma With Contemporary Treatment: A Non-mixture Cure Model Analysis

Jie Chen¹, Yunhong Huang², Ming Jiang³, Zhihua Yao⁴, Yue Wang¹, Wenhui Zhang¹, Jun Zhu¹, Yuqin Song¹, Shujuan Wen⁵, Yunfei Shi⁶, Weiping Liu¹

¹Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Lymphoma, Peking University Cancer Hospital & Institute, Beijing 100142, China, ²The Affiliated Cancer Hospital of Guizhou Medical University, Guiyang, China, ³Department of Medical Oncology, Cancer Center and State Key Laboratory of Biotherapy, West China Hospital of Sichuan University, Chengdu, Sichuan, China, ⁴Department of Internal Medicine, Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, Henan, China, ⁵Xinjiang Medical University Affiliated Tumor Hospital, Wulumuqi, China, ⁶Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Pathology, Peking University Cancer Hospital & Institute, Beijing, China

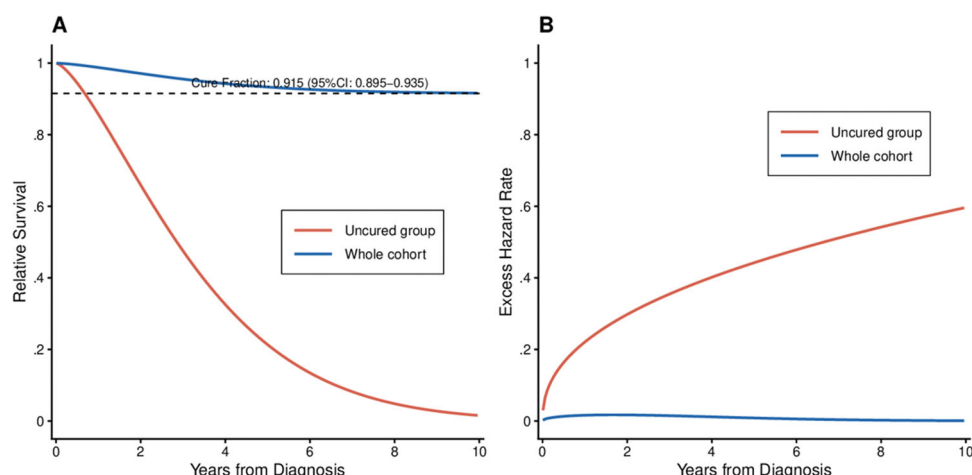


Table 1: Mixture cure model estimates of relative survival and excess hazard rate following diagnosis.

Background: Whether patients with Hodgkin lymphoma (HL) achieve statistical cure in the modern treatment era remains incompletely characterized. The current study was aimed to estimate overall and subgroup-specific cure fractions, determine cure time, and validate 5-year overall survival (OS) as a surrogate for cure fraction in a large multicenter cohort.

Methods: A total of 1,164 HL patients treated between 1996 and 2020 were enrolled. Relative survival was estimated using the Ederer II method with reference to Chinese national life tables. Statistical cure was assessed using a non-mixture cure model; cure fractions were estimated across 13 predefined clinical subgroups. Linear regression evaluated associations between landmark OS rates and cure fractions.

Results: Over a median follow-up of 7.2 years, 166 patients (14.3%) died. The estimated overall cure fraction was 91.5% (95% CI, 89.5%–93.5%), with a cure time of approximately 4 to 5 years. Cure fractions varied substantially across subgroups: age ≥ 60 years (78.7% vs. 93.0%; $\Delta = 14.3$ pp), advanced-stage disease (86.5% vs. 96.1%; $\Delta = 9.6$ pp), ECOG performance status ≥ 2 (83.6% vs. 93.1%; $\Delta = 9.5$ pp), and B symptoms (86.8% vs. 95.8%; $\Delta = 9.0$ pp). In multivariate analysis, advanced-stage disease (adjusted OR = 0.372; $P = 0.013$) and older age (per 10-year increment; adjusted OR = 0.454; $P < 0.001$) were the independent determinants of reduced cure probability. The 5-year OS rate demonstrated the strongest correlation with subgroup-specific cure fractions ($R^2 = 0.92$; $P < 0.001$).

Conclusions: This study provides the first comprehensive population-level evidence of statistical cure in patients with HL, establishing a cure fraction of 91.5% and a cure time of 4 to 5 years. The 5-year OS constitutes a valid surrogate for cure fraction, with direct implications for clinical trial design and individualized survivorship care planning.

Keywords: Hodgkin lymphoma; Statistical cure; Cure model; Relative survival; Conditional survival; Cure fraction.

P095: Chemotherapy-induced peripheral neuropathy and quality of life among Hodgkin lymphoma survivors treated at an older age - A national cross-sectional study

Renate B. Galleberg^{1,2}, Kjersti Lia³, Unn Merete Fagerli^{4,5}, Idu B. Bø^{6,7}, Knut B. Smeland⁸, Siri Rostoft^{9,10}, Marianne J. Hjermsstad^{11,12,13}, Jeanette Johansen¹⁴, Sameer Bhargava^{15,16}, Cecilie E. Kiserud^{11,12,13}, Kari Sørland¹⁷, Floortje Mols^{18,19}, Øystein Fluge^{1,2}, Alexander Fossa^{11,20}

¹Cancer Clinic, Haukeland University Hospital, Bergen, Norway, ²Department of Clinical Science, University of Bergen, Bergen, Norway, ³Medical Department, Bærum Hospital, Vestre Viken Hospital Trust, Gjetsum, Norway, ⁴Department of Oncology, St. Olavs Hospital, Trondheim, Norway, ⁵Institute of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway, ⁶Stavanger University Hospital, Stavanger, Norway, ⁷Institute of Clinical Medicine 2, University of Bergen, Bergen, Norway, ⁸Department of Oncology, Oslo University Hospital, Oslo, Norway, ⁹Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway, ¹⁰Department of Geriatric Medicine, Oslo University Hospital, Oslo, Norway, ¹¹Department of Oncology, Oslo University Hospital, Oslo, Norway, ¹²Department of Oncology, European Palliative Care Research Centre (PRC), Oslo University Hospital, Oslo, Norway, ¹³Institute of Clinical Medicine, University of Oslo, Oslo, Norway, ¹⁴Department of Oncology, University Hospital of North Norway, Tromsø, Norway, ¹⁵Cancer Registry of Norway, Norwegian Institute of Public Health, Oslo, Norway, ¹⁶South-Eastern Norway Regional Health Authority, Oslo, Norway, ¹⁷Cancer Clinic, Haukeland University Hospital, Bergen, Norway, ¹⁸Department of Research and Development, Netherlands Comprehensive Cancer Organisation, Utrecht, The Netherlands, ¹⁹CoRPS - Center of Research On Psychological Disorders and Somatic Diseases, Department of Medical and Clinical Psychology, Tilburg University, Tilburg, The Netherlands, ²⁰KG Jebsen Centre for B-cell Malignancies, University of Oslo, Oslo, Norway

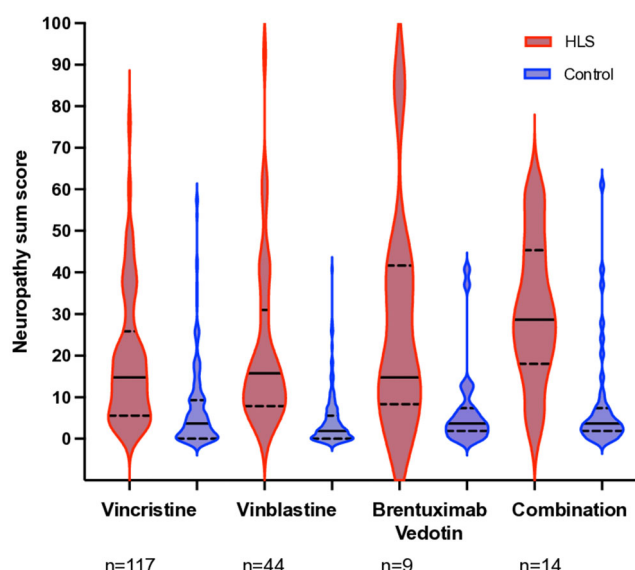


Figure 1: Neuropathy sum score by neurotoxic agent in Hodgkin lymphoma survivors and their controls. Solid and dotted lines represent the median and interquartile range respectively. N denotes number of survivors who have received the relevant neurotoxic agent.

Background: Chemotherapy induced peripheral neuropathy (CIPN) is a potentially debilitating long-term side effect of Hodgkin lymphoma (HL) treatment that can impact health and lead to a reduced quality of life. In this national cross-sectional study, we evaluated the prevalence and severity of CIPN among older tumor-free HL survivors (HLSs) at a median of 8 years after diagnosis.

Methods: Two hundred and ninety HLSs aged >60 years at diagnosis were invited to participate and 193 (67%) completed a 95-item questionnaire including patient-reported outcome measures assessing physical and mental health related quality of life (HRQoL), fatigue, activities of daily living and anxiety/depression. CIPN was assessed via the validated European organisation for research and treatment of cancer, quality of life questionnaire for chemotherapy-induced neuropathy 20 (EORTC QLQ-CIPN20). Findings were compared to a Dutch age- and sex-matched control population. Details regarding treatment were extracted from patient records.

Results: Of the consenting participants 185 (96%) had received at least one treatment regimen containing a potentially neurotoxic compound. At a median of 8 years after diagnosis, HLSs reported a significantly higher neuropathy sum score (NSS) than controls (20.8 versus 7.4, $p < 0.001$), irrespective of the neurotoxic agent received (vincristine, vinblastine, brentuximab vedotin or combinations thereof). Dose reductions due to treatment-emergent CIPN was most commonly done in patients receiving vincristine. Development of CIPN CTCAE grade ≥ 1 during treatment or CIPNCTCAE ≥ 2 one year or more after treatment predicted a higher NSS at time of survey. Multivariable regression analysis showed a significant association between the total doses of neurotoxic drugs received and NSS, most clearly related to the dose of vincristine. Also, a higher total comorbidity score at survey was positively correlated with NSS. Survivors with higher CIPN symptom burden were significantly more fatigued, had higher levels of anxiety and depression and lower HRQoL at survey, but showed similar levels of independence in functions of daily life.

Conclusion: Older HLSs report dose-dependent higher CIPN symptom burden compared to controls at a median of 8 years after treatment. Neuropathy symptom burden was associated with worse fatigue, anxiety, depression and HRQoL, highlighting the long-term impact of treatment-related neuropathy on survivorship outcomes.

P096: Frailty as a predictor of survival in older patients with classical Hodgkin lymphoma: A retrospective, multicenter study from the RELINF Spanish Lymphoma Registry of the GELTAMO Spanish Lymphoma Group

Eva Domingo-Doménech¹, Carmen Martínez Muñoz², Rosa María Rodríguez Nuñez³, Blanca Sánchez González⁴, Miriam Moreno⁵, David Alonso Castronuño⁶, María Jimena Cannata-Ortiz⁷, Pilar Gómez Prieto⁸, Laurentino Benito⁹, Tamara Torrado¹⁰, Joan Buch¹¹, Carolina Arevalo¹, Juan Carlos Caballero¹², Nazaret Dominguez¹³, Raquel Santiago¹⁴, Isabel González-Gascon¹⁵, María Moya Arnao¹⁶, Cecilia Carpio¹⁷, María Dolores Gutiérrez-Meca Maestre¹⁸, Luis Antonio López Gómez¹⁹, Eukene Gainza²⁰, María Rocio Figueroa Mora²¹, Paula Fernández-Caldas²², Paola Villafuerte Gutiérrez²³, Samuel Romero²⁴, Belén Navarro²⁵, Izaskun Zeberio Etxetxipia²⁶, Emilia Pardo²⁷, Antonio Gutiérrez²⁸, Eva Donato²⁹, Javier Nuñez³⁰, Teresa Cobo³¹, Ramón García Sanz²², María Isabel Gómez Roncero³², Cristina Barrenetxea³³, Haridán De La Nuez³⁴, Andrea Dorado López³⁵, Roberto Trelles³⁶, Luis Ignacio Sánchez Val³⁷, Sofía Martín-Consuegra³⁸, María Luisa Bengochea³⁹, Carmen María Alonso Prieto⁴⁰, Elena Ramila⁴¹, María Jesús Peñarubia⁴², Alfonso Ortiz⁴³, Ignacio Mahillo¹², Raul Córdoba⁴⁴

¹ICO. Hospital Duran i Reynals. Barcelona, ²Hospital Clínic de Barcelona, University of Barcelona, IDIBAPS, Barcelona, ³Hospital Universitario Álvaro Cunqueiro de Vigo, Instituto de Investigación Sanitaria Galicia-Sur, ⁴Hospital del Mar. Barcelona, ⁵ICO. Hospital Germans Trias i Pujol. Badalona, ⁶Hospital de Salamanca, ⁷Hospital de la Princesa. Madrid, ⁸Hospital La Paz. Madrid, ⁹Hospital Getafe. Madrid, ¹⁰Complejo Hospitalario Universitario de A Coruña, ¹¹ICO. Hospital Josep Trueta. Girona, ¹²Fundación Jiménez Díaz. Madrid, ¹³Hospital Virgen Macarena, Sevilla, ¹⁴Hospital de Manresa, ¹⁵Hospital Infanta Leonor, Madrid, ¹⁶Hospital Morales Meseguer, Murcia, ¹⁷Hospital Vall d'Hebron. Barcelona, ¹⁸Hospital Santa Lucía, Cartagena, ¹⁹Hospital Universitario Royo Villanova. Zaragoza, ²⁰Hospital Galdakao, Vizcaya, ²¹Clinica Universitaria de Navarra, ²²Hospital Gregorio Marañón, ²³Hospital Príncipe de Asturias, Alcalá de Henares. Madrid, ²⁴Hospital de Manises, Valencia, ²⁵Hospital Puerta de Hierro, Madrid, ²⁶Hospital Donostia, San Sebastián, ²⁷Hospital Virgen del Puerto, Plasencia, ²⁸Hospital Universitari Son Espases, Palma de Mallorca, ²⁹Hospital Universitario Doctor Peset, Valencia, ³⁰Hospital Marqués de Valdecilla, Santander, ³¹Hospital del Sureste, Arganda del Rey. Madrid, ³²Hospital Virgen de la Salud, Toledo, ³³Hospital de Basurto, Bilbao, ³⁴Hospital Doctor Negrín, Las Palmas de Gran Canaria, ³⁵Hospital Universitario Lucus Augusti, Lugo, ³⁶Hospital Fundación Alcorcón, Madrid, ³⁷Hospital Lozano Blesa, Zaragoza, ³⁸Hospital de Alcañiz, Teruel, ³⁹Hospital Severo Ochoa, Leganés. Madrid, ⁴⁰Hospital Arnau Vilanova, Valencia, ⁴¹Hospital Parc Taulí, Sabadell, ⁴²Hospital Clínico Valladolid, ⁴³Hospital HM Sanchinarro, Madrid, ⁴⁴MD Anderson Cancer Cancer, Madrid

Multivariate Analysis			
Variable	HR	(95% CI)	P
Treatment			
Standard	1.00		
Attenuated	0.78	(0.44-1.37)	0.375
Palliative	7.79	(4.06-15.0)	<0.001
ECOG			
0	1.00		
1	1.49	(0.84-2.66)	0.174
2	3.79	(1.86-7.72)	<0.001
3-4	8.32	(4.07-17.0)	<0.001
Smoker			0.002
Never	1.00		
Former	1.07	(0.67-1.70)	0.78
Current	2.80	(1.58-4.97)	0.001
Geriatric syndrome	5.90	(1.30-26.8)	0.022
Age at diagnosis	1.05	(1.01-1.08)	0.005
CIRS-G cardiologic 0	0.50	(0.28-0.89)	0.020
Hemoglobin >12 g/dL	0.89	(0.80-0.98)	0.020

Table 1: Multivariate Analysis.

Introduction: Survival among older patients with classical Hodgkin lymphoma (cHL) has improved in recent decades. However, outcomes remain poor in patients aged ≥ 70 years. Frailty has been associated with inferior outcomes and reduced treatment tolerance in hematologic malignancies. Although geriatric assessment is recommended to guide treatment decisions, its implementation in routine practice remains limited.

Objectives: To evaluate the impact of comorbidities and frailty on clinical outcomes in older patients with cHL included in the Spanish Lymphoma Registry (RELINF) of the GELTAMO group.

Methods: We conducted a retrospective multicenter study including 673 patients aged ≥ 60 years with cHL from 46 Spanish centers. Baseline characteristics, activities of daily living (ADL), instrumental activities of daily living (IADL), geriatric syndromes, and comorbidities were collected. Comorbidities were assessed using the Cumulative Illness Rating Scale-Geriatrics (CIRS-G). Statistical analyses were performed using R.

Results: Median age at diagnosis was 72 years (range, 60–93); 57.8% were male, 65.7% had advanced-stage disease, and 43.9% had extranodal involvement. CIRS scores were available for 417 patients (median, 4; range, 0–13). ADL impairment was present in 13.9%, IADL impairment in 17.7%, and geriatric syndromes in 14.4% of evaluated patients. In the univariate analysis, older age, cardiovascular disease, extranodal involvement, advanced stage, ECOG > 2, ADL and IADL impairment, geriatric syndromes, cardiac and psychiatric comorbidities were associated with worse overall survival. Among laboratory parameters, absolute lymphocyte count, hemoglobin, albumin, and erythrocyte sedimentation rate were associated with survival. No significant differences were observed among treatment approaches except for palliative regimens, which were associated with inferior survival (HR 11.5; 95% CI, 7.73–17.2; $p < 0.001$). In the multivariate analysis, age, ECOG performance status, anemia, geriatric syndromes, and palliative treatment remained independently associated with overall survival.

Conclusions: Functional reserve and resilience significantly influence survival in older patients with cHL. Comprehensive geriatric assessment should be systematically incorporated into routine clinical practice to identify frailty and patients at higher risk. More effective and safer therapeutic strategies are needed to improve outcomes in this population.

P097: The Psychological Impact of Lung Cancer Screening in Hodgkin Lymphoma Survivors

Morgan Brusven¹, Tania Seale¹, Kim Linton^{1,2}, Rachel Broadbent²

¹The University of Manchester, ²The Christie NHS Foundation Trust

Table 1: Mean Scores Over Time

	Baseline	Screening	2 months	6 months	12 months
SF-12 PCS	-0.22	X	X	-0.94	-1.41
SF-12 MCS	-0.94	X	X	0.51	0.28
STAI-6	37.43	34.11	30.78	34.86	35.81
BWS	12.31	12.66	12.19	11.57	11.73
RIES	4.07	4.04	3.04	3.01	4.22

Key: X – timepoint not collected

Table 1: provides the mean scores for each of the five questionnaires utilised in this study. It is broken down into when the scores were collected: baseline, screening, 2-, 6-, and 12- months post-LDCT, respectively.

Background: People previously treated for Hodgkin lymphoma (HL) are at increased risk of developing lung cancer. This study examined the psychological impact of receiving an invitation and undergoing lung cancer screening in HL survivors enrolled in a single-centre low-dose CT (LDCT) screening pilot.

Methods: One hundred and twenty-six HL survivors were invited to complete questionnaires measuring health-related quality of life (Short Form 12 (SF-12)); anxiety (State-Trait Anxiety Inventory (STAI-6)); severity of worry (Brief Worry Score (BWS)), and frequency of cancer worry (Revised Impact of Events (RIES)). Questionnaires were completed at invitation (baseline), pre-LDCT and 2, 6 and 12 months post-LDCT.

Results: Ninety-nine participants completed all questionnaires; a further 24 completed baseline questionnaires before declining further participation in the pilot. Three participants were diagnosed with lung cancer and did not complete follow-up questionnaires. The mean age of participants was 52, and the mean years since treatment completion was 21. 67% were never smokers. Cancer worry severity (BWS) was elevated at baseline and remained elevated during follow-up. Across all questionnaires, higher scores were observed among younger participants, those treated with ABVD chemotherapy compared to other chemotherapy regimens, and those with fewer years since treatment completion. Participants who completed baseline questionnaires only and did not undergo LDCT reported significantly higher baseline anxiety and cancer worry than those who underwent LDCT screening. Identification of indeterminate pulmonary nodules on LDCT was not associated with significant differences in psychological outcomes.

Conclusions: HL survivors demonstrated high cancer worry severity at baseline and over the 12 months following invitation to lung cancer screening. It remains unclear whether these levels reflect pre-existing cancer-related concern or are influenced by the screening process itself, showing a neutral impact on worry. Further research in larger, more diverse cohorts is needed to clarify the impact of lung cancer screening on cancer worry, anxiety, and quality of life and to inform supportive care strategies for this high-risk population.

P098: Impact of Exercise interventions during chemotherapy in functional capacity and patient-reported outcomes in patients with Hodgkin lymphoma

Maren Martinez De Rituerto Zeberio¹, Begoña Mendibil Esquisabel^{2,3}, Helena Goicoechea Pellejero¹, Mikel Tous Espelisin⁴, Iñigo Olazabal Eizaguirre^{2,3}, Jon Madinabeitia¹, June Iriondo Alzola^{2,3}, Sara Maldonado Martín⁵, Izaskun Zeberio Etxetxipia^{2,3}

¹Department of Physical Education and Sport, Faculty of Education and Sport, University of the Basque Country (UPV/EHU), Vitoria-Gasteiz, Basque Country, Spain
²Biopuzkoa Health Research Institute. Donostia-San Sebastian, Basque Country, Spain, ³Hematology Department, Donostia University Hospital. Donostia-San Sebastian, Spain, ⁴Department of Physical Education and Sport, Faculty of Education and Sport, University of the Basque Country (UPV/EHU), Vitoria-Gasteiz, Basque Country, Spain
⁵Bioaraba Health Research Institute, Physical Activity, Exercise, and Health group.

CLINICAL VARIABLES			TOTAL PATIENTS	GROUPS		PATIENTS DISAGGREGATED BY SEX		
			(n= 10)	Control (n = 6)	Intervention (n = 4)	Male (n = 2)	Female (n=8)	
Demographics	Age (median ± IQR)		44 [31, 50]	47 [34, 62]	38 [32, 44]	43 [34, 51]	44 [30, 58]	
	Sex (n, %)	Male	2 (20%)	0 (0%)	2 (50%)	-	-	
		Female	8 (80%)	6 (100%)	2 (50%)	-	-	
	Group (n, %)	Control	6 (60%)	-	-	0 (0%)	6 (75%)	
		Intervention	4 (40%)	-	-	2 (100%)	2 (25%)	
ANAMNESIS	Arterial Hypertension (n, %)	Yes	1 (10%)	1 (17%)	0 (0%)	0 (0%)	1 (13%)	
		No	9 (90%)	5 (83%)	4 (100%)	2 (100%)	7 (88%)	
	Diabetes mellitus (n, %)	Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
		No	10 (100%)	6 (100%)	4 (100%)	2 (100%)	8 (100%)	
	Dyslipidaemia (n, %)	Yes	1 (10%)	1 (17 %)	0 (0%)	0 (0%)	1 (13%)	
		No	9 (90%)	5 (83%)	4 (100%)	2 (100%)	7 (88%)	
	Hyperuricemia (n, %)	Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
		No	10 (100%)	6 (100%)	4 (100%)	2 (100%)	8 (100%)	

Physical Capacity	MSWT (median ± IQR)	Pic Heart rate	157 [137, 176]	140 [124, 151]	176 [171, 182]	181 [170, 191]	150 [131, 175]	
		Distance (m)	920 [625, 1005]	690 [365, 865]	1085 [1005, 1165]	1115 [1068, 1162]	850 [495, 960]	
	CARDIO (median ± IQR)	Pic Heart rate	150 [143, 165]	145 [140, 157]	159 [150, 173]	172 [161, 182]	148 [141, 162]	
		VO2 Relative	23.2 [20.6, 28.0]	21.01 [19.46, 23.93]	29.8 [26.4, 32.0]	32.4 [32.0, 32.9]	21.6 [20.0, 25.4]	
		VO2 Absolut	1.41 [1.25, 2.01]	1.27 [1.24, 1.41]	2.33 [1.88, 2.64]	2.67 [2.64, 2.71]	1.33 [1.24, 1.56]	
FATIGUE	QLQ-FA12 (median ± IQR)	Total	17 [14, 23]	14.0 [14.0, 23.0]	17.0 [16.5, 20.0]	22 [19, 26]	17 [14, 20]	
HM-PRO	Part A (median ± IQR)	Total	10 [8, 20]	10.0 [8.0, 15.0]	14.5 [8.8, 21.5]	17 [13, 22]	10 [9, 18]	
	Part B (median ± IQR)	Total	4 [2, 10]	2.0 [1.0, 10.0]	6.0 [3.8, 11.2]	12 [8, 17]	4 [2, 9]	

Group	Distance (m)		
	Delta (Δ)	IQR	
Control	55	85	
Intervention	80	195	
	Quality of life		
	HM PRO Part A	Part B	

Table 1: Patient characteristics and results.

Background: Exercise interventions (EI) during chemotherapy may improve functional capacity (FC) and patient-reported outcomes in patients with Hodgkin lymphoma (HL). However, the relationship between objective exercise performance, fatigue, and quality of life (QL) after treatment completion remains insufficiently characterized. The aim of this preliminary analysis from the EDONOLA study was to examine the subgroup of patients with HL and explore associations between functional capacity and QL outcomes.

Methods: QL questionnaires (HM-PRO and QLQ-FA12) and functional capacity assessments (Modified Shuttle Walk Test [MSWT] and Cardiopulmonary Exercise Testing [CPET]), were analysed. Patients were evaluated before (T0) and after (T2) ABVD CT combined with either an EI or usual care. Ten adults with HL requiring systemic treatment were included (mean age: 44 years; 80% female).

Descriptive statistics were used to summarize the data and are presented as medians and interquartile ranges (IQR). Changes from T0 to T2 were explored descriptively, and Spearman's rank correlation coefficients were calculated to assess associations.

Results: The EI group demonstrated greater improvements in FC than the control group. The median increase in MSWT distance was 80 m in the EI group compared with 50 m in the control group (Table 1).

Correlation analyses revealed weak-to-moderate associations between changes in FC and changes in QL for fatigue, although none reached statistical significance. A moderate negative correlation was observed between changes in MSWT distance and HM-PRO Part A scores ($r = -0.44$, $p = 0.38$), suggesting that greater improvements in walking performance may be associated with better perceived health status.

The EI group showed larger improvements in both absolute and relative VO_{2peak} values.

Conclusions: Comparison of changes from T0 to T2 showed a favourable trend in the EI group relative to the control group. Median changes in FC measures suggest greater improvements following the EI.

The observed negative correlation between MSWT distance and HM-PRO Part A scores may indicate that improved FC is associated with fewer limitations in daily activities and better perceived QL. Although the EI group demonstrated enhanced cardiorespiratory fitness, considerable inter-individual variability was observed, and no statistically significant associations were confirmed.

Given the limited sample size, these findings should be considered exploratory.

P099: Factors Associated with Survivorship Care Engagement Among Pediatric Hodgkin Lymphoma Survivors

Ksenya Shliakhtsitsava^{1,2}, Anandini Rao^{3,2}, Lynn Gargan⁴, Cindy Cochran^{3,2}, Tanya Watt^{1,2}, Eman Rettig^{5,6}, Daniel Bowers^{1,2}, Rebecca Eary^{7,2}, Amy Hughes^{8,2}

¹Department of Pediatrics, Division of Pediatric Hematology & Oncology, Harold C. Simmons Comprehensive Cancer Center, ²University of Texas Southwestern Medical Center, Dallas, TX, ³Department of Pediatrics, Division of Pediatric Hematology & Oncology, ⁴Gill Center for Cancer and Blood Disorders, Children's Medical Center of Dallas, Dallas, TX, ⁵Gill Center for Cancer and Blood Disorders, Neuropsychology Department, Children's Medical Center, Dallas, TX, ⁶Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas TX, ⁷Department of Family and Community Medicine, ⁸Department of Epidemiology, O'Donnell School of Public Health

Background: Childhood Hodgkin lymphoma (HL) survivors remain at risk for treatment-related late effects and require long-term survivorship follow-up. Factors associated with sustained survivorship care engagement remain poorly characterized. We leveraged a longitudinal cohort of childhood HL survivors to identify factors associated with ongoing engagement in survivorship care.

Methods: We conducted a retrospective cohort study of pediatric HL survivors diagnosed before age 19 years who attended at least one survivorship clinic visit between 2013 and 2024. Demographic, treatment, and survivorship data were obtained from an electronic health record-based survivorship database. Survivors were risk-stratified for late effects based on chemotherapy and radiation exposures. Survivorship engagement was assessed using the Attendance Continuity Score (ACS), defined as the ratio of observed to expected survivorship visits according to institutional follow-up recommendations. Survivors were categorized as engaged or disengaged based on longitudinal attendance patterns.

Results: Fifty-four HL survivors were included. Median age at diagnosis was 10.9 years, and median time from therapy completion to first survivorship visit was 3.0 years. All survivors received chemotherapy, 53.7% received radiation therapy, and 7.4% underwent hematopoietic stem cell transplantation. Overall, 51.9% were classified as high risk for severe late effects, while 29.6% were at high risk for infertility and 29.6% for secondary breast cancer. Forty-one survivors (75.9%) were classified as engaged and 13 (24.1%) as disengaged. Disengaged survivors were younger at survivorship referral (11.8 vs 14.2 years, $p = 0.030$), first survivorship visit (12.5 vs 14.9 years, $p = 0.036$), and last survivorship visit (15.3 vs 17.6 years, $p = 0.022$). ACS was significantly lower among disengaged survivors (0.54 vs 1.31, $p < 0.001$). Treatment exposures and late-effects risk profiles did not differ between groups.

Conclusions: Nearly one-quarter of pediatric HL survivors disengaged from survivorship care despite substantial risk for treatment-related late effects. Younger age at survivorship referral and program entry was associated with subsequent disengagement, whereas treatment intensity and late-effects risk were not. Earlier entry into survivorship care alone may be insufficient to ensure long-term engagement, highlighting the need for developmentally and culturally tailored survivorship and transition strategies.

P100: Long-term follow up after Lymphoma treatment in young adults

Urska Rugelj¹, Lorna Zadavec Zaletel¹, Danijela štrbac¹, Miha Toplak¹

¹Institute of Oncology Ljubljana, Slovenia

Background: In Slovenia, a specialized late-effects follow-up clinic for childhood cancer survivors has been in operation for 40 years. During the past 20 years, we have also included survivors treated for lymphoma in young adulthood. Given the excellent cure rates of Hodgkin lymphoma and the long life expectancy of survivors, long-term follow-up is essential. Active surveillance for treatment-related late effects and their timely management can help reduce morbidity and improve quality of life among survivors. At our institution, we analyzed data on late effects among patients with Hodgkin lymphoma treated in Slovenia between 1983 and 2010.

Methods: The Cancer Registry of the Republic of Slovenia provided data on all patients diagnosed with and treated for Hodgkin lymphoma in Slovenia aged 18 to 30 years. Data on late effects were obtained from the medical records of the Late Effects Follow-up Clinic and subsequently analyzed statistically.

Results: We analyzed the data of 413 patients. At the time of data cut-off, 337 patients were alive, and 76 patients had died. In 46 patients, the cause of death was lymphoma, in 16 a second malignant disease, 4 died because of acute myocardial infarction, 1 had GVHD, and 10 died of other causes. Among patients in follow-up, 37.5% had at least one manifestation of cardiovascular disease. A total of 79 patients developed a second malignant neoplasm. The most common second malignancy was breast cancer ($n = 13$), followed by non-melanoma skin cancer ($n = 12$), thyroid cancer ($n = 11$), gynecological cancers ($n = 11$), hematologic malignancies ($n = 5$), lung cancer ($n = 4$), melanoma ($n = 4$), other lymphomas ($n = 3$), central nervous system tumors ($n = 3$), and head and neck cancers ($n = 3$). Two patients developed prostate cancer, while one patient each developed colorectal cancer, liver cancer, bladder cancer, and sarcoma. In survivors exposed to abdominal irradiation, colonoscopy has been advised and has been performed in 60% of eligible patients. Carcinoma was detected in one patient and lymphoma in another, while other findings included benign

and premalignant lesions. Additional late effects evaluated included gonadal dysfunction, thyroid disease, metabolic syndrome, chronic kidney disease, chronic pulmonary disease, and psychological disorders.

Conclusion: Hodgkin lymphoma survivors face significant late morbidity. Risk-adapted lifelong follow-up is crucial for detecting and managing treatment-related complications.

NLPHL

T101: Single-Nuclei and Spatial Transcriptomic Analysis of Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)

Hua Dong¹, Samira Rambow-Makhzami¹, Max Vorneweg², Finn Wichmann², Philipp Jurmeister³, Ina Bühnen^{4,5}, Andreas Rosenwald⁶, Wolfram Klapper⁷, Bastian Von Tresckow⁸, Christian Reinhardt⁸, Frederik Klauschen³, Heinz-Wolfram Bernd⁹, Martin-Leo Hansmann¹⁰, Dennis Eichenauer^{4,5}, Sylvia Hartmann², Florian Rambow¹

¹Department of Applied Computational Cancer Research, Institute for AI in Medicine (IKIM), University Hospital Essen, Essen, Germany, ²Institute of Pathology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany, ³Institute of Pathology, Ludwigs-Maximilians-Universität München, Germany, ⁴University of Cologne, First Department of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Dusseldorf, Cologne, Germany, ⁵German Hodgkin Study Group (GHSG), University Hospital Cologne, Cologne, Germany, ⁶Institute of Pathology, Julius-Maximilians-Universität Würzburg, Germany, ⁷Institute of Pathology, Hematopathology Section and Lymph Node Registry, University Hospital Schleswig-Holstein Campus Kiel, Kiel, Germany, ⁸Department of Hematology and Stem Cell Transplantation, University Hospital Essen, University Duisburg-Essen, German Cancer Consortium (DKTK partner site Essen), Essen, ⁹Hematopathology Lübeck, Lübeck, Germany, ¹⁰Frankfurt Institute of Advanced Studies, Frankfurt am Main, Germany.

Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) typically exhibits favorable prognosis compared to classical Hodgkin lymphoma. However, a subset of patients experience disease relapse, which can be difficult to manage, particularly in early relapses. The molecular mechanisms underlying relapse remain poorly understood. Characterization of lymphoma (LP) cells and their spatial interactions within the tumor microenvironment is crucial for understanding relapse biology and developing precision medicine approaches.

We performed single-nuclei RNA sequencing and spatial transcriptomic profiling on FFPE samples from NLPHL patients stratified by relapse status, revealing cellular heterogeneity at single cell resolution. Nuclei from 17 patients (n = 9 R, n = 8 NR) were analyzed, yielding 80,855 high-quality nuclei after quality control. Following Harmony integration (by patient) to correct batch effects, nuclei were clustered using Seurat's Louvain algorithm to identify nine distinct major cell types using marker gene combinations. Single-nuclei analysis revealed distinct transcriptional profiles distinguishing LP cells from normal B cells, with candidate biomarker genes showing expression differences between relapse and non-relapse patients. CellChat analysis based on snRNA-seq data identified complex intercellular communication networks involving multiple ligand-receptor pairs across different cell types. Spatial transcriptomics was performed using the 10x Genomics Xenium platform, followed by cell type annotation through label transfer from snRNA-seq data, identifying 30 cellular subtypes at single-cell resolution and revealing the characteristic popcorn-like structures where LP cells are encircled by T cells. Our integrated approach combining single-cell transcriptomics with spatial validation provides comprehensive insights into NLPHL relapse mechanisms at cellular and molecular levels. The spatially validated intercellular communication networks suggest candidate therapeutic targets, potentially informing future approaches in NLPHL treatment.

T102: Malignant LP cells build a stroma-poor, avascular niche that concentrates IDO1+ macrophages and excludes regulatory T cells in NLPHL and THRLBCL

Ilja Kalashnikov¹, Suvi-Katri Leivonen², Kerttu Kalander², Matias Autio³, Johannes Dunkel³, Anniina Färkkilä⁴, Sirpa Leppä¹

¹University of Helsinki and Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland, ²Research Programs Unit, Applied Tumor Genomics, University of Helsinki, Helsinki, Finland., ³Department of Pathology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland, ⁴Research Program in Systems Oncology, University of Helsinki, Finland

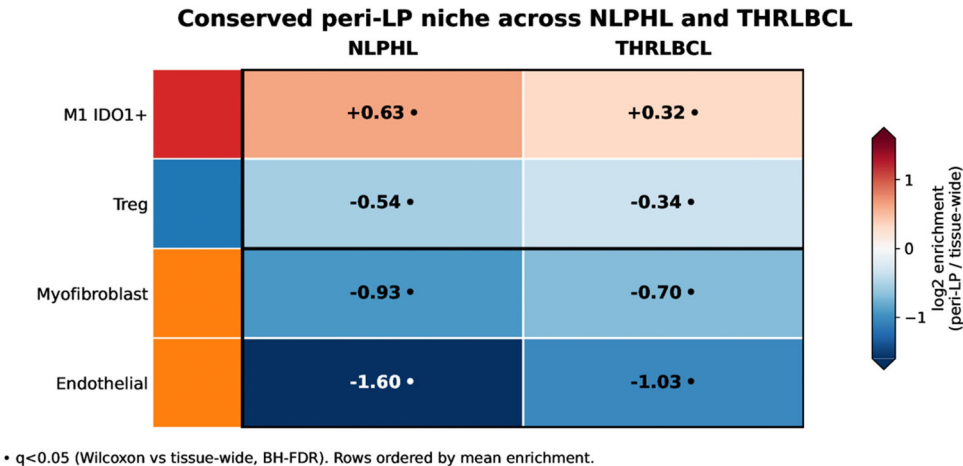


Figure 1: Conserved peri-LP niche. The 4/33 phenotypes significant in both entities. Log2 enrichment within 50 µm of LP cells vs tissue-wide, NLPHL and THRLBCL (red=enriched, blue=excluded; dot=q < 0.05, Wilcoxon vs tissue-wide, BH-FDR).

Background: Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a rare B-cell malignancy in which infrequent neoplastic lymphocyte-predominant (LP) cells reside within an immunologically active tumor microenvironment (TME) typically surrounded by T-follicular helper (Tfh) rosettes. In contrast, THRLBCL loses these rosettes and shifts to a macrophage-rich TME. Whether the LP cell reprograms its neighbors remains unknown.

Design: We performed 20-marker cyclic immunofluorescence (CyCIF) on 1.53 million cells from 27 patients (16 NLPHL and 11 THRLBCL). Cells were segmented, scored for per-marker positivity with an in-house phenotyping pipeline, and assigned to 33 single-cell phenotypes using a fixed marker-rule scheme spanning lymphoid, myeloid, and functional states. We compared cellular composition across entities. For each phenotype, we quantified enrichment within 50 μm of LP cells relative to the tissue-wide background (per-patient log2 fold change, Wilcoxon vs tissue-wide, BH-FDR) and related spatial features to event-free survival (EFS).

Results: Median age was 53 years (range 16–75), and most patients were male (24/26). Over a median 17-year follow-up, 7 relapses (NLPHL 4, THRLBCL 3), 1 transformation (NLPHL), and 9 deaths (NLPHL 5, THRLBCL 4) occurred. From NLPHL to THRLBCL, bystander B cells were depleted (41% to 6%, $q < 0.001$) and all macrophage subsets increased, most markedly IDO1+ macrophages (0.7% to 3.0%, $q < 0.01$). Four phenotypes showed peri-LP enrichment or exclusion that was significant in both entities, defining a conserved niche. IDO1+M1-like macrophages were enriched within 50 μm of LP cells, whereas regulatory T cells, myofibroblasts, and endothelial cells were excluded ($q < 0.05$). In NLPHL, the niche was further enriched for PD1+CD4+ Tfh rosettes, dendritic cells, and activated helper and cytotoxic T cells. In THRLBCL, these enrichments were absent, and the peri-LP niche was instead enriched for IDO1+M2-like macrophages.

The disease entity was not prognostic (for EFS, $P = 0.62$). Within NLPHL, peri-LP macrophage features showed a consistent but FDR-nonsignificant trend toward worse EFS ($q = 0.3$).

Conclusion: Across NLPHL and THRLBCL, LP cells organize a conserved local niche by recruiting IDO1+ macrophages and excluding regulatory T cells and stroma. CD4+PD1+ rosettes also mark this niche in NLPHL and are replaced by an IDO1+ macrophage program toward THRLBCL. Spatial prognostic biomarkers will require larger cohorts.

P103: Data Scarcity in Rare Lymphoma: Synthetic Patient Generation and Survival Analysis in NLPHL

Gabriele Santangelo¹, Eleonora Fresi², Virginia Ferretti³, Martha Berliner⁴, Sofia Pedrali⁴, Alessandro Mazzacane³, Arianna Dagliati¹, Manuel Gotti³

¹Department of Electrical, Computer, and Biomedical Engineering, University of Pavia, Pavia, Italy, ²Biostatistics Clinical Trial Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, ³Department of Hematology Oncology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, ⁴Department of Molecular Medicine, University of Pavia, Pavia, Italy

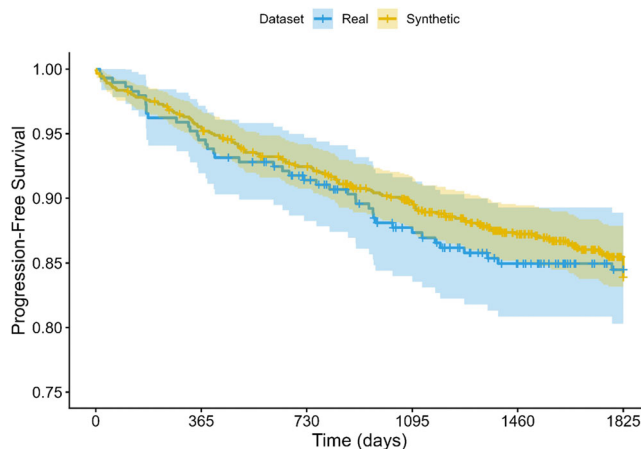


Figure 1: Progression-free survival curves obtained with real data (blue) and synthetic data (yellow).

Background: Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a rare B-cell lymphoma with generally favorable survival but risk of relapse and transformation, and limited evidence for standardized treatment due to small cohorts. Rituximab is a key therapeutic option, but data scarcity restricts robust clinical conclusions. In this context, synthetic data generation is investigated as a strategy to address data scarcity by expanding data availability while preserving the statistical and clinically relevant properties of real-world cohorts, enabling more reliable survival and treatment-response analyses in rare disease settings.

Methods: Real-world anonymized NLPHL patient data derived from a multicenter data collection coordinated by IRCCS Policlinico San Matteo in Pavia were used, including longitudinal clinical, laboratory, treatment, and outcome variables.

Synthetic data were generated using a diffusion-based architecture for mixed-type tabular data, with generation conditioned on treatment type (rituximab-based vs conventional therapy). Synthetic data quality was assessed through replication of Kaplan-Meier progression-free survival (PFS) analyses compared with the real cohort, using disease progression as the event of interest and time from treatment initiation to progression as survival time.

Results: The real-world cohort comprised 292 patients, while the synthetic dataset included 1000 patients after post-processing removal of anomalous samples. Preliminary survival analyses compared PFS between real and synthetic cohorts. Kaplan–Meier PFS curves and corresponding confidence intervals were evaluated; log-rank test showed no significant difference between curves ($p = 0.9$).

Conclusion: This study evaluated a conditional diffusion model for synthetic data generation in NLPHL, a rare disease with limited cohort sizes. Conditioning on treatment allowed generation of synthetic cohorts preserving clinically relevant distributions, with utility supported by agreement between real and synthetic Kaplan–Meier survival curves.

However, results are limited by the retrospective single-cohort design and small sample size, and synthetic data should be considered complementary to real data. Future work should explore outcome-conditioned generation and multi-center validation to improve time-to-event modeling and robustness.

P104: Pembrolizumab in Relapsed/Refractory Nodular Lymphocyte-Predominant Hodgkin Lymphoma: A Case Report

Pedro Rodrigues Santos¹, Francesca Pierdomenico¹, Pedro Sousa¹, Gonçalo Esteves², José Cabeçadas², Maria Gomes Da Silva¹

¹Departamento de Hematologia, Instituto Português de Oncologia de Lisboa Francisco Gentil, ²Serviço de Anatomia Patológica, Instituto Português de Oncologia de Lisboa Francisco Gentil

Background: Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a rare B-cell malignancy, accounting for 5–6% of Hodgkin lymphomas, usually with very favorable outcomes. However, 20–30% of patients will relapse, with a 10-year risk of transformation into an aggressive large B-cell Lymphoma of 4–10%. The management of relapsed/refractory (R/R) NLPHL remains challenging. While PD-1 blockade has established activity in classical Hodgkin lymphoma, data in NLPHL are scarce.

Case Report: A 24-year-old male presented in 2018 with stage IIA NLPHL (unknown histological variant at diagnosis), located in the inguinal region. He was first treated with 4 cycles of ABVD and involved-field radiotherapy but relapsed 2 years later, with retroperitoneal disease and B symptoms. A new biopsy confirmed NLPHL and he received rituximab monotherapy (4 infusions), achieving a partial response. A year later he complained of lumbar pain and stage IV disease was demonstrated, with multiple extranodal sites (pleural, peritoneal and bone marrow). Third line with ESHAP was started, with the intention to consolidate with high dose chemotherapy and autologous stem cell transplantation (SCT), but no response was obtained. At this time a new biopsy excluded transformation and showed a type D histological variant. Stage IV disease was present. The patient started a fourth line with rituximab-bendamustine, again progressing under treatment and requiring dorsal radiotherapy for pain control. A new biopsy confirmed persistence of NLPHL with PD1 expression in tumor microenvironment T-Cells. At this time a sixth line treatment was proposed with pembrolizumab monotherapy. After 6 cycles complete metabolic response (CMR) was achieved, with resolution of extensive nodal, pleural, pulmonary, paravertebral and bone disease. Patient then underwent consolidation with allogeneic SCT with a matched unrelated donor and reduced intensity conditioning in March 2026. Complete metabolic response is ongoing.

Conclusion: This case illustrates the potential use of PD-1 blockade as an effective salvage and bridging strategy to allogeneic SCT in the rare instance of heavily pre-treated NLPHL. Durable CMR was achieved in this patient, previously refractory to five chemotherapy regimens. This data support further investigation of checkpoint inhibition at earlier lines in this uncommon lymphoma subtype.

P105: Management and Outcomes in Pediatric Nodular Lymphocyte-Predominant Hodgkin Lymphoma: Evidence from a Brazilian Multicenter Cohort

Adriana Morais¹, Juliana Costa², Ana Rosa Costa³, Monica Palese⁴, Michael Binkley⁵, Jamie Flerlage⁴

¹Hospital Universitário Oswaldo Cruz, Centro de Oncohematologia Pediátrica, Recife, Brazil, ²Consorcio Latinoamericano de Enfermedades Hemato-Oncológicas Pediátricas (CLEHOP), Salvador, Brazil, ³Consorcio Latinoamericano de Enfermedades Hemato-Oncológicas Pediátricas (CLEHOP), Seattle, WA, United States of America, ⁴University of Rochester Medical Center, Division of Pediatric Hematology/Oncology, Rochester, NY, United States of America, ⁵Stanford University, Department of Radiation Oncology, Stanford, CA, USA

Childhood nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a rare, indolent lymphoma lacking an evidence-based standard of care worldwide. In Brazil, where resources can be scarce, non-specific therapeutic protocols developed for other lymphoma subtypes are often used, but there are no data to understand current practices and patient outcomes. A retrospective analysis of data from patients treated for NLPHL at Brazilian centers is necessary to assess these fundamental baseline data.

This multicenter retrospective study aims to analyze the clinical, histopathological, and therapeutic profile of pediatric NLPHL cases in Brazil. Secondary objectives include characterizing immunohistochemistry findings and evaluating clinical outcomes.

In partnership with Global nLPHL One Working Group (GLOW) and the Consorcio Latinoamericano de Enfermedades Hemato-oncologicas Pediatricas (CLEHOP) members, 27 Brazilian institutions were invited to participate in a retrospective study of NLPHL. Patients aged <19 years diagnosed with NLPHL between January 2023 and June 2025 were included. Data were extracted from physical and electronic medical records using standardized electronic spreadsheets. Statistical analysis was descriptive.

Preliminary analysis includes 15 patients from 7 institutions. The cohort has male predominance (80%). Most patients were diagnosed at early stages: 47% at stage I, 47% at stage II, and 6% at stage IV. Immunohistochemistry showed CD20 positivity in 100% of cases and CD30 positivity in 27% of cases. Management strategies included observation after surgical resection in 27% (4/15), chemotherapy + radiotherapy in 6% (1/15) and chemotherapy alone in 67% (10/15), with primarily CVP-based regimens. Rituximab was added in 90% of these chemotherapy regimens (10/11). With a median follow-up of 22.6 months, 80% achieved a complete response, while 3 patients (20%) experienced disease

recurrence, with one death after disease progression. Notably, 2 of the 3 patients who relapsed had been managed with observation alone, and all of them were rescued with chemotherapy afterward.

Preliminary results from this Brazilian registry indicate that although pediatric NPLHL appears to have an excellent overall outcome, disease recurrence remains a significant issue even in early-stage patients. This systematic collection of this multicenter data is essential for building evidence to understand how to support strategies for this rare cancer.

Relapsed and refractory

T106: Phase 1 PRIMAVERA Study of the PRMT5 Inhibitor AZD3470 in Patients with Relapsed/Refractory Classic Hodgkin Lymphoma

Pier Luigi Zinzani¹, Franck Morschhauser², Vincent Ribrag³, Elizabeth H. Phillips⁴, Herve Ghesquieres⁵, Hun Ju Lee⁶, Peter Borchmann⁷, Paul J. Bröckelmann⁷, Tae Min Kim⁸, Katharine Lewis⁹, Jakub Svoboda¹⁰, Antonia Rodriguez Izquierdo¹¹, Won Seog Kim¹², Anna Sureda¹³, Graham P. Collins¹⁴, Kaitlyn Beyfuss¹⁵, Cedric Dos Santos¹⁶, Richard F. Olsson¹⁷, Enrico Derenzini¹⁸

¹Policlinico Sant'Orsola-Malpighi, University of Bologna, Bologna, Italy, ²Centre Hospitalier Universitaire de Lille, Lille, France, ³Institut Gustave Roussy, Villejuif, France, ⁴Christie NHS Foundation Trust and Division of Cancer Sciences, University of Manchester, Manchester, UK, ⁵Hospital Lyon Sud, Lyon, France, ⁶MD Anderson Cancer Center, Houston, TX, USA, ⁷Universitätsklinikum Köln, Cologne, Germany, ⁸Seoul National University Hospital, Seoul, Republic of Korea, ⁹Linear Clinical Research, Sir Charles Gairdner Hospital, and University of Western Australia, Perth, Australia, ¹⁰Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA, ¹¹Hospital Universitario 12 de Octubre, Madrid, Spain, ¹²Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, ¹³Instituto Catalán de Oncología - Hospital Duran i Reynals, Barcelona, Spain, ¹⁴Oxford Cancer and Haematology Centre, Oxford, UK, ¹⁵Hematology R&D, AstraZeneca, Mississauga, Canada, ¹⁶Hematology/Oncology R&D, AstraZeneca, South San Francisco, CA, USA, ¹⁷Hematology R&D, AstraZeneca, Gothenburg, Sweden, ¹⁸IEO European Institute of Oncology IRCCS, Milan, Italy

Background: Protein arginine methyltransferase 5 (PRMT5) is critical for cell proliferation and differentiation and its dysregulation is associated with cancer development. Methylthioadenosine (MTA), an endogenous partial inhibitor of PRMT5, accumulates in cancer cells deficient in MTA phosphorylase (MTAP). In classic Hodgkin lymphoma (cHL), >80% of primary patient (pt) tumor samples are MTAP deficient (Urosevic J, ASH 2023). The MTA-cooperative PRMT5 inhibitor AZD3470 preferentially binds to MTA-bound PRMT5, increasing its target engagement to MTAP-deficient cancer cells. We present safety and preliminary efficacy of AZD3470 from a Phase 1 study in relapsed/refractory (r/r) cHL (NCT06137144).

Methods: Eligibility: ≥18 years; r/r cHL; ≥3 prior lines of therapy (including brentuximab vedotin (BV) and anti-PD-1). Pts received oral AZD3470 monotherapy QD in ascending dose levels (DLs) using an mTPI-2 design. Primary endpoints: incidence and severity of treatment-emergent adverse events (TEAEs) and dose-limiting toxicity (DLT). Secondary endpoints: overall response rate (ORR) and complete response rate (CRR) (Lugano 2014 criteria).

Results: As of 25/11/25, 39 pts (male, 62%; stage IV, 77%; median age, 42 [range 25–78] years; median prior lines of anticancer therapy, 6 [range 3–14]) had received AZD3470 at DL 1 to 8. All pts had had prior BV and anti-PD1 therapy; 20 (51%) and 5 (13%) pts had had prior autologous and allogeneic hematopoietic stem cell transplantation, respectively. All pts evaluable for MTAP protein expression were MTAP deficient. Median duration of exposure was 15 weeks (range 0.1–45.1), with treatment ongoing in 16 pts (41%). TEAEs occurred in 85% of pts, predominantly grades 1 or 2. The most common TEAEs (any grade) were anemia (28%) and nausea (15%). Grade ≥3 TEAEs occurred in 28% of pts, most commonly neutropenia (related) and hypokalemia (n = 2 each). Serious TEAEs occurred in 5 pts (13%). Two pts had dose reductions due to TEAEs (grade 4 hypertriglyceridemia and grade 3 esophagitis). No DLTs, treatment discontinuations nor deaths due to TEAEs were reported. Of 31 evaluable pts, 14 had an objective response, with responses at ≥DL4. The highest response rate was observed at ≥DL7 (n = 10) with ORR 80% and CRR 50%.

Conclusions: AZD3470 monotherapy was well tolerated, with no DLTs and mainly low-grade AEs. Both ORR and CRR were dose-dependent and notably high in this heavily pretreated cHL population. Dose optimization is ongoing.

T107: Treatment patterns and survival outcomes of patients relapsing after frontline Nivolumab-AVD in advanced stage classical Hodgkin lymphoma (cHL)

Harsh Shah¹, Allison Bock¹, Peirong Hao², Xi Qiao², Robert Stuver³, Swetha Thiruvengadam⁴, Azra Borogovac⁴, Reid Merryman⁵, Nicole Araujo⁶, Ayo Falade⁷, Samin Houshyar⁸, Daniel Reef⁹, Gordon Smilnak¹⁰, Kanithra Sekaran¹¹, Efrat Luttwak³, Dahlia Sano¹², Ajay Major¹³, Ritwick Mynam¹⁴, Grace Baek¹⁵, John Sharp¹⁶, John Vaughn¹⁷, Praveen Ramakrishnan Geethakumari¹⁸, Sanjal Desai¹⁹, Jessica Allen¹, Kelsey Baron¹, Tiffany Chang³, Nivetha Ganesan³, Vrutti Patel²⁰, Marisa Palmeri²¹, Anuja Abhyankar²², Drew Gerber²³, Madiha Iqbal²⁴, Hua-Jay Cherng²³, Alex Niu²², Joanna Rhodes²¹, Jakub Svoboda²⁰, Catherine Diefenbach¹⁷, Timothy Voorhees¹⁶, Mengyang Di¹⁵, Priyanka Pophali¹⁴, Yasmin Karimi¹², Reem Karmali¹¹, Krithika Shanmugasundaram¹⁰, Natalie Grover⁹, Urshila Durani⁷, Ivana N. Micallef⁷, Jonathan W. Friedberg⁸, Tatyana Feldman⁶, Matthew Mei⁴, Pallawi Torka³, Philippe Armand⁵, Alison Moskowitz³, Alex Herrera⁴, Narendranath Epperla¹

¹Huntsman Cancer Institute at University of Utah, ²University of Utah, Division of Epidemiology, ³Memorial Sloan Kettering Cancer Center, ⁴City of Hope Cancer Center, ⁵Dana Farber Cancer Center, ⁶Hackensack University Medical Center, ⁷Mayo Clinic Rochester, ⁸University of Rochester, ⁹University of North Carolina, ¹⁰University of Virginia, ¹¹Northwestern University, ¹²University of Michigan, ¹³University of Colorado, ¹⁴University of Wisconsin, ¹⁵Fred Hutchinson Cancer Center, ¹⁶Ohio State University, ¹⁷New York University, ¹⁸UT Southwestern Medical Center, ¹⁹University of Minnesota, ²⁰University of Pennsylvania, ²¹Rutgers University, ²²Roswell Park, ²³Columbia University, ²⁴Mayo Clinic Florida

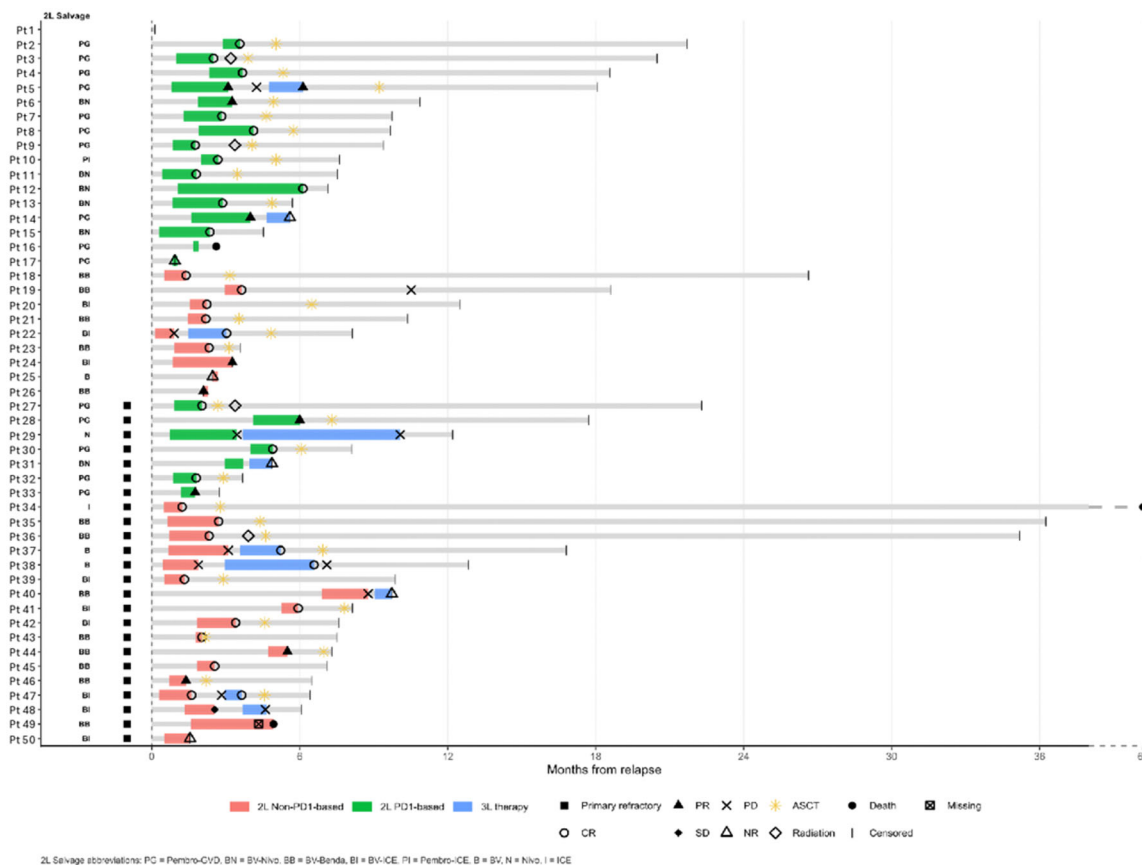


Figure 1: Swimmer plot showing treatment duration and response among patients relapsed/refractory to 1 L Nivo-AVD.

Background: Nivolumab (nivo) with AVD (NAVD) is standard-of-care for frontline (1L) treatment (tx) of advanced stage (AS) cHL in the U.S. There is a gap in data on patients (pts) relapsing after 1L NAVD and the utility of re-challenge with checkpoint inhibitors (CPI). Thus, we sought to evaluate tx patterns and outcomes of pts with cHL relapsing after 1L NAVD.

Methods: Pts included had cHL treated with 1L NAVD between 2018 and 2025 at 23 US sites. Primary refractory disease was defined as less than a complete response (CR) at end of treatment (EOT) PET-CT. Second line (2L) tx was considered CPI-based if it included CPI with chemotherapy (chemo) or Brentuximab Vedotin (BV) and non-CPI based if BV +/- chemo. PFS was calculated from date of auto-SCT (ASCT).

Results: Overall, 50 pts were included, 52% were male, 24 (48%) were primary refractory to 1L tx and 15 (30%) had relapse <12 months (mo) from EOT. 47 (94%) had biopsy proven relapse. The median age at relapse was 55 (17–84). At relapse, 78% had AS disease, 15% had B symptoms, and 42% had extranodal involvement. 49 pts (98%) received 2L tx; 23 pts (47%) received CPI-based tx and 26 pts (53%) received non-CPI based tx (Figure 1). Non-CPI tx included BV-bendamustine (benda) (n = 13, 50%), BV-ICE (n = 9, 35%), BV monotherapy (n = 3), and ICE (n = 1). CPI-based tx included CPI with chemo (n = 16, 70%), BV+nivo (n = 6, 26%) and nivo monotherapy (n = 1). Among all response-evaluable pts (n = 43/49), the ORR/CR rates were 86% and 65%, respectively. ORR (95% vs 78%) and CR rates (70% vs 61%) were numerically higher for CPI-based vs non-CPI based 2L tx. 71% (17/24) of primary refractory pts received non-CPI 2L tx. Among evaluable primary refractory pts (n = 21/24), ORR was 76% and CRR was 57% (CPI-based vs non-CPI CRR was 50 vs 60%, respectively). 10 pts (20%) required third line tx. Of these, 8 pts had PD after 2L tx. The other 2 pts had inadequate response to 2L. With a median follow up (f/up) of 8.1 mo (0.1–60), there were 12 total events with 9 progressions and 3 deaths (1 cHL, 2 unknown during salvage). 31 patients (62%) proceeded to ASCT. Median f/up post ASCT was 5.3 mo (0.3–57.3). 6-month PFS/OS post ASCT was 100%, with 1 late relapse/death from cHL post-ASCT at 60 months. Two pts were ineligible for ASCT.

Conclusions: Both CPI-based and non-CPI-based therapies remain effective at achieving disease control and bridging to ASCT post NAVD relapse. Outcomes after ASCT appear similar to prior literature with longer f/up needed.

T108: Primary Analysis of the GHSG Pembro-CORE Trial: PET-Adapted PD-1-Based Salvage Therapy Omitting High-Dose Chemotherapy in First-Relapsed Hodgkin Lymphoma

Hishan Tharmaseelan¹, Ina Bühnen¹, Helen Kaul¹, Sarah Gillessen¹, Carsten Kobe², Karin G. Schrenk^{3,4}, Philipp Ernst^{3,4}, Max S. Topp⁵, Ulf Schnetzke^{3,4}, Nico Freund⁶, Stephanie Sasse⁶, Wolfram Klapper⁷, Michael Fuchs¹, Sven Borchmann¹, Paul J. Bröckelmann¹, Peter Borchmann¹, Bastian Von Tresckow^{1,6}

¹University of Cologne, Faculty of Medicine and University Hospital of Cologne, Department I of Internal Medicine, and Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf (CIO ABCD), and German Hodgkin Study Group (GHSG), Cologne, Germany, ²Department of Nuclear Medicine, University Hospital of Cologne, Kerpener Straße 62, 50937, Cologne, Germany, ³Klinik für Innere Medizin II, Abteilung für Hämatologie und Internistische Onkologie, Universitätsklinikum Jena, Jena, Germany, ⁴Comprehensive Cancer Center Central Germany, Campus Jena, Jena, Germany, ⁵Medical Department II, University Hospital Würzburg, Würzburg, Germany, ⁶Department of Haematology and Stem Cell Transplantation, West German Cancer Center and German Cancer Consortium (DKTK partner site Essen), University Hospital Essen, University of Duisburg-Essen, Essen, Germany, ⁷Department of Pathology, Hematopathology Section, University Hospital Schleswig-Holstein Campus, Kiel, Germany

Flowchart of the Pembro-CORE trial

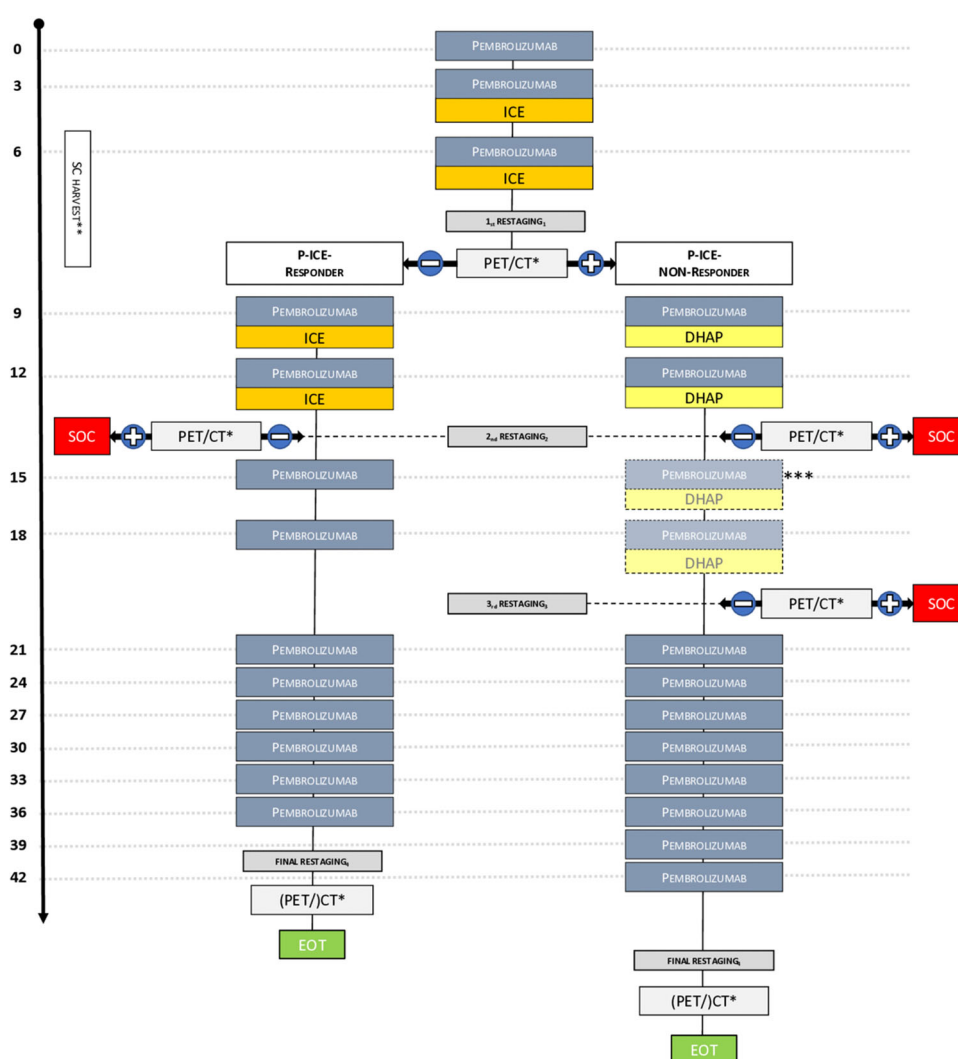


Figure 1: Trial Flowsheet of the GHSG Pembro-CORE trial [SOC: Standard of Care (usually high-dose chemotherapy), EOT: End of Treatment, P-ICE: (Pembrolizumab, Ifosfamide, Carboplatin, Etoposide), P-DHAP: (Pembrolizumab, Dexamethasone, High-Dose Cytarabine, Cis).

Background: Standard therapy for relapsed/refractory classical Hodgkin lymphoma (r/r cHL) consists of salvage chemotherapy followed by high-dose chemotherapy (HDCT) and autologous stem-cell transplantation (ASCT). Although effective, this approach is associated with substantial acute and long-term toxicity, and a major unmet need for HDCT-free strategies remains. Anti-PD1-

based salvage combinations have shown high complete metabolic response rates (CMR) and may allow selected patients to avoid HDCT/ASCT.

Methods: Pembro-CORE is a prospective, open-label, multicenter phase II trial conducted at four German sites. Transplant-eligible patients aged 18–65 years with first relapsed or primary refractory cHL received 1x pembrolizumab followed by chemoimmunotherapy adapted by interim PET after 1x pembrolizumab and 2x P-ICE. PET-negative patients received 2 additional P-ICE, whereas PET-positive patients switched to 4x P-DHAP. Patients achieving PET negativity received 8x pembrolizumab maintenance. Stem-cell apheresis was mandatory; patients with persistent PET positivity were recommended to undergo off-trial HDCT/ASCT. The primary endpoint was centrally reviewed CMR after completion of 4x chemoimmunotherapy.

Results: 29 patients were enrolled (median age 38 years; 59% male; 52% advanced-stage at initial diagnosis; 93% BEACOPP-like-pretreated; 14% primary refractory). At the primary endpoint restaging CMR was achieved in 26/29 patients (90%). After 2 cycles of chemoimmunotherapy, the CMR rate was 57%. Only 5/29 patients (17%) subsequently underwent HDCT/ASCT. With a median follow-up of 13.2 months, 9 patients (31%) experienced progression/relapse, including 7 patients who had achieved CMR at the primary endpoint assessment. No deaths occurred. All patients experienced at least one adverse event. Serious adverse events occurred in 10/29 (34%), mainly infections (n = 5), while one patient developed autoimmune colitis (all events resolved).

Conclusions: PET-adapted pembrolizumab-chemotherapy induces a high CMR rate of 90% in first r/r cHL. However, the substantial relapse rate despite short follow-up, including relapses among patients who achieved PET-negativity at the primary endpoint restaging indicates that Deauville score-based stratification alone appears insufficient to identify patients who can safely omit HDCT. Further studies exploring HDCT-free strategies, tailored by biologically defined patient subgroups and dynamic response assessment, are warranted.

P109: Immune Checkpoint Inhibitor Combined with Radiotherapy for Relapsed/Refractory Classical Hodgkin Lymphoma: A Transplant-Free Retrospective Study

Yue Liu¹, Jingnan Wang², Yunpeng Wu¹, Xin Liu¹, Yongwen Song¹, Shu-Nan Qi¹, Ye-Xiong Li¹

¹Department of Radiation Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, ²Department of Radiation Oncology, The First Affiliated Hospital of Bengbu Medical University, Bengbu, China

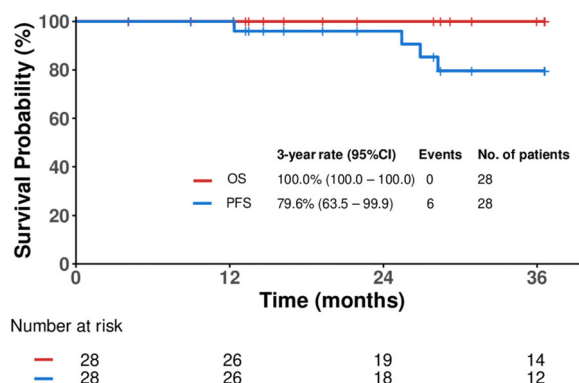


Figure 1: Kaplan-Meier Curves for PFS and OS of the 28 patients included with refractory or relapsed cHL received ICI combined with RT. Kaplan-Meier estimates of progression-free survival (PFS, blue) and overall survival (OS, red) in all 28 patients.

Background: Despite advances with immune checkpoint inhibitors (ICIs) in relapsed or refractory classical Hodgkin lymphoma (r/r cHL), many patients still require intensive consolidation. Combining ICIs with modern radiotherapy (RT) may provide a non-transplant salvage alternative.

Methods: We retrospectively analyzed patients with biopsy-proven r/r cHL treated at a single institution (2018–2024) who received ICIs (with or without chemotherapy) and modern RT (volumetric modulated arc therapy or tomotherapy), delivered concurrently or sequentially (interval ≤ 3 months). The treatment outcomes were analyzed according to clinical factors, and toxicities were displayed.

Results: Twenty-eight patients were included, and 64.3% had primary refractory disease and 78.6% relapsed after frontline ABVD. Ten patients (35.7%) received ICI monotherapy, while the remainder received ICI-based combinations. All patients completed modern RT. At a median follow-up of 36.5 months (range 4.1–75.4), the estimated 3-year progression-free survival (PFS) and overall survival (OS) rates were 79.6% and 100%, respectively. Six relapses (21.4%) occurred exclusively outside irradiated fields. PFS was significantly associated with stage IV disease and high GHSG score (both $P < 0.001$). Treatment was well tolerated, with no grade ≥ 3 radiation-related adverse events.

Conclusion: ICIs combined with modern RT achieved high rates of durable disease control in selected patients with r/r cHL and may represent a viable non-transplant salvage strategy. Prospective studies are warranted to define optimal patient selection and integration with systemic therapy.

P110: How to manage BrECADD failure? Early Outcomes of Second-Line Treatment in classic Hodgkin Lymphoma

Christian Peter Jaworek^{1,2}, Janina Jablonski^{1,2}, Lisa Marie Sgonina³, Annika Rudat³, Pascal Fichtel⁴, Thomas Melchardt^{5,6}, Susanne Ghandili⁷, Andreas Rank⁸, Matthias Hänel⁹, Julia Meissner¹⁰, Theresa Halbsguth¹¹, Hishan Tharmaseelan^{1,2}, Justin Ferdinandus^{1,2}, Paul J. Bröckelmann^{1,2,12}, Peter Borchmann^{1,2}, Bastian Von Tresckow^{13,2}

¹University of Cologne, Faculty of Medicine and University Hospital of Cologne, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD), Cologne, Germany, ²German Hodgkin Study Group (GHSG), Cologne, Germany, ³University of Münster, Department of Hematology, Oncology and Pneumology, University Hospital Münster, Münster, Germany, ⁴Dresden University of Technology, Department of Medicine I, University Hospital Carl Gustav Carus, Dresden, Germany, ⁵Department of Internal Medicine III with Haematology, Medical Oncology, Haemostaseology, Infectiology and Rheumatology, Paracelsus Medical University, Salzburg, Austria, ⁶Cancer Research Laboratory of the Department of Internal Medicine III, Salzburg, Austria, ⁷Department of Oncology, Hematology and Bone Marrow Transplantation with Section Pneumology, University Cancer Center Hamburg, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, ⁸Department of Internal Medicine II, University Hospital Augsburg, Augsburg, Germany, ⁹Department for Internal Medicine III, Klinikum Chemnitz, Chemnitz, Germany, ¹⁰University of Heidelberg, Medicine V, Heidelberg, Germany, ¹¹Goethe University Frankfurt, Division of Hematology and Oncology, Department of Medicine II, Goethe University Hospital Frankfurt, Frankfurt, Germany, ¹²MV Zentrum Hämatologie und Onkologie, Sachsenring 69, 50677 Cologne, Germany, ¹³Department of Hematology and Stem Cell Transplantation, West German Cancer Center, University Hospital Essen, University of Duisburg-Essen, Essen, Germany



Figure 1: Swimmer plot of treatment courses after BrECADD failure in cHL.

While PET-guided BrECADD achieves high primary cure rates in classic Hodgkin lymphoma (cHL), the few relapsing or primary refractory cases may be difficult to treat. In this setting, high-dose chemotherapy (HDCT) followed by autologous stem cell transplantation (autoSCT) is usually indicated. Herein, we analyze salvage strategies and early outcomes in patients after failure of BrECADD.

To better understand the optimal salvage strategy after BrECADD failure, we performed a retrospective multicenter real-world study. Inclusion criteria were (1) BrECADD as 1st line therapy, (2) refractory/relapsed cHL, (3) HDCT in 2nd line planned (intention-to-HDCT) or performed. Centers in Austria, Germany, Israel, and Switzerland were invited to contribute eligible cases. For this early-results analysis, data collection focused on patient and disease characteristics, salvage treatment approaches, treatment response and outcomes with descriptive analyses.

19 eligible patients were included at data cutoff on 22 April 2026. 13 (68%) completed therapy and for 6 (32%), treatment is ongoing. Salvage comprised conventional chemotherapy in 13 patients (68%; DHAP, n = 10; DHAC, n = 2; ASHAP, n = 1) and PD1 inhibitor-based

regimens in 6 patients (32%; Pembro-GVD, $n = 5$; Nivo-ICE, $n = 1$). Among patients who completed upfront conventional salvage, 3/10 (30%) experienced further progression and were subsequently switched to PD1 inhibitor-based therapy. After completion of therapy, relapse occurred in 1/10 patients (10%) treated with upfront conventional salvage, while no relapse was observed after upfront PD1 inhibitor-based salvage. Radiotherapy was administered in 4/13 patients (31%). Consolidation therapy included brentuximab vedotin in 4/13 (31%; received or ongoing), and pembrolizumab in 2/13 (15%; received or ongoing). Febrile neutropenia occurred in 5/19 patients (26%; grade 3 $n = 4$, grade 4 $n = 1$), neuropathy in 3/19 (16%; grade 2 $n = 3$), and mucositis after HDCT in 2/13 (15%; grade 1 $n = 1$, grade 2 $n = 1$). Median observation time was 11 months (range 0–64; $n = 19$) and median follow-up after HDCT was 12 months (range 2–63, $n = 13$).

In conclusion, early outcomes after BrECADD failure appear overall favorable, with responses to both conventional and PD1 inhibitor-based salvage in selected patients. PD1-based approaches show activity, including in chemotherapy-refractory cases. Subgroup analyses remain limited by small numbers.

P111: KEYFORM-008: Randomized Phase 2 Study of Coformulated Favezelimab/Pembrolizumab Versus Chemotherapy in Participants With Relapsed or Refractory Classic Hodgkin Lymphoma

Paul J. Bröckelmann¹, David Lavie², Guilherme Perini^{3,4}, Muhit Ozcan⁵, Nathalie Johnson⁶, Won Seog Kim⁷, Carolina Mahuad⁸, Norma Gutiérrez⁹, Senem Maral¹⁰, Cecile Borel¹¹, Tae Min Kim¹², Lara Goncalves¹³, Deepa Jagadeesh¹⁴, Yasmin Karimi¹⁵, Nina Wagner-Johnston¹⁶, John Timmerman¹⁷, Ryan Lynch¹⁸, Graham P. Collins¹⁹, Yulia Sidi²⁰, Pallavi Pillai²⁰, Rushdia Yusuf²⁰, Alex Herrera²¹

¹University Hospital of Cologne, Germany, ²Hadassah Medical Center, Jerusalem, Israel, ³Instituto Américas, São Paulo, Brazil, ⁴Einstein Hospital Israelita, Sao Paulo, Brazil, ⁵Ankara University School of Medicine, Ankara, Türkiye, ⁶Jewish General Hospital, Montreal, Canada, ⁷Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, ⁸Hospital Alemán, Buenos Aires, Argentina, ⁹Hospital Universitario de Salamanca, IBSAL, Centro de Investigación del Cáncer, Salamanca, Spain, ¹⁰Medipol University Faculty of Medicine, Istanbul, Türkiye, ¹¹Institut Universitaire du Cancer Toulouse-Oncopole, Toulouse, France, ¹²Seoul National University Hospital, Seoul, Republic of Korea, ¹³Fundação Pio XII-Hospital de Câncer de Barretos, São Paulo, Brazil, ¹⁴Cleveland Clinic, Cleveland, OH, USA, ¹⁵University of Michigan, Ann Arbor, MI, USA, ¹⁶Johns Hopkins University School of Medicine, Baltimore, MD, USA, ¹⁷UCLA Medical Center, Los Angeles, CA, USA, ¹⁸Fred Hutchinson Cancer Center and University of Washington, Seattle, Washington, USA, ¹⁹GenesisCare Cancer Centre, Oxford, United Kingdom, ²⁰Merck & Co., Inc., Rahway, NJ, USA, ²¹City of Hope, Duarte, CA, USA

	Favezelimab/pembrolizumab	Chemotherapy
	n = 104	n = 99
PFS, median (90% CI), months	6.4 (5.7-8.4)	5.7 (5.6-6.2)
HR (90% CI)	0.757 (0.575-0.996)	
12-month PFS rate, %	32	14
OS, median, months	Not reached	Not reached
HR	0.67	
12-month OS rate, %	92	88
ORR (95% CI), %	44.2 (34.5-54.3)	67.7 (57.5-76.7)
Complete response, %	13.5	36.4
Partial response, %	30.8	31.3
Stable disease, %	23.1	4.0
Progressive disease, %	26.0	25.3
DOR, median (range), months	11.0 (0.0+ to 21.8+)	5.4 (0.0+ to 27.6+)
Pts with response lasting ≥ 12 months, %	43	21

Table 1: Efficacy measures.

Background: PD-1 blockade (eg, pembrolizumab) is standard treatment for relapsed or refractory (R/R) classic Hodgkin lymphoma (cHL), but most patients experience progressive disease (PD), and optimal post-PD-1 therapy is undefined. Favezelimab (anti-LAG3) plus pembrolizumab showed promising activity and manageable safety in participants (pts) with anti-PD-1-refractory R/R cHL in a phase 1/2 study. We report results from KEYFORM-008 (NCT05508867), a randomized, open-label, phase 2 study of coformulated favezelimab/pembrolizumab vs chemotherapy in anti-PD-1-refractory R/R cHL.

Methods: Adults with R/R cHL, ECOG PS 0–2, and PD per investigator ≤ 12 weeks from last dose of anti-PD-(L)1-based therapy (received for ≥ 3 months with ≥ 2 doses) were randomly assigned 1:1 to favezelimab 800 mg/pembrolizumab 200 mg IV Q3W or chemotherapy (gemcitabine 800–1200 mg/m² IV on days 1 and 8 of a 21-day cycle or bendamustine 90–120 mg/m² IV on days 1 and 2 of a 21- or 28-day cycle). Prior brentuximab vedotin and autologous stem cell transplant were required. Crossover to favezelimab/pembrolizumab was allowed for pts who received chemotherapy with PD per Lugano criteria by BICR. Primary end point was PFS per Lugano criteria by investigator. Secondary end points included OS, ORR, and DOR per Lugano criteria by investigator, and safety. Primary hypothesis for PFS was evaluated using a stratified log-rank test and at 5% (1-sided) alpha level.

Results: Overall, 203 pts were randomly assigned to favezelimab/pembrolizumab ($n = 104$) and chemotherapy ($n = 99$); 52 pts in the chemotherapy arm crossed over, with 17 ongoing treatment. At data cutoff (Sept 3, 2025), median follow-up was 17.6 months (range, 7.9–34.3). Efficacy data are reported in the table. Treatment-related AEs (TRAEs) occurred in 79 pts (76.0%) with favezelimab/pembrolizumab and 81 pts (83.5%) with chemotherapy. Grade 3–5 TRAEs occurred in 19 (18.3%) and 39 pts (40.2%). One treatment-related death occurred in the chemotherapy arm only (sepsis).

Summary/Conclusion: Primary end point was met, with improved PFS and late curve separation at 6 months, although few pts at risk thereafter warrant caution. DOR was longer; OS trended favorably but remains immature. ORR was lower for favezelimab/pembrolizumab, but disease control rates (CR+PR+SD) were similar between arms. KEYFORM-008 was discontinued due to sponsor's business decision to end the entire favezelimab clinical development program and was unrelated to safety or efficacy.

P112: Preliminary Results of Nivolumab and Axatilimab in Patients with Relapsed/Refractory Classical Hodgkin Lymphoma refractory to anti-PD-1 therapy

Harsh Shah¹, Dipenkumar Modi², Kenneth Boucher¹, James Marvin¹, Jerry Zak¹, Anthony Pomicter¹, Kelsey Baron¹, Daniel Ermann¹, Alison Moskowitz³, Radhakrishnan Ramchandren⁴, Deborah Stephens⁵, Boyu Hu¹

¹HCI, ²KCI, ³MSKCC, ⁴Reading Hospital, ⁵UNC

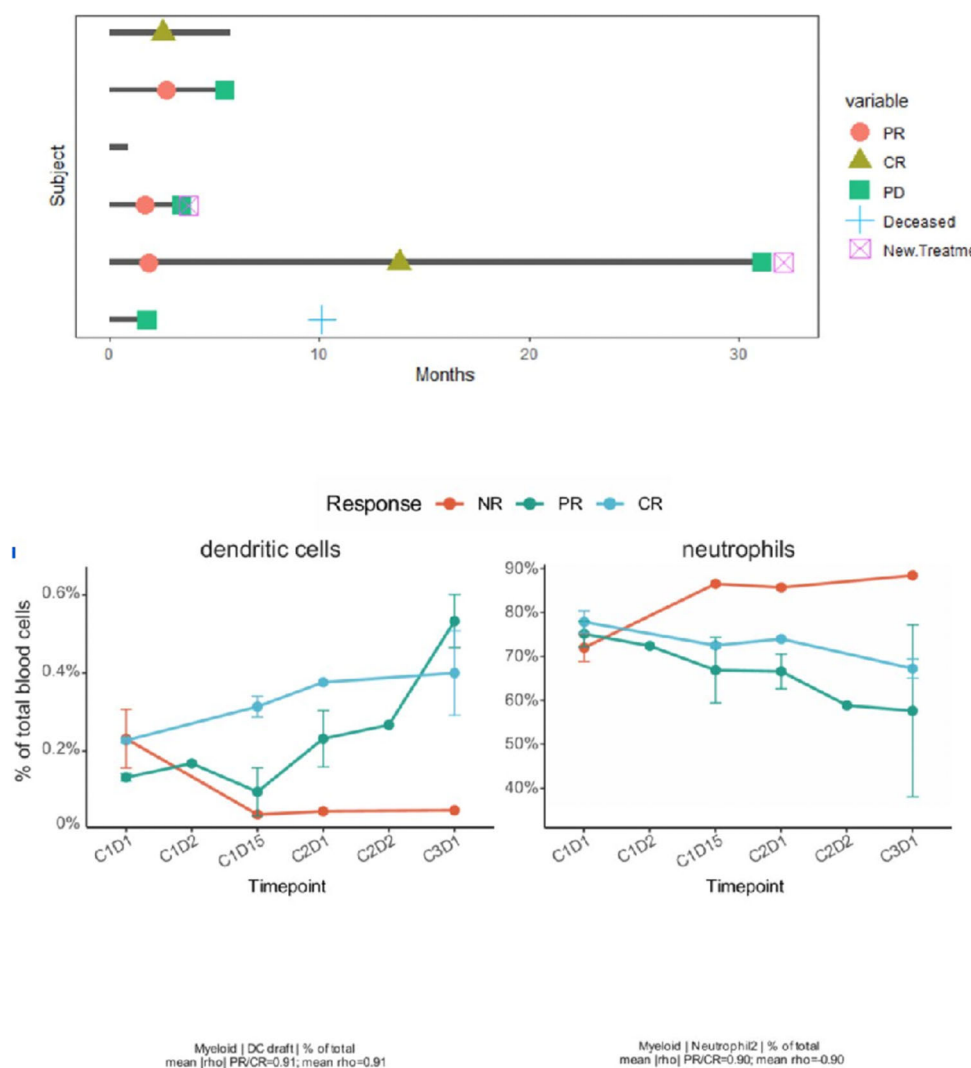


Figure 1: Top Panel: Swimmer plot of first six patients enrolled. Bottom Panel: Analysis of dendritic cells and neutrophils in responding vs non-responding patients.

Background: Patients (pts) with relapsed/refractory (r/r) classical Hodgkin lymphoma (cHL) progressing on anti-PD-1 therapy have poor outcomes. Tumor Associated Macrophages (TAMs) expressing colony stimulating factor 1 receptor (CSF1-R) have been implicated in resistance to anti-PD-1 therapy through (i) direct inhibition of cytotoxic T lymphocytes (CTLs) and (ii) phagocytosis of the anti-PD-1 antibody. Pre-clinical studies suggest that combination of anti-PD-1 and anti-CSF1-R blockade can result in upregulation of CTLs and increased PD-L1 expression.

Methods: We designed a phase 2 dose de-escalation trial of nivolumab and axatilimab (anti-CSF1-R monoclonal antibody) in pts with r/r cHL who have sub-optimal response to anti-PD-1-based therapy to determine the safety and efficacy of the combination (NCT05723055). Pts received axatilimab 3 mg/kg (with DL-1 dose of 2 mg/kg) and nivolumab 480 mg Q4 weeks until progression or toxicity.

Results: Six pts have been enrolled with a median age of 46 years (range, 27–78). The median lines of prior therapy were 4 (range, 2–8) and 50% had prior autologous stem cell transplant. Five pts had progressive disease and 1 pt had partial response (PR) on anti-PD-1 based therapy as the last line of treatment. No dose limiting toxicities were observed. Three pts had G 1–2 periorbital edema. There were 4 treatment-related G3 adverse events (AEs) including: asymptomatic CPK elevation (2), hypotension (1), and meningitis (1). Immune-related AEs were G 1–2 rash (2), G1 pneumonitis (1), and G3 meningitis (1). The pt with G3 meningitis was in complete response (CR) after 17 cycles of treatment and discontinued further treatment after developing meningitis.

Of the 5 pts evaluable for response, the best ORR was 80% (40% CR and 40% PR) (Figure 1, top panel). Median time to response was 2.2 months (mo). Median duration of response was 16 mo (95% CI 1.8 mo – NA) and median duration of response in complete responders was 17.3 mo. With a median follow up of 5.75 mo, median PFS was 5.5 mo (95% CI 3.5 mo– NA) with 1-year PFS of 40% (95% CI 14%–99%). In the correlative blood analysis, we observed an increase in dendritic cells and a decrease in neutrophils in responders (Figure 1, bottom panel).

Conclusions: The combination demonstrated a manageable safety profile and encouraging preliminary antitumor activity, including durable CR in a subset of pts. Anti-CSF1-R treatment can restore or enhance the effectiveness of immune checkpoint blockade.

P113: Eight-year outcomes after nivolumab discontinuation in patients with relapsed/refractory classic Hodgkin lymphoma

Liudmila Fedorova¹, Kirill Lepik¹, Polina Kotselyabina¹, Elena Kondakova¹, Andrey Chekalov¹, Evgeniya Borzenkova¹, Natalia Mikhailova¹, Alexander Kulagin¹

¹RM Gorbacheva Research Institute, Pavlov University

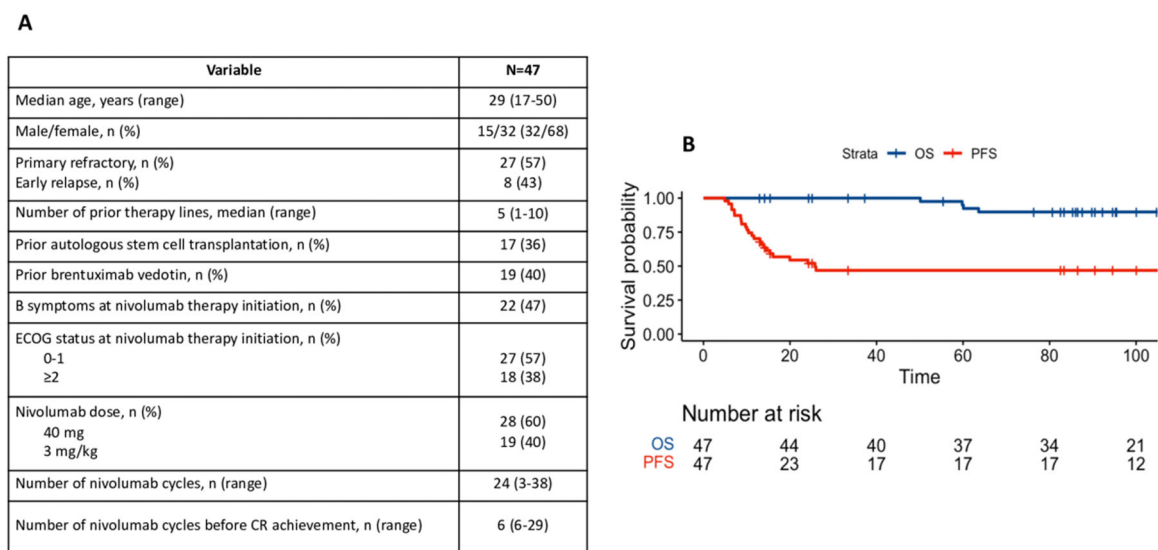


Table 1: (A) Patient characteristic, (B) overall and progression-free survival after nivolumab discontinuation.

Background: The optimal duration of immune checkpoint inhibitor (ICI) therapy in relapsed/refractory classic Hodgkin lymphoma (r/r cHL) and its curative potential remain uncertain. Limited data suggest that discontinuation of therapy after achievement of complete response (CR) may lead to durable remissions, while ICI retreatment can be effective. We analyzed long-term outcomes in an expanded cohort of patients who discontinued nivolumab (nivo) in CR and evaluated the efficacy and safety of nivo retreatment.

Methods: This retrospective study included 47 patients with r/r cHL treated with nivo at a dose of 3 mg/kg (60%) or 40 mg (40%) (Table 1). All patients discontinued therapy in CR. At relapse, nivo monotherapy was reinitiated in 19 pts. After discontinuation, patients were monitored every 6 months for 2 years, then clinically with imaging as indicated. Responses were assessed by PET/CT using LYRIC criteria; adverse events (AEs) by CTCAE 5.0. PFS and OS were evaluated after discontinuation, and ORR, PFS, OS, and AEs were evaluated after retreatment. Univariate Cox regression assessed clinical factors associated with PFS (primary r/r, sex, prior auto-HCT, prior brentuximab vedotin, number of prior therapy lines, presence of B symptoms, ECOG PS at nivo initiation, nivo dose, occurrence of severe AEs, completion of 24 cycles of nivo, and early CR at 3 mo).

Results: Median follow-up was 95 (13–111) mo. Nivo was discontinued due to AEs (n = 5, 11%), cessation of the national nivo compassionate use program (n = 19, 40%), or patient/physician decision (n = 23, 49%). Relapse occurred in 24 (51%) pts. Median PFS was 25.8 mo (95% CI: 14.5-NA); 8-y PFS was 46.8% (95% CI: 34.2–64.2). Median OS was not reached; 8-y OS was 89.8% (95% CI: 80.8–99.8). No clinical factors were significantly associated with PFS.

ORR after nivo retreatment ($n = 19$) was 74% (CR 47%). Median follow-up was 68 (25–96) mo. Median PFS was 22.7 mo (95% CI: 16.5–NA); 5-y PFS was 34.7% (95% CI: 18.4–65.5). Median OS was not reached; 5-y OS was 76.5% (95% CI: 58.7–99.5). AEs during retreatment occurred in 42% of patients, with grade 3–4 in 16%.

Conclusion: Long-term follow-up of patients with r/r CHL who discontinued nivo in CR demonstrates that a substantial proportion of patients remain relapse-free, raising the possibility of cure in this population. These findings should be considered when developing treatment strategies, including decisions regarding the role of consolidative allogeneic HCT.

P114: Low-Dose Nivolumab Combined with Salvage Chemotherapy in Relapsed/Refractory Classic Hodgkin Lymphoma: Outcomes from a Tertiary Care Centre in North India

Charanpreet Singh¹, Aditya Jandial¹, Arihant Jain¹, Alka Khadwal¹, Rajender Basher¹, Amanjit Bal¹, Gaurav Prakash¹, Pankaj Malhotra¹

¹Postgraduate Institute of Medical Education and Research, Chandigarh, India

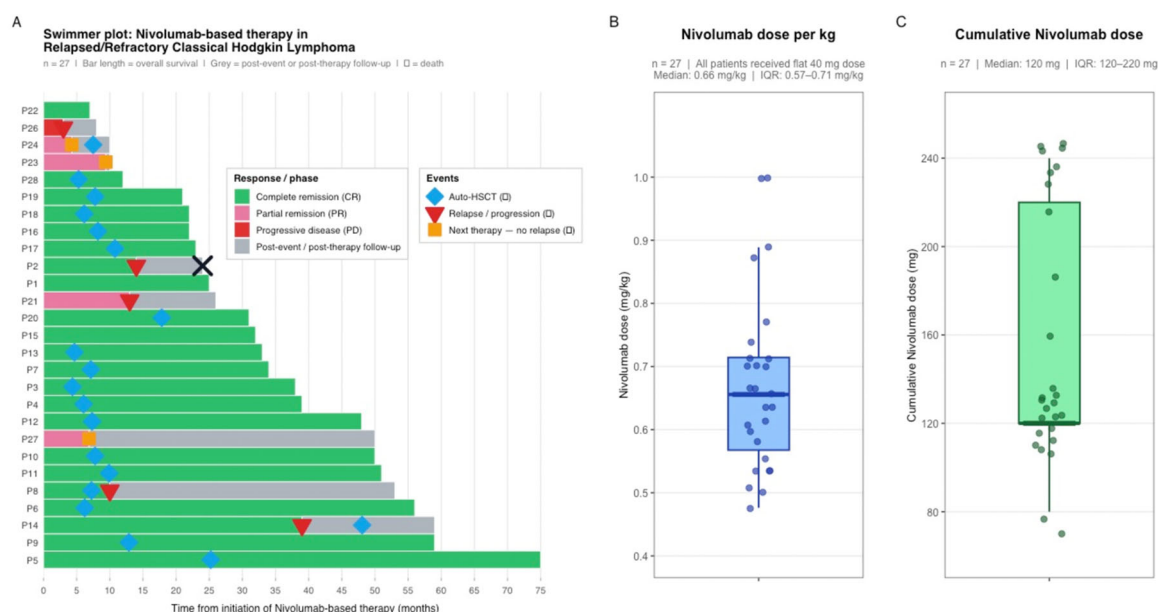


Figure 1: Nivolumab-based therapy outcomes in relapsed/refractory classical Hodgkin Lymphoma ($n = 27$). (A) Swimmer plot of individual treatment timelines (B) Nivolumab dose per kg (C) Cumulative Nivolumab dose.

Background: Immune checkpoint inhibitors (ICIs) have established activity in relapsed/refractory classic Hodgkin lymphoma (r/r CHL). Outcomes of patients receiving salvage with a combination of ICIs with chemotherapy are excellent. However, ICIs are often unavailable to a large population globally due to their high cost, leading to regional innovations including utilisation of a lower dose of these drugs. We report outcomes of low-dose nivolumab combined with salvage chemotherapy in r/r CHL at a tertiary care centre in North India.

Methods: This was a retrospective analysis of patients with r/r CHL treated with low dose nivolumab-based therapy between 2020 and 2026. Nivolumab was given at a fixed dose of 40 mg per cycle along with chemotherapy (without steroids). Progression-free survival (PFS), event-free survival (EFS, with receipt of next therapy counted as an event), and overall survival (OS) were calculated by the Kaplan–Meier method.

Results: The cohort comprised of 27 patients: 15 males (55.6%) and 12 females; median age 27 years (IQR 22–31). Most patients had advanced-stage disease at baseline ($n = 17$, 63.0%) and refractory disease to ABVD ($n = 20$, 74.1%). Nivolumab was used as second-line therapy in 16 patients (59.3%), third-line in 8 (29.6%), and fourth-line in 3 (11.1%). The median Nivolumab dosing was 0.66 mg/kg per patient (IQR- 0.57–0.71) with a median cumulative Nivolumab dose of 120 mg (IQR- 120–240 mg). Patients received a median of 3 cycles of therapy (range 2–6). Chemotherapy combinations included gemcitabine and cisplatin ($n = 9$) or vinorelbine, ifosfamide, bendamustine and etoposide ($n = 18$).

Complete response (CR) was achieved in 22 patients (81.5%) and overall response rate was 96.3% ($n = 26$). Nineteen patients (70.4%) proceeded to auto-HSCT. At a median follow-up of 31 months (range 3–75), 2-year PFS was 83.6% (95% CI 61.9–93.6%), 2-year EFS was 73.0% (95% CI 51.5–86.2%), and 2-year OS was 94.4% (95% CI 66.6–99.2%). Grade III/IV toxicity occurred in 3 patients (11.1%); there were no treatment-related deaths.

Conclusion: Low-dose nivolumab combined with chemotherapy achieves high response rates and favourable survival with acceptable toxicity in patients with r/r CHL. In settings where standard-dose ICIs are inaccessible, this is a practical and cost-effective bridging approach to auto-HSCT. Prospective evaluation in larger cohorts is warranted.

P115: Outcomes in Double-Exposed Classical Hodgkin Lymphoma: The Impact of Treatment Sequence and Salvage Strategies After Brentuximab Vedotin and Checkpoint Inhibitor Failure

Massimiliano Marinoni^{1,2}, Tomohiro Aoki¹, Sita Bhella¹, Inna Gong¹, Robert Kridel¹, Vishal Kukreti¹, Anca Prica¹, Abi Vijenthira¹, Chloe Yang¹, Woodrow Wells³, Danielle Rodin³, David Hodgson³, Michael Crump¹, John Kuruvilla¹

¹Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, Ontario, Canada, ²Hematology, Department of Biomedicine and Prevention, Tor Vergata University of Rome, Rome, Italy, ³Department of Radiation Medicine, Princess Margaret Cancer Centre, Toronto, Ontario, Canada

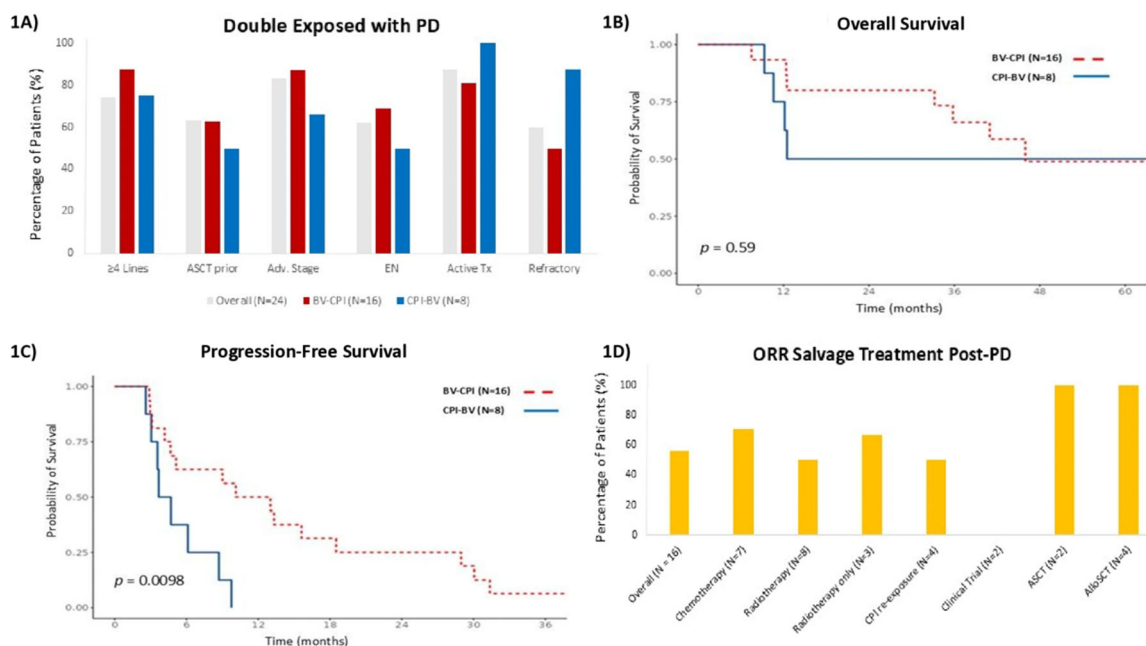


Figure 1: Patient characteristics at progression after treatment with Brentuximab Vedotin and CPI; OS after second novel agent exposure; PFS after second novel agent exposure; ORR for patients receiving therapy after progression to second novel agent.

Background: Brentuximab Vedotin (BV) and checkpoint inhibitors (CPIs) revolutionized classical Hodgkin lymphoma (cHL) treatment, improving outcomes in both relapsed/refractory (RR) and primary treatment setting. The outcomes of patients (pts) with active disease after exposure to both agents are unclear and the impact of treatment sequencing is not well understood. We aimed to characterize RR-cHL pts with progressive disease (PD) after both BV/CPI to describe subsequent treatment outcomes, treatment sequencing and survival.

Methods: We conducted a retrospective analysis of RR-cHL pts with PD after treatment with BV and CPI (pembrolizumab or nivolumab) at Princess Margaret from 2012 to 2024. Patients exposed to both novel agents were classified as “Double Exposed” (DE).

Results: We identified 24 DE cHL patients with PD after treatment with sequential BV and CPI. Median age: 40 years (20–75 years); 62% male. 74% had received 4+ lines of therapy (median 4, 2–6) and 63% had undergone ASCT. Advanced stage: 83% - Extranodal disease: 62%. 71% were actively on treatment with a novel agent at PD (BV-CPI 81%, CPI-BV 100%, $p = 0.526$). A trend in disparity of refractoriness to the most recent novel agent was observed (CPI-BV: 87.7%, BV-CPI: 50%, $p = 0.178$) [Figure 1A]. Median follow-up was 37.9 months (3–121 mo); median overall survival (OS) was 46 mo for the entire cohort (7–121 mo). Median OS for subgroups: BV-CPI 46 mo; CPI-BV 12.5 mo ($p = 0.59$). [Figure 1B]. The median progression-free survival (PFS) after the second agent was 7.4 mo (2–107 mo): BV-CPI 11.6 mo; CPI-BV 4.2 mo ($p = 0.0098$) [Figure 1C]. Time to next treatment (TTNT) was longer for CPI-BV (35.41 vs 13.33 mo; $p = 0.025$). 16 pts (67%) received further treatment while 8 (33%) went on to palliative therapy. Overall response rate (ORR) was 56% for pts receiving treatment with a variety of options used [Figure 1D].

Conclusions: DE BV/CPI pts represent a young, clinically aggressive, heavily treated RR- cHL population with progressive disease with poor outcomes. While the order of drug administration did not significantly impact OS, it may affect PFS and TTNT, highlighting the importance of studying treatment sequencing. With a proportion of pts transitioning to palliative care or not responding to subsequent therapy, BV/CPI DE pts have a need for novel treatment approaches. Our preliminary data underscore the critical need to optimize sequencing and salvage strategies to improve outcomes in this challenging population.

P116: PD-1 Inhibitor maintenance after Auto-HCT in r/r Classical Hodgkin lymphoma with prior PD-1 exposure: interim phase II results

Polina Kotselyabina¹, Aminat Balaeva¹, Liudmila Fedorova¹, Vladimir Bogatyrev², Nikita Shorokhov², Nikita Mochkin², Mobil Akhmedov³, Mariya Vernyuk³, Irina Cherkashina³, Azat Karabekov⁴, Vladislav Sarzhevskiy², Elena Demina², Vadim Keimakin⁴, Natalia Mikhailova¹, Alexander Kulagin¹

¹RM Gorbacheva Research Institute, Pavlov University, Saint Petersburg, Russia, ²N. I. Pirogov National Medical and Surgical Center, Moscow, Russia, ³PA Hertsen Moscow Oncology Research Institute, Moscow, Russia, ⁴National Research Oncology Center, Astana, Kazakhstan

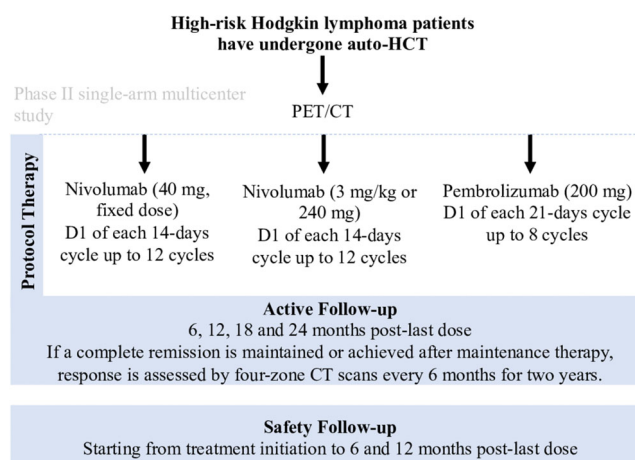


Figure 1: Study design.

Background: Maintenance therapy with PD-1 inhibitors after auto-HCT shows promising activity in relapsed/refractory classical Hodgkin lymphoma (r/r cHL). We report interim results of a prospective multicenter study evaluating PD-1 maintenance in patients previously exposed to PD-1 inhibitors.

Methods: This international multicenter phase 2 trial included adult patients with histologically confirmed r/r cHL who underwent auto-HCT after second or later lines of therapy (NCT06812858). Patients received PD-1 inhibitor maintenance per center choice (Figure 1): nivolumab (nivo) 40 mg, 3 mg/kg, or 240 mg IV every 14 days (up to 12 cycles), or pembrolizumab (pembro) 200 mg IV every 21 days (up to 8 cycles). Response evaluation is performed by PET/CT after auto-HCT and following the completion of maintenance therapy (LYRIC).

Results: Forty-seven patients (median age 34 [range 19–56]) were enrolled across four centers (2024–2026). All patients had at least one AETHERA risk factor (median 2, range 1–4). Primary refractory disease occurred in 53% (n = 25), early relapse in 28% (n = 13). All patients received PD-1 inhibitors prior to auto-HCT, with the last salvage regimen before auto-HCT also including PD-1 inhibitors. Brentuximab vedotin was given before auto-HCT in 32% (n = 15). Prior to auto-HCT, the best response to PD-1 inhibitor-based salvage therapy was complete response (CR) in 87% (n = 41) and partial response (PR) in 13% (n = 6). Pre-HCT status included CR in 83% (n = 39), PR in 15% (n = 7), and indeterminate response in 2% (n = 1). Auto-HCT was performed as consolidation of second-line therapy in 43% (n = 20) and third-line or later in 57% (n = 27). All patients were in CR prior to the maintenance (PET/CT). Maintenance consisted of full-dose nivo in 36% (n = 17), nivo 40 mg in 43% (n = 20), and pembro in 21% (n = 10). During maintenance, grade 1–2 adverse events (AEs) based on CTCAE v5.0 occurred in 49% (n = 23) and grade 3–4 in 4% (n = 2), with no treatment-related deaths. The most common AEs were fatigue (13%), thrombocytopenia (13%), upper respiratory tract infection (11%), leukopenia (11%), anemia (9%), and rash (9%). Three patients required therapy discontinuation due to immune-related AEs (grade 3 pneumonitis, grade 4 diarrhea, grade 2 hypothyroidism). After a median follow-up of 10 months (range 1–35), no relapses or deaths were observed.

Conclusion: Interim results demonstrate high efficacy and manageable toxicity in r/r cHL post auto-HCT.

P117: Association of prior PD-1 inhibitor exposure with pre-engraftment syndrome after ASCT in relapsed/refractory Hodgkin lymphoma

Dávid Tóthfalusi^{1;2;3}, Gréta Melani Csatlós¹, Boglárka Dobó^{1;2;3}, Fanni Borics^{1;2;3}, László Imre Pinczés^{1;2;3}, Árpád Illés^{1;2;3}, Zsófia Miltényi^{1;2;3}

¹Division of Haematology, Department of Internal Medicine, Faculty of Medicine, University of Debrecen, 4032, Debrecen, Hungary, ²Doctoral School of Clinical Medicine, University of Debrecen, 4032, Debrecen, Hungary, ³Member of ERN-EuroBloodNet (European Reference Network on Rare Haematological Diseases)

Background: PD-1 inhibitors are increasingly incorporated into salvage treatment strategies before autologous stem cell transplantation (ASCT) in relapsed/refractory Hodgkin lymphoma (R/R HL). However, inflammatory complications during the early peri-transplant period remain insufficiently characterized. We evaluated inflammatory events after ASCT, focusing on engraftment syndrome (ES)-like manifestations occurring before neutrophil recovery.

Methods: We retrospectively analyzed 64 consecutive adult HL patients undergoing ASCT at a single center between 2018 and 2025. ES was assessed according to Spitzer and Maiolino criteria. ES-compatible manifestations developing before neutrophil engraftment were classified as pre-engraftment syndrome (pre-ES). Clinically significant events were defined as inflammatory episodes requiring systemic corticosteroid treatment after exclusion of infection.

Results: Conventional ES after ASCT was infrequent. No patient fulfilled Spitzer criteria within the standard engraftment period, while three patients (4.7%) met Maiolino criteria without requiring corticosteroid therapy. When the conventional engraftment timeframe was disregarded, pre-ES manifestations were identified in 34 patients (53.1%) according to Maiolino criteria, although most cases were mild and self-limiting. Three patients developed steroid-requiring pre-ES; each fulfilled Spitzer criteria outside the standard engraftment window. All severe pre-ES cases occurred exclusively in patients previously exposed to PD-1 inhibitors. Prior PD-1 inhibitor therapy was significantly associated with steroid-requiring pre-ES ($P = 0.0007$), although interpretation is limited by the small number of events. Patients with severe pre-ES also exhibited higher early post-transplant CRP levels.

Conclusions: While classical ES after ASCT in HL was uncommon, pre-ES manifestations were frequent. Steroid-requiring pre-ES occurred exclusively in PD-1-exposed patients, suggesting a distinct inflammatory phenotype in this setting. Early recognition and prompt corticosteroid treatment after exclusion of infection may help prevent severe complications. Prospective studies are warranted to better define risk factors, underlying mechanisms, and optimal monitoring strategies in this high-risk population.

P118: Autologous hematopoietic cell transplantation remains relevant despite PD-1 inhibitor-based second-line therapy in classic Hodgkin lymphoma: interim results from the Prolgo-HL study

Liudmila Fedorova¹, Polina Kotselyabina¹, Kirill Lepik¹, Andrey Chekalov¹, Vladislav Markelov¹, Valeria Shpirko², Anastasia Semenova², Gayane Tumyan², Stanislav Volchenkov³, Angelina Piletskaya³, Ilya Zyuzgin³, Natalia Konoplya⁴, Natalia Mikhailova¹, Alexander Kulagin¹

¹RM Gorbacheva Research Institute, Pavlov University, ²N.N. Blokhin National Medical Research Center of Oncology, ³NN Petrov National Medical Cancer Research Center,

⁴N. N. Alexandrov National Cancer Center of Belarus

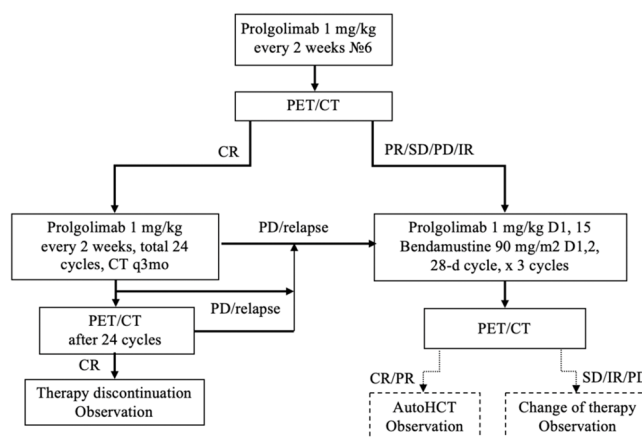


Figure 1: Study protocol.

Backgrounds: Recent advances in 2d-line treatment, particularly the incorporation of PD-1 inhibitors (iPD-1) into salvage regimens before auto-HCT, have markedly improved outcomes in classic Hodgkin lymphoma (cHL). These changes have prompted a re-evaluation of high-dose chemotherapy and auto-HCT, with growing interest in alternative consolidation strategies. This study aimed to assess the feasibility of omitting auto-HCT in patients who achieved an early complete response (CR) to prolgolimab (prolgo).

Methods: This prospective, multicenter, single-arm phase II trial included adult cHL pts after first-line therapy without prior iPD-1 (NCT05757466). The study protocol is shown in Figure 1. Response was assessed every 3 months by PET-CT (LyRIC). Primary endpoint was ORR, secondary - OS, PFS, DoCR. Intention-to-treat (ITT) population was used for safety, per-protocol (PP) for efficacy. Four pts were excluded from PP due to protocol deviation ($n = 2$), consent withdrawal ($n = 1$), gr 3 AE ($n = 1$).

Results: 32 pts with r/r cHL were enrolled (04.2023–05.2026); 28 were included in the PP analysis. The median follow-up was 24 mo (8–37). After 6 cycles of mono-prolgo, CR was achieved in 9 pts (32%). Among patients with CR, 8 pts (89%) had completed 24 cycles of therapy. In this cohort, relapse occurred in 5 pts (63%). The median PFS was 24 mo (95%CI 24–NA); 2-y PFS was 71% (95%CI 45–100).

Eighteen of 19 pts without CR were switched to the prolgo-bendamustine (benda) arm, where ORR was 89% (CR 83%). Among patients who achieved a response, auto-HCT was performed in 7 pts (39%) after prolgo+benda, while 1 pt was preparing for auto-HCT. Ten patients did not undergo auto-HCT after completion of the protocol due to patient preference ($n = 7$) or progression ($n = 1$). In patients proceeding directly to auto-HCT, the only event was early post-transplant death; no relapses occurred. Median OS and PFS were not reached; 2-year OS and PFS were 83% (95% CI, 58–100%).

Overall, 26 pts completed therapy per protocol. ORR at the end of treatment was 92% ($n = 24$, CR 88%); 2 y PFS was 60% (95%CI 43–85); 2 y OS was 88% (95%CI 75–100%).

Conclusion: Despite the high CR rates observed with mono-prolgo and prolgo-benda, a high relapse rate was noted, likely associated with omission of auto-HCT in both cohorts, underscoring the importance of this treatment component. Further risk stratification is required to identify a genuinely low-risk subgroup in whom omission of auto-HCT may be a safe and reasonable option.

P119: Efficacy of Ultra-Low-Dose Nivolumab in Combination with Gemcitabine and Cisplatin as Remission-Induction Therapy in Primary Progressive and Relapsed Hodgkin Lymphoma: A Randomized Phase II study with two ultra-low-dose schedules

Mithun Prakash¹, Nutan Joshi¹, Sujith Karumathil¹, Sushil Selvarajan¹, Sharon Lionel¹, Uday Kulkarni¹, Aby Abraham¹, Biju George¹, Vikram Mathews¹, Anu Korula¹

¹Christian Medical College Vellore

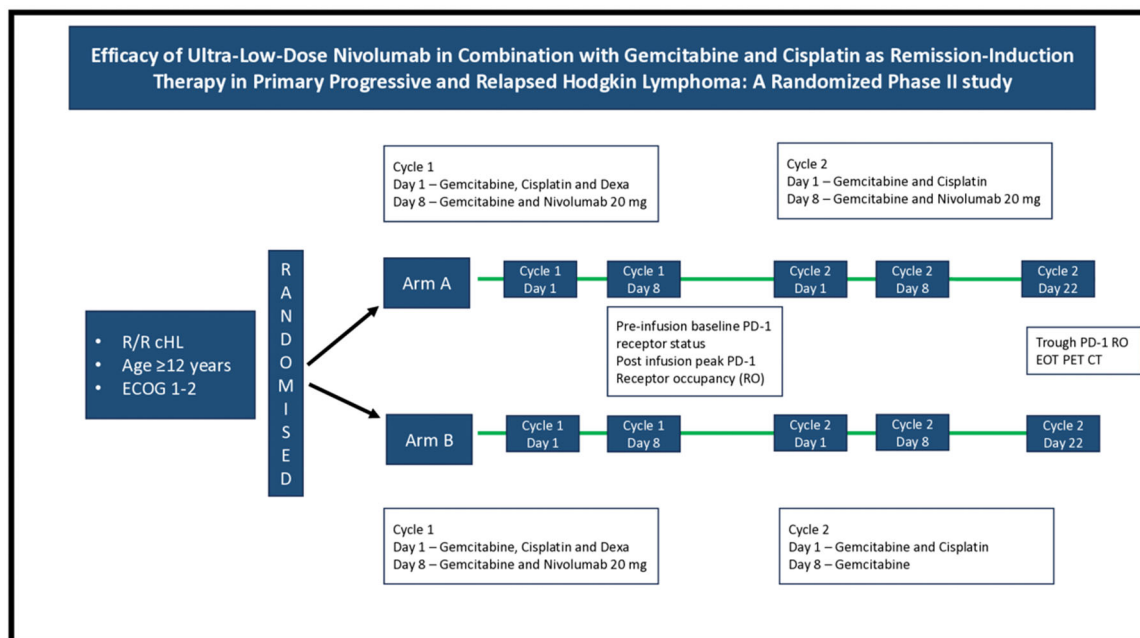


Figure 1: Trial schema showing patients with relapsed/refractory cHL randomised to receive ultra-low-dose nivolumab (20 mg) with gemcitabine/cisplatin for either 2 cycles (Arm A) or 1 cycle only (Arm B) with serial PD-1 receptor occupancy assessments.

Background: Patients with relapsed/refractory (R/R) classical Hodgkin lymphoma (cHL), achieve complete remission (CR) in only 40–50% of cases with first-line salvage chemotherapy. Although nivolumab is highly effective in R/R cHL, the minimum biologically effective dose remains unknown. In a prior phase II study, we demonstrated a 90% overall response rate (ORR) using low-dose nivolumab (40 mg) with standardized flow cytometric analysis showing near-complete PD-1 receptor saturation and persistence of receptor occupancy at trough time-points (<https://doi.org/10.1016/j.bict.2025.100011>). In-vitro, we have also demonstrated complete PD-1 receptor saturation with lower doses of nivolumab (20 mg and 10 mg). These findings suggest that efficacy may be retained with further dose and schedule de-escalation, potentially improving affordability and access to PD-1 blockade.

Methods: This investigator-initiated, single-centre, randomized phase II trial evaluates ultra-low-dose nivolumab combined with gemcitabine, cisplatin, and dexamethasone (GCD) in patients aged ≥12 years with R/R cHL. Patients are randomized 1:1 to receive GCD plus nivolumab 20 mg for two cycles (Arm A) or GCD plus a single 20 mg dose during cycle 1 only (Arm B). The primary endpoint is ORR by end-of-treatment FDG-PET. Secondary endpoints include CR rate, toxicity, PD-1 receptor saturation, proportion proceeding to autologous stem cell transplantation, and 2-year PFS. Peripheral blood samples collected before and 2 hours after nivolumab administration, and at response assessment, will be analyzed for PD-1 receptor occupancy and T-cell activation. Patients achieving less than CR after two cycles will discontinue protocol therapy.

Statistical Considerations: Salvage chemotherapy alone yields ORRs of approximately 40–50%, whereas PD-1-based chemo-immunotherapy achieves ORRs approaching 85%. Assuming an ORR of 85% with ultra-low-dose nivolumab plus GCD, a sample size of 30 patients (15 per arm) provides 80% power at a two-sided significance level of 0.05 to demonstrate significant improvement over historical chemotherapy outcomes, while generating preliminary comparative data regarding the adequacy of single versus repeated ultra-low-dose nivolumab administration.

Current Status: Registered, Currently recruiting; Clinical Trials Registry of India, [CTRI/2025/06/089253 [20/06/2025].

Off-Label Disclosure: Nivolumab is being evaluated at a dose of 20 mg (1–2 doses), below the FDA-approved dosing regimen.

P120: From Clinical Trials to Clinical Practice: A Decade of Experience with Nivolumab in Relapsed/Refractory Classical Hodgkin Lymphoma

Alice Sykorova¹, Jan Koren², Eva Maule³, Lubica Gaherova⁴, Marie Lukasova⁵, Juraj Duras⁶, Katerina Steinerova⁷, Pavla Stepankova¹, Blanka Vackova², Jozef Michalka³, Jana Markova⁴, Vit Prochazka⁵, Barbara Brizova⁷, Marek Trneny², Zdenek Kral³, Petra Blahovcova², Heidi Mocikova⁴

¹th Department of Internal Medicine, University Hospital and Faculty of Medicine – Hematology, Hradec Kralove, Czech Republic, ²st Department of Medicine-Department of Hematology, Charles University, General Hospital, Prague, Czech Republic, ³Department of Internal Medicine, Hematology and Oncology, University Hospital Brno and Faculty of Medicine, Masaryk University Brno, Brno, Czech Republic, ⁴Department of Clinical Hematology, University Hospital Kralovske Vinohrady and Third Faculty of Medicine, Charles University, Prague, Czech Republic, ⁵Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic, ⁶Department of Hemato-Oncology, University Hospital and Faculty of Medicine, Ostrava, Czech Republic, ⁷Department of Hematology and Oncology, University Hospital, Pilsen, Czech Republic

Fig 1

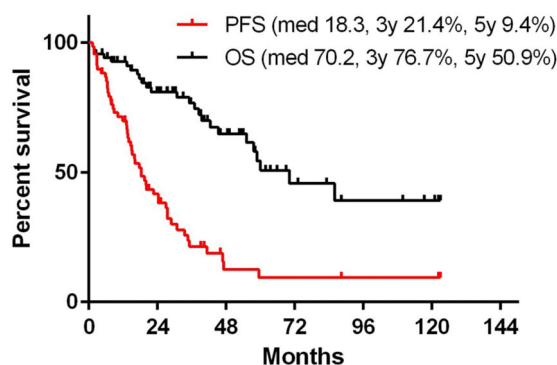


Figure 1: Progression-free survival (PFS) and Overall survival (OS).

Background: Nivolumab (nivo) is an established treatment option for patients (p) with relapsed/refractory classical Hodgkin lymphoma (R/R CHL).

Methods: Among 82 p treated with nivo between 2015 and 2025, 69 p receiving nivo monotherapy were analyzed. Clinical characteristics, treatment responses, survival, outcomes, and toxicity were evaluated in this retrospective analysis.

Results: Median age at nivo initiation was 42 years (y) (range, 20–77), with 52% aged ≤ 60 y, most p were male (n = 45; 65%). Patients received median of 3 (range, 1–12) prior treatment lines, 64% had advanced stage, 51% extranodal involvement, 5.7% bulky disease and 19% B symptoms. Prior autologous SCT was performed in 78% of p, while 67% were previously exposed to brentuximab vedotin (BV). Median time from diagnosis to first nivo dose was 34.7 months (range, 6–299). Median number of nivo administrations was 19 (range, 1–165). Median dose was 240 mg (range, 165–480 mg) with administration every 2 weeks in 64p. Best overall response rate (ORR) was 75% (complete remission, CR 42%). Treatment-related toxicity occurred in 22 p (32%); grade 3–4 in 7 (32%) of these p. Reasons for nivo discontinuation were CR (n = 12), partial remission (PR; n = 2), stable disease (n = 1), progression (PD; n = 33), toxicity (n = 6), and other reasons (n = 7). Ten p underwent nivo retreatment (8p were evaluable for BOR). Two p achieved CR and 3 p remain in treatment. Median treatment duration was 5.5 months (range, 2–15). During follow-up, 10 p received allogeneic SCT.

After median follow-up of 49.2 months, median progression-free survival (PFS) and overall survival (OS) were 18.3 and 70.2 months. 3 y PFS and OS were 21.4% and 76.7% (Figure 1). Median duration of response was 19.2, 30 and 12.8 months for ORR, CR and PR. Previous treatment with BV did not influence survival. At last follow-up, 24 p were in CR (22 p remained alive). Causes of death (n = 25) included PD (n = 10), infections (n = 7), secondary malignancies (n = 3), allogeneic SCT-related complications (n = 1), other (n = 2) and unknown causes (n = 2).

Conclusion: Our findings support nivo monotherapy as an effective and well-tolerated option for heavily pretreated patients, with improved outcomes over the past decade, although its role may evolve as immunotherapy shifts to earlier treatment lines.

This work was supported by the grant AZV NU22-03-00182 from the Ministry of Health of the Czech Republic and by the Cooperatio Program, research area “Oncology and Haematology”.

P121: Brentuximab vedotin as bridging and maintenance therapy in hematopoietic cell transplant in a national access program for relapsed or refractory classical Hodgkin lymphoma patients

Omar Fernandez-Vargas¹, Silvia Rivas-Vera¹, Gladys Agreda-Vásquez², Ingrid Mucius³, Marco Balandrán-Ruiz³, David Gómez-Almaguer⁴, Jorge Cruz-Rico⁵, Perla Colunga-Pedraza⁴, Carolina Balderas-Delgado⁶, Carlos Best⁷, Gabriel Barragán⁸, Mariela Cardiel⁹, María Luisa Alcivar¹⁰, Sergio Galvez-Acosta¹¹, Rosa Elena Sosa¹², Daniela Pérez Karen¹³, Ana Lucía Ron-Magaña¹⁴

¹Hematology Department, Instituto Nacional de Cancerología, Mexico City, Mexico, ²Hematology and Oncology Department, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, ³Medical Affairs, Takeda Mexico, Mexico City, Mexico, ⁴Hematology Service, Hospital Universitario de la Universidad Autónoma de Nuevo León, Nuevo León, Mexico, ⁵Hematology Service, Hospital Juárez de México, Mexico City, Mexico, ⁶Hematology Department, Hospital Regional de Alta Especialidad de Ixtapalapa, Mexico, Mexico, ⁷Hematology, Hospital General de Occidente, Jalisco, Mexico, ⁸Hematology Service, Hospital Regional de Alta Especialidad de Oaxaca, Oaxaca, Mexico, ⁹Hematology Department, Hospital General Zona 1, Aguascalientes, Mexico, ¹⁰Hematology, ISSSTE Hospital Regional de Alta Especialidad Bicentenario de la Independencia, Mexico, Mexico, ¹¹Hematology Department, Health Services of Instituto Mexicano del Seguro Social para el Bienestar, Hospital General,

Tijuana, Mexico, ¹²Hematology Service, Hospital General del Estado de Sonora, Sonora, Mexico, ¹³Hematology, Centro Estatal de Cancerología, Chihuahua, Mexico, ¹⁴Hematology Department, Hospital Civil de Guadalajara Fray Antonio Alcalde, Jalisco, Mexico

Background: Hematopoietic cell transplantation (HCT) is standard treatment for people with relapsed or refractory classical Hodgkin lymphoma (R/RcHL), but controlling the disease before HCT is crucial for success. Brentuximab vedotin (BV), an anti-CD30 antibody-drug conjugate, has proven useful as maintenance after HCT. We examined BV as bridging and post-HCT maintenance therapy through Mexico's Patient Access Program (PAP) in R/RcHL.

Methods: We retrospectively analyzed data from R/RcHL patients in the PAP from January 2017 to December 2021. Of 231 people identified, 193 (83.5%) were deemed eligible for HCT (autologous or allogeneic) by their physicians. We collected demographic data, disease status, prior therapy, BV use (doses, purpose, timing), transplant type, eligibility, completion, and outcomes (relapse, death, survival). Patients were grouped by BV use as bridging and/or maintenance therapy. Main outcomes included HCT completion rate, post-HCT relapse, relapse-free survival (RFS), and overall survival (OS).

Results: Among 193 eligible patients, 71 (36.8%) underwent HCT (59 autologous, 12 allogeneic [9 matched related, 3 haploidentical]). Two patients had an allo-HCT after relapsing from an auto-HCT. The rest (n = 122) missed HCT due to limited access (62), progression (42), refusal (6), death (3), stem-cell mobilization failure (3), or other reasons. BV was used as bridging in 46/193 (23.8%); 28/46 (60.9%) later had HCT, vs. 43/147 (29.3%) without BV bridging (p < 0.001). Of 71 who had HCT, 28 got BV as a bridge; 12/28 (42.9%) also received BV as post-HCT maintenance. Of those not given BV as a bridge, 17/43 (39.5%) still got BV as maintenance. In total, 29 people had post-HCT BV maintenance (median 12 doses). Post-HCT relapse happened in 19 (median time: 10.5 months); 24.1% (7/29) relapsed in the maintenance group vs. 28.6% (12/42) without it (p = 0.6780). No significant RFS (p = 0.4917) or OS (p = 0.3529) differences were seen with BV maintenance. Of maintenance patients, 41.4% also had BV as bridging. The 36-month OS rate was higher in HCT vs. non-HCT patients (100% vs. 85.9%).

Conclusions: BV use as bridge to HCT may increase the likelihood of undergoing HCT. While post-HCT maintenance with BV did not significantly improve OS or RFS, several factors could explain this result, including prior BV exposure or insufficient power of the study.

P122: BCL-2 Inhibition Combined with Other Therapeutic Agents Demonstrates Synergistic Efficacy in Hodgkin Lymphoma Cells

Alex Niu¹, Noah Brosnick¹, Cory Mavis¹, Matthew Cortese¹, Francisco Hernandez-Ilizaliturri¹

¹Roswell Park Comprehensive Cancer Center, Department of Medicine (Lymphoma Section)

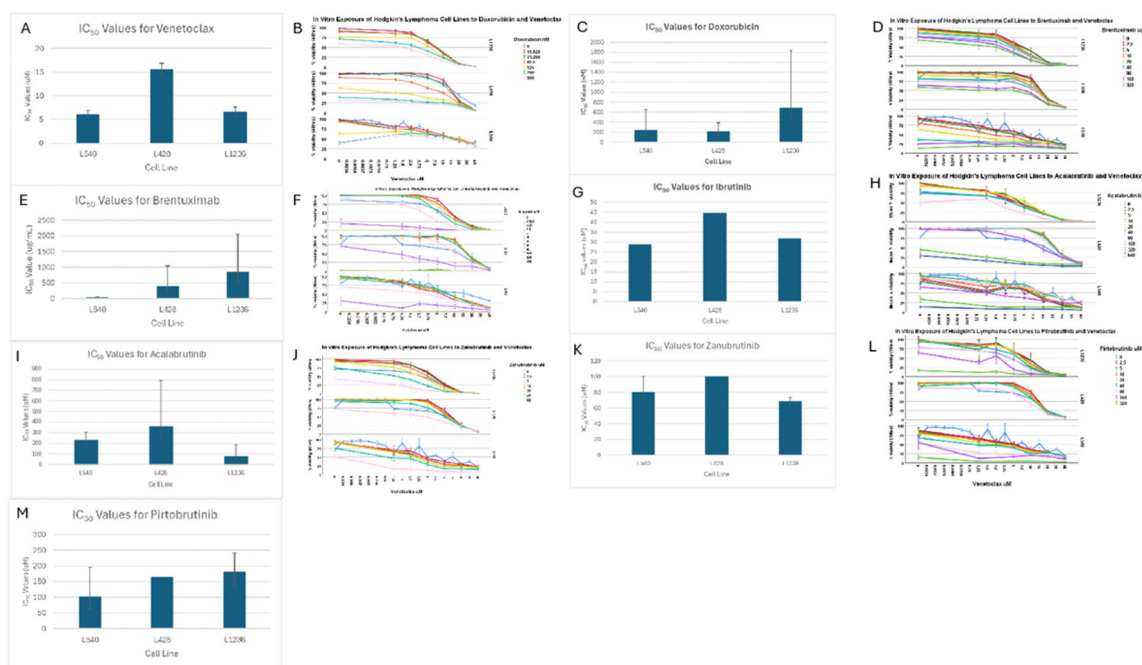


Figure 1: A, C, E, G, I, K, M: IC₅₀ value for venetoclax monotherapy and combined with other agents across HL cell lines; B, D, F, H, J, L: Respective dosage curves and percent viability of HL cell lines exposed to venetoclax and others agents in vitro.

Background: Relapsed/refractory (R/R) Hodgkin lymphoma (HL) remains difficult to treat, with particularly poor outcomes following relapse post-autologous stem cell transplant and check point inhibitors, and limited treatment options. The shift of active agents into the frontline setting further underscores the need for new therapies in R/R HL. B-cell lymphoma 2 inhibition (BCL2i) has shown activity, but remains underexplored, particularly in combination strategies. Similarly, Bruton's tyrosine kinase inhibitors (BTKi) have demonstrated preliminary efficacy in R/R HL. Thus, we aimed to evaluate BCL2i with venetoclax (ven) in combination with other agents, including BTKi, to assess cytotoxic effects in HL cell lines.

Methods: HL cell lines L1236, L428 and L540 were utilized for this analysis. Ven was combined with Ibrutinib (ibr), acalabrutinib (acal), zanubrutinib (zanu), pirtobrutinib (pir), brentuximab vedotin (bv) and doxorubicin (doxo) to assess synergistic cytotoxicity. HL cells were exposed for 48 hours. Cell viability changes were determined by measuring adenosine triphosphate content using Cell Titer-Glo Assay. The half maximal inhibitory concentration (IC50) was calculated with Graph Pad Prism Software. Experiments were performed in triplicates on three separate occasions. Data was analyzed using SPSS 21.0 software. Synergy coefficients for ven combinations were calculated by CalcuSyn software.

Results: Ven monotherapy demonstrated activity across all three HL cell lines, with the lowest IC50 observed in L540 (Figure 1A). Ven was subsequently combined with dox producing synergistic cytotoxicity across all cell lines, with the lowest IC50 in L428 (Figure 1B & 1C). Ven was then paired with bv with similar synergistic killing of all HL cells, with the lowest IC50 seen in L540 (Figure 1D & 1E). Ven also showed synergistic activity when combined with multiple BTKis, all of which showed synergistic efficacy in HL cell killing, with the lowest IC50 values observed with ibr and pir (Figure 1F-1M).

Conclusions: In this study, we evaluated the synergistic activity and potential efficacy of BCL2i (ven) in combination with other agents in HL cell lines. We found that ven combined with doxo, bv, and multiple BTKi's consistently produced synergistic cytotoxicity across HL models. These findings highlight BCL2i-based combinations as a potential therapeutic approach for R/R HL and support further investigation to enable progression toward clinical trials.

P123: Real-World Data on the Single-Agent Pembrolizumab Therapy in Relapsed /Refractory Classic Hodgkin Lymphoma Patients in the Czech Republic

Jozef Michalka¹, Heidi Móciková², Katarína Hradská³, Alice Sýkorová⁴, Vít Procházka⁵, František Folber¹, Eva Maule¹, Iubica Gahérová², Juraj Ďuraš³, Barbora Obadalová¹, Pavla štěpánková⁴, Marie Lukášová⁵, Zdeněk Král¹

¹Department of Internal Medicine, Hematology and Oncology, University Hospital Brno and Faculty of Medicine, Masaryk University Brno, Czech Republic, ²Department of Hematology, University Hospital Kralovské Vinohrady and 3rd Faculty of Medicine, Charles University, Prague, Czech Republic, ³Department of Haematology, University Hospital Ostrava, Ostrava, Czech Republic, ⁴Department of Internal medicine - Hematology, University Hospital and Faculty of Medicine, Hradec Kralove, Czech Republic, ⁵Department of Hematology, University Hospital Olomouc and Palacky University Olomouc, Czech Republic

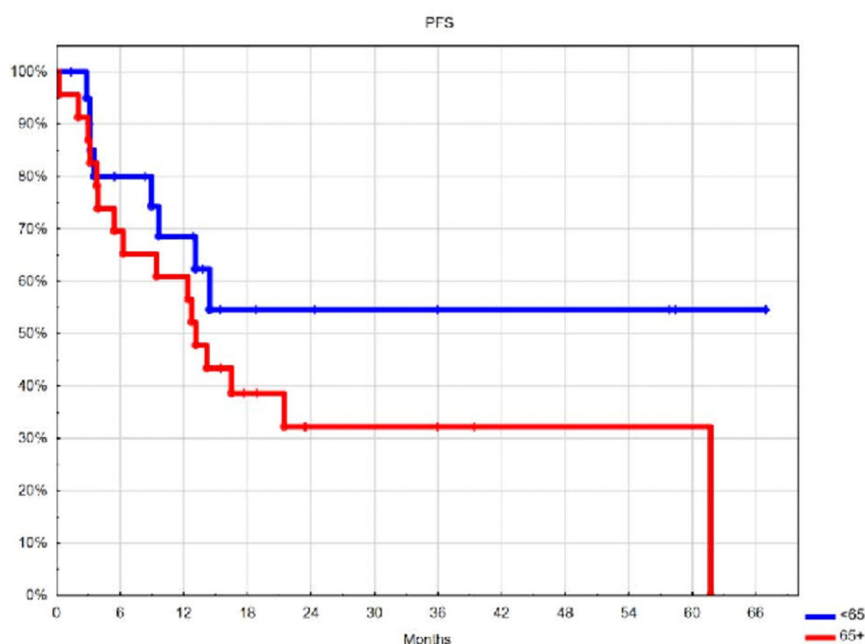


Figure 1: pembrolizumab, progression-free survival depending on age.

Background: Pembrolizumab has demonstrated significant anti-tumour activity and durable long-term disease control in patients (pts) with relapsed or refractory classic Hodgkin lymphoma (R/R cHL). Herein we present retrospective analysis on efficacy and safety of pembro treatment including optional approach with autologous hematopoietic stem cell transplantation (ASCT).

Patients and methods: We've analysed data of 44 R/R cHL pts after at least 2 lines of treatment between June 2019 and May 2026 in the Czech Republic. Pembro was administered every 3 weeks until disease progression, unacceptable toxicity or a maximum of 35 cycles.

Results: There were 28 men and 16 women, median age was 65 years (20–83). Median number of previous therapies was 3 (2–13) and the majority of pts (71%) started pembro in an advanced stage of the disease (III–IV). The median number of pembro courses was 10 (1–35), and the median duration of treatment was 8.2 months. Response was evaluated in 41 pts (93%) and assessed per Lugano criteria. Overall response rate (ORR) was 68% with a complete response (CR) rate in 46% and a partial response (PR) in 22%. In the subgroup of pts <65 years the ORR was 75% (CR 60%, PR 15%) while pts ≥65 years had ORR 62% (CR 33%, PR 29%). The most common reason for withdrawal was disease progression (50%) and ASCT (16%). With a median follow-up (FU) of 22 months, the 2year progression-free survival (PFS) was 41% (median PFS 14 months) and the

2year overall survival (OS) 88% (median OS not reached). In the pts <65 years, the 2year PFS was 55% whilst in ≥65 years 32%, but the difference was not statistically significant (Figure 1). Two pts with localized disease underwent radiation therapy after pembro and 7 of the responding pts in CR proceeded to ASCT and subsequent 8 cycles of pembro maintenance per treating physician's discretion. All of them remain in CR at the last FU. Treatment-related adverse events were reported in 12 pts (27%), but only 4 cases (9%) were grade 3. Eight pts died (18%), one of COVID-19, one of pneumocystis pneumonia, but always in the context of progressive lymphoma.

Discussion: Even though response rates were lower in the subgroup of pts ≥65 years, pembro often represents the only reasonable therapeutic option for them in the 3rd line setting. For the younger pts it may represent an efficient salvage therapy prior to ASCT. Increasing use of protocols combining pembro with chemotherapy can change current therapeutical landscape.

P124: Activity of Nivolumab with Decitabine Cedazurine (DEC-C) in Relapsed/Refractory Hodgkin Lymphoma (cHL): Results from an ETCTN Phase 1 Study

Justin Kline¹, Joseph Tuscano², Guarav Goyal³, Matthew Mei⁴, Alison Davis⁵, Geoff Shapiro⁶, Catherine Diefenbach⁵

¹University of Chicago School of Medicine, ²UC Davis Comprehensive Cancer Center, ³The University of Alabama at Birmingham, ⁴City of Hope Cancer Center, ⁵Perlmutter Cancer Center at NYU Langone School of Medicine, ⁶Dana Farber Cancer Institute

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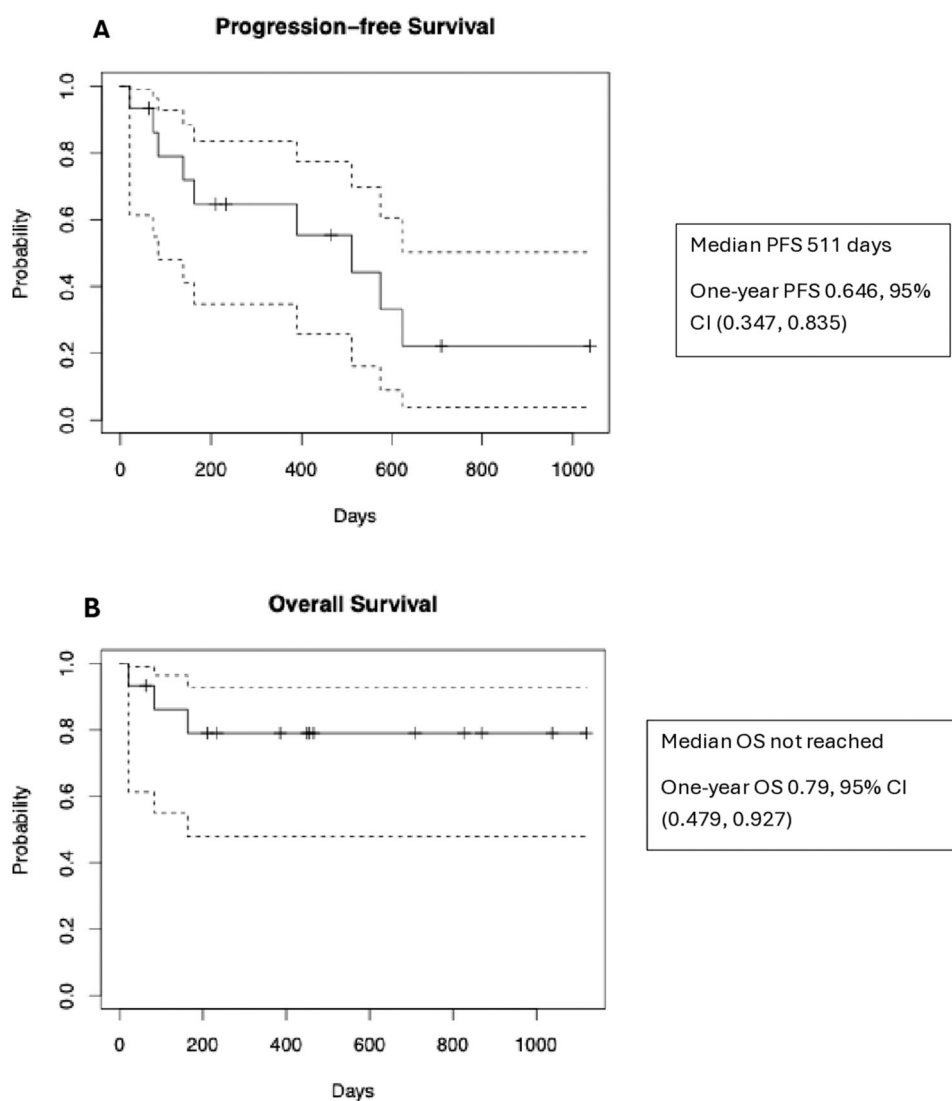


Figure 1: Progression Free Survival (A) and Overall Survival (B).

Patients with classic Hodgkin lymphoma (cHL) who relapse after checkpoint inhibitor (CPI) have limited treatment options; effective therapies remain an unmet need. Epigenetic silencing leading to exhausted T-cells is a mechanism of CPI resistance.

We tested the combination of oral decitabine and cedazuridine (DEC-C) a fixed-dose formulation of the hypomethylating agent decitabine, in combination with the checkpoint inhibitor (CPI) Nivolumab (Nivo) in a Phase 1 multicenter NCI/CTEP study of patients with R/R cHL and DLBCL. We present the cHL cohort here. A total of 15 patients were treated between 07/23 and 3/26.

DEC-C was given at a dose of 35 mg/100 mg daily x 5 (DL 1) or x 3 (DL-1) with standard dose Nivo. Two patients were treated in DL 1 and 13 patients in DL-1. Patients were heavily pre-treated with a median of 4 prior lines of therapy (range 2 to 16); 10 patients had prior hematopoietic stem cell transplant (HCT): 7 auto, 3 allo. 12 patients received prior CPI; all CPI treated patients relapsed after CPI, and 10 were considered refractory. 15 patients are evaluable for safety.

All patients had adverse events (AEs) across all grades which were low grade and included anemia, thrombocytopenia, nausea, headache, dyspnea, fatigue, and transaminase elevation. Gr 3 and 4 AEs considered at least possibly related were primarily hematologic and included neutropenia (7), anemia (2), thrombocytopenia (2), leukopenia (5), lymphocytopenia (2), and neutropenic fever (2); Gr 3 and 4 non-hematologic AEs included: dyspnea (2), hypokalemia (2), hyperkalemia (1), and cardiomyopathy (1). 12 of 15 patients are currently evaluable for response, of the 3 who are not evaluable, one died within a month of starting therapy due to disease, one came off treatment due to AEs, and one is too early for assessment. The overall response rate was 8/12 (66.7%) with 1 CR and 7 PR; an additional 4 (33.33%) patients had stable disease for a clinical benefit rate of 100%.

The 12-month PFS is 64% with a median PFS of 511 days, 95% CI (0.347, 0.835). The median OS is not reached, with one year OS of 79%, 95% CI (0.479, 0.927). DEC-C in combination with Nivo had manageable toxicity with durable clinical benefit in heavily pretreated predominantly HCT and CPI refractory cHL patients, for whom PFS is generally short. Future platforms could build on this strategy to maximize efficacy for these patients with limited treatment options.

P125: Three cycles of nivolumab (N) before BGD chemotherapy improves the remission rate before autologous hematopoietic cell transplantation (aHCT) in relapsed/refractory Hodgkin Lymphoma: N-BURGUND trial of the Polish Lymphoma Research Group (PLRG)

Michał Taszner^{1,2}, Ewa Paszkiewicz-Kozik³, Adam Wyszomirski⁴, Justyna Rybka⁵, Karolina Chromik⁶, Agnieszka Kołkowska-Leśniak⁷, Edyta Subocz⁸, Łukasz Targoński³, Paulina Ceklarz⁹, Magdalena Witkowska¹⁰, Ryszard Swoboda¹¹, Katarzyna Domańska-Czyż³, Agnieszka Giza⁹, Małgorzata Kobylecka¹², Conrad-Amadeus Voltin¹³, Joanna Romejko-Jarosińska³, Beata Ostrowska³, Monika Świerkowska³, Agnieszka Druzd-Sitek³, Michał Kurlapski^{1,2}, Marta Bednarek¹⁴, Bogdan Małkowski¹⁵, Grzegorz Romanowicz¹⁶, Janusz Hałka⁸, Tomasz Wróbel⁵, Sebastian Giebel¹¹, Grzegorz Helbig⁶, Ewa Lech-Marańda⁷, Jan Maciej Zaucha^{1,2}

¹Department of Hematology, Transplantology and Cell Therapies, Medical University of Gdansk, Gdansk, Poland, ²University Clinical Center, Gdansk, Poland, ³Department of Lymphoid Malignancies, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland, ⁴Department of Adult Neurology, Medical University of Gdansk, Poland, ⁵Department and Clinic of Hematology, Cellular Therapies and Internal Medicine, Wrocław Medical University, Wrocław, Poland, ⁶Department of Hematology and Bone Marrow Transplantation, Medical University of Silesia, Katowice, Poland, ⁷Department of Hematology, Institute of Hematology and Transfusion Medicine, Warsaw, Poland, ⁸Department of Hematology and BMT, Clinical Hospital of the Ministry of Internal Affairs and Administration with the Warmia-Mazury Oncology Centre in Olsztyn, ⁹Department of Hematology, Jagiellonian University Medical College, Krakow, Poland, ¹⁰Department of Hematology, Medical University of Lodz, Lodz, Poland, ¹¹Department of Bone Marrow Transplantation and Oncohematology, Maria Skłodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland, ¹²Department of Nuclear Medicine, The National Institute of Medicine of the Ministry of the Interior and Administration, Warsaw, Poland, ¹³Department of Nuclear Medicine, University Hospital of Cologne, Cologne, Germany, ¹⁴nd Department of Radiology, Medical University, Medical University of Gdansk, Gdansk, Poland, ¹⁵Department of Nuclear Medicine, Oncology Center, Bydgoszcz, Poland, ¹⁶Department of Nuclear Medicine, Medical University of Gdańsk, Gdańsk, Poland

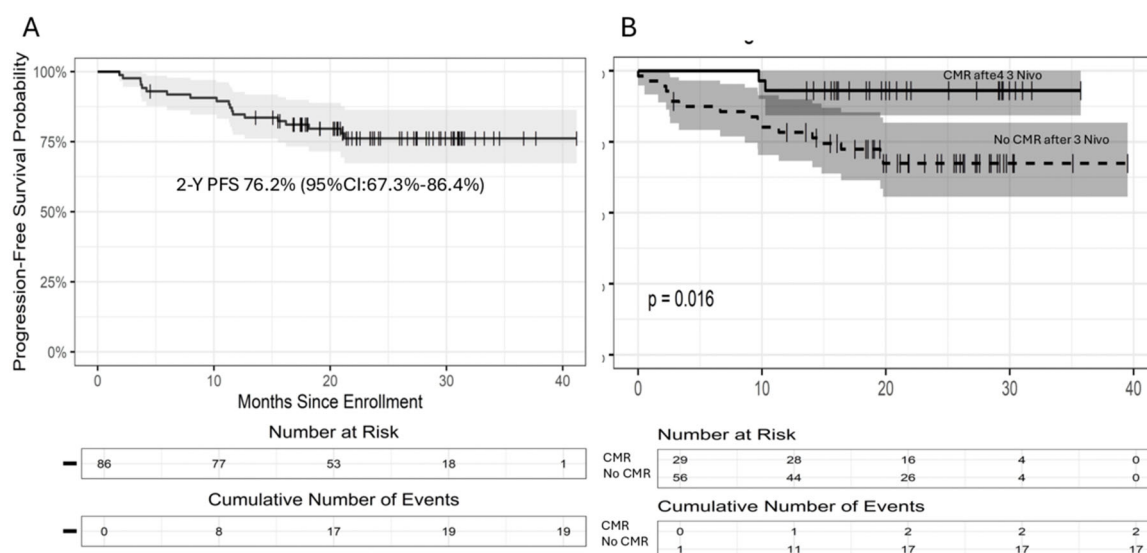


Figure 1: Two-year PFS in intention to treat (ITT) patient population (A) and 2-year PFS according to the presence or absence of CMR after 3 cycles of Nivolumab (B).

Introduction: Achieving complete metabolic response (CMR-Deauville score-DS1-3) before aHCT in patients (pts) with relapsed/refractory classical Hodgkin Lymphoma (r/r cHL) improves the long-term outcomes. BGD chemotherapy (bendamustine 90 mg/m² D1,2; gemcitabine 800 mg/m² on D1,4; dexamethasone 40 mg on D1-4.) in the 2nd line induces CMR in ca.70% of r/r HL pts. In the phase-2 N-BURGUND trial (EudraCT 2021-002630-17), we test the hypothesis that short exposure to Nivolumab (Nivo) prior to BGD increases CMR rate by 15%.

Methods: Patients aged ≥18 years with r/r stage (IIAX + IIB-IV) HL after 1st-line treatment were eligible and received N 240 mg IV Q2W for 3 cycles followed by PETNIVO and 2xBGD combined with CD34+ cell mobilization, followed by PETBGD. Responding pts (DS1-4 assessed centrally) are subjected to aHCT and post-transplant brentuximab (BV) if eligible. The primary endpoint is CMR in PETBGD. The secondary endpoints: PETNIVO response and 2-year progression-free survival (2-Y PFS).

Results: Between 12/22 and 11/24, 86 pts (50% female) with r/r cHL were enrolled across 9 PLRG centers. Median age was 36 years (20–71); 71 (83%) pts received ABVD, 2 (2%) BV+AVD, and 13 (15%) BEACOPPesc as 1st line therapy. 56 (65%) pts were primary refractory, including 12 to BEACOPPesc and 2 to BV+AVD; 50 (58%) pts had an early relapse (<12 months). All pts, except 1, have completed 3xN and 2xBGD. The negative (-) PETNIVO rate was 34,5% (96%CI:23.9%–44.7%), whereas the (-) PETBGD 84% (95%CI 73.9%–90.7%). After 2xBGD all (-) PETNIVO pts had also (-) PETBGD; Out of 55 (+) PETNIVO pts: 41 became (-), the rest remained (+) PETBGD. AHCT was not performed in 10 (12%) pts: 6 because of early progression, 2 because of withdrawal of consent, 1 due to myocardial infarction, and 1 due to lack of compliance. 50 (66%) pts received BV after aHCT at median number 13 (1–16). After median follow-up 24 months 16 pts progressed:1 who withdrew the consent for aHCT, 6 before and 9 after aHCT. 2 pts died: 1 from tuberculosis and 1 from myocardial infarction. 2-Y PFS in ITT population is 76.2% (95%CI:67.3%–86.4%) and per protocol 79% (95%CI:70.2%–88.9%). 2-Y PFS in pts with (-) PETNIVO is 93.1% (95%CI:84.3%–100%) and significantly better compared to (+) PETNIVO 67.4% (95% CI: 55.6%–81.7%) with HR: 0.20 (95% CI:0.05–0.86), p = 0.016, Figure.

Conclusion: A short Nivo prior to standard 2nd line BGD improves CMR from historical 70% to 84%. CMR after 3xNivo identifies pts with excellent 93% PFS.

P126: Real World Efficacy and Safety Comparison of Salvage Regimens Combining Brentuximab Vedotin and Chemotherapy in Second-Line Hodgkin Lymphoma: A LYSA Multicenter Retrospective Study

Juliette Wence¹, Arnaud Pages², Florian Cheillon³, Robin Noël⁴, Lucie Laemmel⁵, Maxime Vignac¹, Emilie Corvilain⁶, Pamela Sfeir⁷, Milena Kohn⁸, Guillemette Fouquet^{9,10,11}, Maxence Lohez⁹, Baptiste Delapierre¹², Gaétan Basile⁵, Gaele Laboure¹³, Amina Cherait¹⁴, Carole Soussain¹⁵, Adrien Grenier¹⁶, Thorsten Braun¹⁷, Laure Ricard¹⁸, Axel Andre¹⁹, Bénédicte Deau²⁰, Morgane Cheminant¹, Jean Galtier⁵, Pilar Dutari⁴, Loïc Renaud^{7,21}

¹Necker-Enfants Malades University Hospital, Department of Hematology, Paris, France, ²Department of Biostatistics, Gustave Roussy, Villejuif, France., ³Hôpitaux Universitaires Paris Nord, Department of AJA, Paris, France, ⁴Institut Paoli-Calmettes, Department of Hematology, Marseille, France, ⁵CHU de Bordeaux, Department of Hematology-Transplantation, Pessac, France, ⁶Hôpital Saint- Louis, Department of Immunopathology, Paris, France, ⁷Gustave Roussy Cancer Campus, Department of Hematology, Villejuif, France, ⁸Centre Hospitalier de Versailles, Department of Hematology, Versailles, France, ⁹CH Sud Francilien, Department of Hematology, Corbeil-Essonnes, France, ¹⁰Gustave Roussy Institute, UMR 1287, Villejuif, France, ¹¹CH Sud Francilien, Paris Saclay University, Corbeil-Essonnes, France, ¹²CHU de Caen, Department of Hematology, Caen, France, ¹³Centre hospitalier de Libourne, Department of Hematology, Libourne, France, ¹⁴Argenteuil Hospital, Department of Hematology, Argenteuil, France, ¹⁵Institut Curie, Department of Hematology, St Cloud, France, ¹⁶Pitié- Salpêtrière Hospital, Department of Hematology and cellular therapies, Paris, France, ¹⁷Hôpital Avicenne, Department of Hematology, Paris, France, ¹⁸Hôpital Universitaire St. Antoine, Paris, France, ¹⁹Centre Henri Mondor, Department of Hematology, Créteil, France, ²⁰Cochin, Department of Hematology, Paris, France, ²¹Hôpital Cochin, Department of Hematology, Paris, France

PFS among patients treated with Brentuximab Vedotin associated with Bendamustine, ICE, or DHAC/X/P

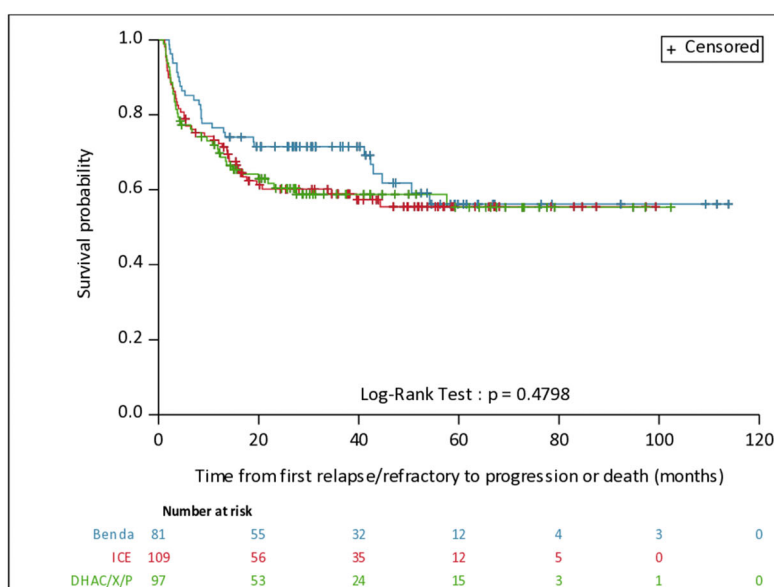


Figure 1: PFS among patients treated with Brentuximab Vedotin associated with Bendamustine, ICE, or DHAC/X/P.

The treatment of R/R HL involves polychemotherapy combined with Bv or anti-PD1 followed by ASCT for eligible patients. Polychemo combinations are based on phase II studies. No direct comparison allows for an evidence-based choice and treatment selection reflects habits.

Aim: To compare the efficacy and toxicity of Bv-chemo regimens in patients with R/R HL who have been treated in a second line setting.

Method: This retrospective multicenter study included patients with R/R Hodgkin lymphoma treated with Bv-chemo with intent to proceed to ASCT across 19 LYSA centers in France between 2014 and 2025.

Result: 288 patients were included: 81 (28%) treated with Bv-benda, 110 (38%) with Bv-ICE and 97 (34%) with Bv-DHAC/X/P (Bv-DHA). The median age was 33 years, and median follow-up was 41 months. ABVD first line treatment was more frequent in patients receiving Bv-benda ($p < 0.01$). Age, stage at relapse and time to relapse were also significantly different ($p < 0.01$, $p < 0.01$ and $p = 0.01$). 97 patients (34%) had a refractory disease and 118 (41%) relapsed more than 1 year after EOT. 215 patients (75%) underwent ASCT after second line, 24 (8%) after third line. CR was observed in 72.4% of patients without difference between treatment groups (78% for Bv-benda, 76% for Bv-ICE and 67% for Bv-DHA; $p = 0.21$). Similarly, 3 years PFS was 62% (712% (IC95% 61–80) for Bv-benda, 59% (IC95% 50–68) with Bv-ICE, 59% (IC95% 48–68) with Bv-DHA), with no significant difference in PFS (log rank $p = 0.48$). In multivariable Cox analysis adjusted for first-line treatment, age, time to relapse, and stage at relapse, PFS was not significantly ($p = 0.20$): using Bv-DHA as the comparator, the HR for the Bv-benda group was 0.6 (95% CI, 0.3–1.1) and 0.8 (95% CI, 0.5–1.4) for Bv-ICE group. Hematological toxicity was higher with Bv-ICE in terms of both RBC ($p < 0.001$) and platelet transfusions ($p < 0.001$). Hospitalization median duration was significantly shorter in patients treated with Bv-benda (1.7 days/cycle) compared to those treated with Bv-ICE (4.3 days/cycle) or Bv-DHA (3.2 days/cycle). Severe infections rates were similar between the groups ($p = 0.81$). Recruitment is ongoing and updated data will be presented at conference.

Conclusion: Bv-benda, Bv-ICE and Bv-DHA showed similar efficacy as 2nd line salvage treatments for HL, with Bv-ICE being associated with significantly increased toxicity. These results provide real-world comparative data that may guide treatment selection among Bv-based salvage regimens.

P127: (Bv)DHAP + G-CSF as an effective peripheral stem cell mobilization regimen in adult patients with relapsed/refractory Hodgkin lymphoma

Maryia Shapetska¹, Igar Iskrau², Marta Valevskaya¹, Olga Gerasimovich¹, Victoria Smolnikova¹

¹Minsk Scientific and Practical Center for Surgery, Transplantology, and Hematology, ²Belarusian State Medical University

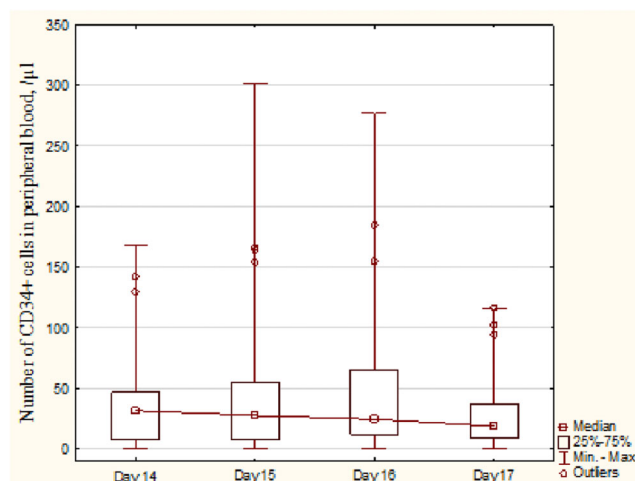


Figure 1: Median peak count of circulating CD34+ cells in peripheral blood using the (Bv)DHAP + G-CSF HSC mobilization regimen.

High-dose chemotherapy with autologous stem cell transplantation (auto-HSCT) remains the accepted standard of care for patients with Hodgkin lymphoma (HL) that has failed or relapsed after first-line chemotherapy. Mobilization of hematopoietic stem cells (HSCs, CD34+ cells) into the peripheral blood is a crucial step. In 5–40% of patients with relapsed or refractory HL, mobilization is ineffective. The use of chemomobilization regimens (chemotherapy followed by the administration of G-CSF) can be highly effective.

Aim: to determine the dynamics of CD34+ cells in peripheral blood and evaluate the effectiveness using peripheral stem cell mobilization regimen (Bv)DHAP + G-CSF in adult patients with HL.

Material and methods: the study included 115 adult patients with refractory form or a relapse of HL, treated at the Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology from 2019 to 2025. As a peripheral stem cell mobilization regimen (Bv)DHAP + G-CSF (10 mcg/kg/day from the 9th day until the mobilization effect was achieved) was administered. The number of CD34+ cells in peripheral blood was determined from days 14 to 17 using flow cytometry. Mobilization was considered effective when the CD34+ cell level reached 10

cells/ μ l. Continuous and categorical variables are presented as median (interquartile range) and abs. (%); for categorical variables, when demonstrating differences in the compared groups, the odds ratio (OR) is determined.

Results: 60 women (52.2%), 55 men (47.8%); median age 35 years. After salvage therapy 73 (63.5%) patients had a complete response. The number of previous lines of therapy in patients ranged from 2 to 5. Mobilization effect was achieved in 93 patients (80.9%) from days 14 to 17, while no effect was achieved in 22 (19.1%). The median maximum number of circulating CD34+ cells in peripheral blood using the (Bv)DHAP + G-CSF HSC mobilization regimen is shown in Figure. The following statistically significant risk factors for unsatisfactory mobilization were identified: 3 or more lines of chemotherapy (OR 4.26 [1.6–11.8]), platelet count less 200 (OR 2.9 [1–8.5]); leukocyte count 4.5 or less (OR 3.26 [1.15–8.5]) in patients before the mobilization regimen.

Conclusion: (Bv)DHAP + G-CSF was found to be an effective peripheral stem cell mobilization regimen in adult patients with relapsed/refractory Hodgkin lymphoma. The mobilization effect may be achieved in 80.9%.

P128: EHA-4448 Real-World Outcomes of Pembrolizumab Plus GVD as Salvage Therapy and Bridge to Autologous Stem Cell Transplantation in Relapsed/Refractory Classical Hodgkin Lymphoma: A Multicenter Gatla Study

Astrid Pavlovsky¹, Fernando Warley², Luciano Salvano³, Maria Orlova², Luciana Guanchiale⁴, Laura Korin⁵, Carolina Mahuad⁶, Jose Ignacio Trucco⁷, Amalia Cerutti⁸, Florencia Negri Aranguren⁹, Guadalupe Antelo Perez¹⁰, Bruno Wannesson¹, Javier Romano¹¹, Lautaro Sardu¹², Veronica Musso¹³, Etelvina Lucia Macchiavello¹⁴, Nadia Scebbba¹⁵, Trinidad Viviani¹⁶, Lorena Fiad¹⁵

¹Centro de Hematología Pavlovsky/FUNDALEU, Ciudad Autónoma de Buenos Aires, Argentina, ²Hospital Italiano de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina, ³Clínica Universitaria Reina Fabiola, Córdoba, Argentina, ⁴Hospital Privado Universitario de Córdoba, Córdoba, Argentina, ⁵Instituto Alexander Fleming, Ciudad Autónoma de Buenos Aires, Argentina, ⁶Hospital Alemán, Ciudad Autónoma de Buenos Aires, Argentina, ⁷Hospital Austral, Buenos Aires, Argentina, ⁸Sanatorio Británico, Rosario, Argentina, ⁹Instituto Privado de Hematología y Hemoterapia, Paraná, Argentina, ¹⁰CEMIC, Ciudad Autónoma de Buenos Aires, Argentina, ¹¹Hospital Posadas, Buenos Aires, Argentina, ¹²Hospital El Cruce, Buenos Aires, Argentina, ¹³Instituto de Trasplante y Alta Complejidad, Buenos Aires, Argentina, ¹⁴Sanatorio La Pequeña Familia, Buenos Aires, Argentina, ¹⁵Hospital Italiano de La Plata, Buenos Aires, Argentina, ¹⁶GATLA, Buenos Aires, Argentina

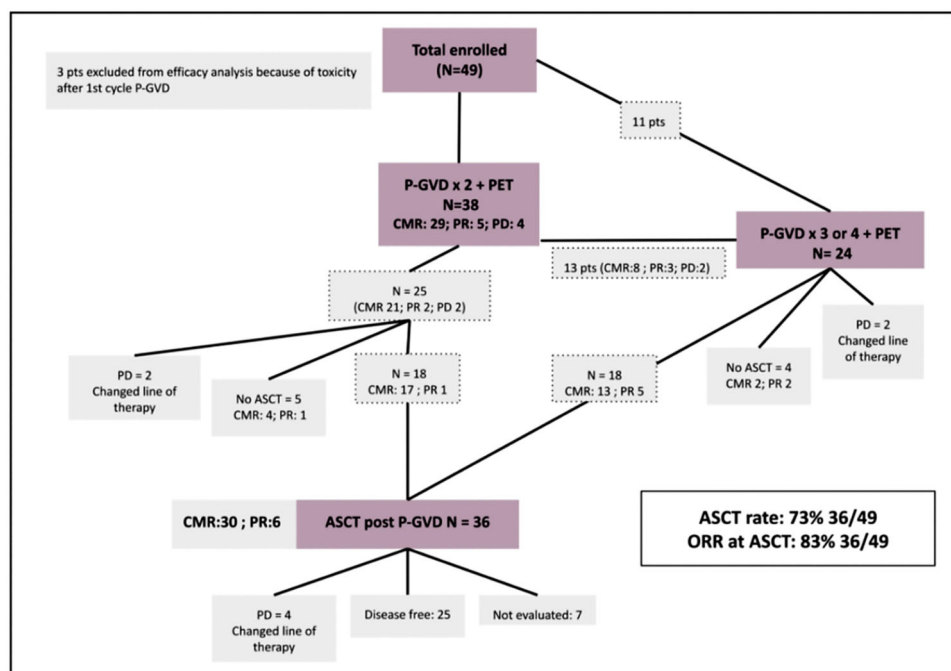


Figure 1: Flow chart. CMR: complete metabolic response, PR: partial response, PD: progressive disease, ASCT: autologous stem cell transplant, P-GVD: Pembrolizumab, Gemcitabine, Vinorelbine, Liposomal Doxorubicine, ORR: overall response rate.

Background: In a phase 2 study of 39 pts. with R/R classical Hodgkin lymphoma (R/R cHL) candidates for autologous stem cell transplantation (ASCT), pembrolizumab plus gemcitabine, vinorelbine and liposomal doxorubicin (P-GVD) achieved a complete metabolic response (CMR) rate of 95%, with 95% proceeding to ASCT, supporting P-GVD as a highly effective bridge to transplant.

Aims: To report real-world outcomes in a broader, unselected population of pts. with R/R cHL eligible for ASCT treated with P-GVD.

Methods: Retrospective multicenter study within the GATLA cooperative group of consecutive pts. with R/R cHL eligible for ASCT treated with P-GVD. Baseline characteristics, PET response, immune-related adverse events (irAEs) and transplant rates were analyzed.

Results: 52 pts. initiated P-GVD (median age 32 years, IQR 17–69). 46 (88.5%) received ABVD as first-line and 6 (11.5%) BV-AVD. AETHERA high-risk features were present in 88.5%: 69.2% primary refractory, 11.5% relapsed within the first year, 36.5% extranodal relapse; B symptoms in 65.4% and bulky disease in 32.7%. P-GVD was given as first salvage in 35 pts (67.3%) and second salvage in the remainder. PET assessment was available in 49 pts (94.2%); 3 discontinued after 1 cycle due to toxicity.

After 2 cycles, 38 pts underwent PET/CT: 29 (76%) CR, 5 (13%) PR, 4 (11%) PD; 25 did not receive further P-GVD (CR 21, PR 2, PD 2). 13/38 received additional cycles and re-evaluated after 3–4 cycles (CR 8, PR 3, PD 2); 24 pts had PET/CT after 3–4 cycles total.

Overall, 36/49 pts (73.5%) achieved CMR. 36 (73.5%) proceeded to ASCT (30 CMR, 6 PR); 6 CMR pts did not undergo ASCT; 1 received allogeneic transplant; 4/36 relapsed post-ASCT. (Figure 1)

Median follow-up 14.7 months (IQR 10.3–26.2); 3/52 died: 1 COVID-19 during P-GVD, 1 GVHD post-allogeneic transplant, 1 sudden death. IrAEs in 8/52 pts (15.4%), manageable with standard interventions.

Summary/Conclusion: P-GVD produced a CMR rate of 73.5% and enabled 77.6% to proceed to ASCT, lower than the 95% reported by Moskowitz et al. in the phase 2 trial. These differences likely reflect a less selected population, including 2nd salvage pts. and a higher proportion of primary refractory disease. Nonetheless, P-GVD remained an effective bridge to transplantation in routine practice, providing real-world context for PD-1-based chemo-immunotherapy as a bridge to ASCT. Our cooperative group is now conducting a prospective trial to more clearly define its safety profile and efficacy.

P129: You Don't Always Need a Transplant: Checkpoint Inhibitors Can Deliver Lasting Remissions in Relapsed and Refractory Classical Hodgkin Lymphoma

Vivek Radhakrishnan¹, Rida Shakeel¹, Deedar Singh¹, Robert Lown¹, Sean Lim², David Dutton¹, Angharad Pryce¹, Luke Bennett¹, Andrew Bates¹, Andrew Davies², Peter Johnson²

¹Cancer Care Group, University Hospital of Southampton, ²School of Cancer Sciences, University of Southampton

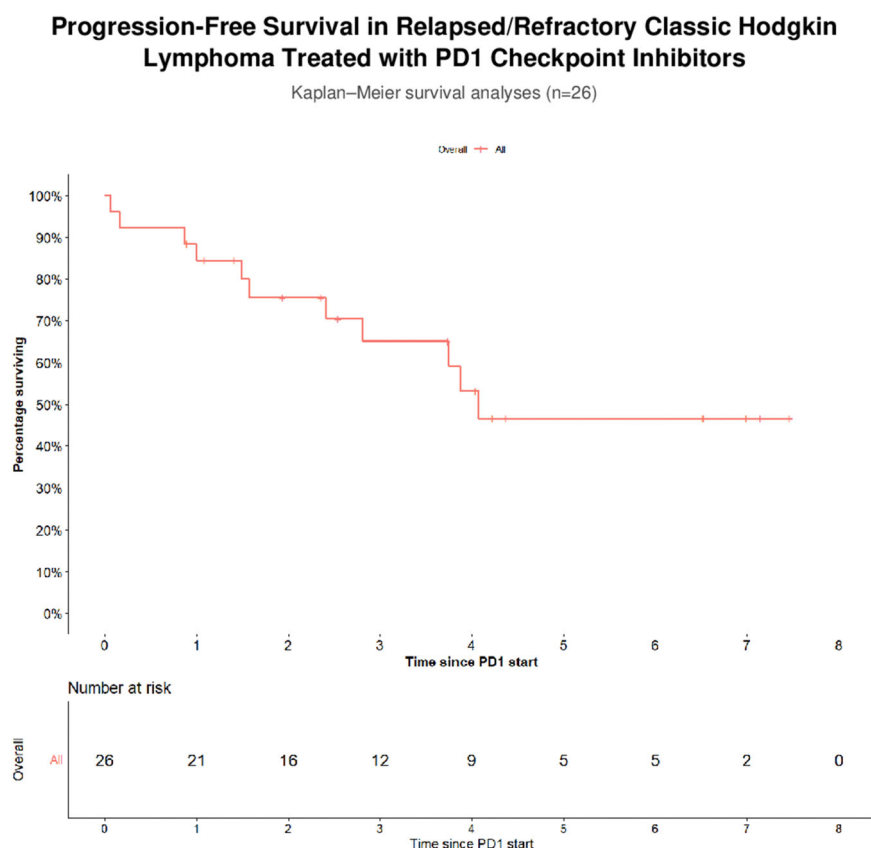


Figure 1. Kaplan–Meier estimate of progression-free survival (PFS) for the entire cohort (n=26). The 5-year PFS estimate was 47% (95% CI 23–67) and the median PFS was 4.07 years (95% CI 2.4–NE). Time is measured in years from initiation of PD1 checkpoint inhibitor (CPI) therapy. The risk table shows the number of patients at risk at each yearly interval.

Figure 1: Kaplan–Meier estimate of progression-free survival (PFS) for the entire cohort (n = 26).

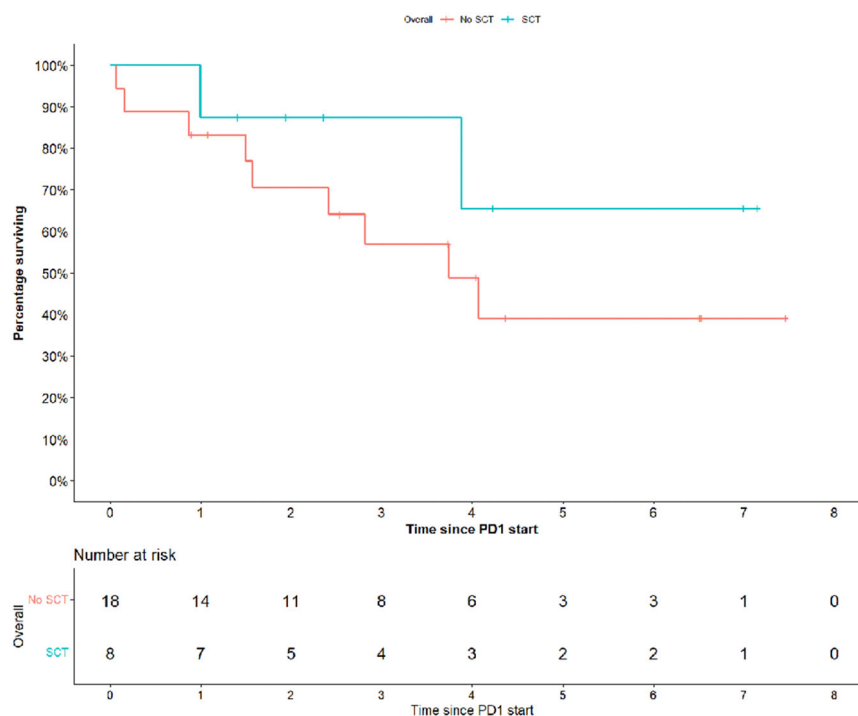


Figure 2. Kaplan-Meier estimate of progression-free survival (PFS) stratified by stem cell transplant (SCT) consolidation status: patients consolidated with allogeneic SCT after CPI (SCT; n=8) versus those not consolidated (No SCT; n=18). The 5-year PFS estimate was 66% (95% CI 16–91) in the SCT group. Time is measured in years from initiation of PD1 checkpoint inhibitor (CPI) therapy. The risk table shows the number of patients at risk in each group at yearly intervals.

Figure 2: Kaplan-Meier estimate of progression-free survival (PFS) stratified by stem cell transplant (SCT) consolidation status.

The PD1-targeting checkpoint inhibitors (CPI) nivolumab and pembrolizumab are established treatments for relapsed/refractory (R/R) classical Hodgkin Lymphoma (cHL) (Keynote-087/204, Checkmate-205). We retrospectively studied CPI-treated R/R cHL patients, evaluating survival, response, toxicity and post-CPI therapy in R.

Between 2015–2025, 26 patients received CPI monotherapy (pembrolizumab n = 16, nivolumab n = 10) for R/R cHL. Median age was 40 (range 22–87) and 14 were female. The median number of prior treatments was 3 (2–11); 69% had advanced stage at diagnosis. The commonest first-line treatment was ABVD (n = 19); 19 had primary refractory disease. Second-line treatments were ICE (n = 10) or GDP (n = 7), and third-line: brentuximab (n = 10) or chemotherapy (n = 8). Nine had autologous and 5 allogeneic stem cell transplant (SCT) pre-CPI (2 had both). CPI was salvage therapy in third line (n = 5) or fourth line and beyond (n = 21). Median CPI treatment duration was 13 months.

For the cohort, ORR, complete response (CR), partial response (PR), stable disease (SD) and progression (PD) were 73.07%, 69.23% (n = 18), 3.8% (n = 1), 3.8% and 11.53% (n = 3) respectively; 3 died before assessment. Median response duration was 21.9 months (95% CI 8.2–46.9). Eight proceeded to SCT as consolidation in CR (n = 6), PR (n = 1) or SD (n = 1); median time from last CPI to transplant was 8.15 weeks. Post-transplant, 5 remain in CR, 3 progressed/relapsed. GVHD occurred in 6 patients, all grade 1–2. Of 12 in CR without SCT, 9 remain in CR (median treatment 13.4 months).

Eight CPI-associated immune-related adverse events (AE) occurred in 6 patients (hepatitis, colitis, autoimmune haemolytic anaemia, panhypopituitarism, arthropathy, pneumonitis, neurotoxicity and thyrotoxicosis).

At a median follow-up of 4 years, 14 patients remain in CR. Median PFS was 4.07 years (95% CI 2.4–NE); 5-year Kaplan-Meier PFS was 47% (95% CI 23–67) overall and 66% (95% CI 16–91) in the SCT group. Median OS not reached; estimated 5-year OS 59% (95% CI 30–79). On Cox regression, older age was associated with significantly higher progression risk (HR 1.06, 95% CI 1.02–1.10; p = 0.001) on univariate and multivariate analysis.

Our study demonstrates the real-world effectiveness of CPIs, with unselected patients achieving durable responses and an acceptable AE profile. It confirms that heavily pretreated patients can be safely consolidated with SCT, while many non-SCT patients in CR maintain durable remission. A UK-wide study is ongoing.

P130: Second-Generation Epigenetic Clocks Reveal Accelerated Biological Aging in Relapsed/Refractory Hodgkin Lymphoma

Mahek Shah¹, Anuja Abhyankar², Nour Nassour², Francisco Hernandez-Ilizaliturri², Joyce Ohm¹, Alex Niu²

¹Department of Cancer Genetics, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA, ²Department of Medicine (Lymphoma), Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

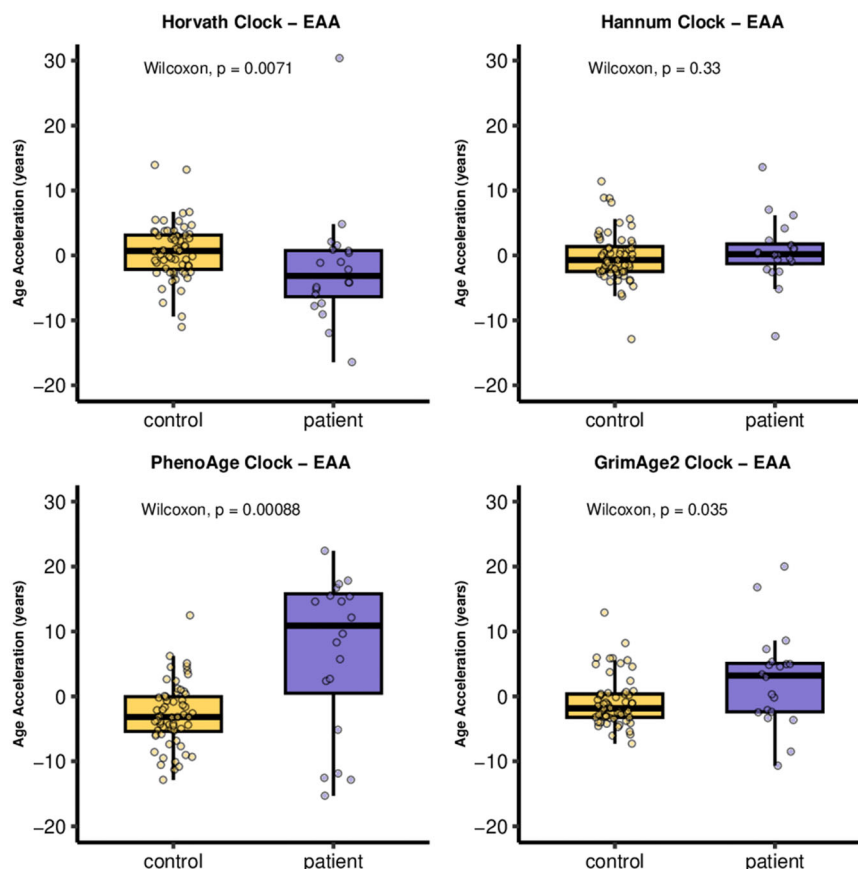


Figure 1: Epigenetic Age Acceleration in Relapsed/refractory (R/R) Hodgkin lymphoma (HL) patients.

Background: Relapsed/refractory (R/R) Hodgkin lymphoma (HL) is associated with poor clinical outcomes arising from multiple contributing factors. Biological aging has recently emerged as an area of interest; however, its role in driving R/R HL is not well defined. Epigenetic age acceleration (EAA), derived from DNA methylation-based clocks, may capture treatment- and disease-related aging processes in HL. First-generation epigenetic clocks predict chronological age, whereas second-generation clocks are designed to reflect biologic aging and health-related outcomes. Thus, we conducted a single-center study comparing EAA in R/R HL patients to that of healthy individuals.

Methods: EAA was evaluated in 20 patients with R/R HL diagnosed from 2020 to 2022, and 60 healthy, non-cancer controls. Pre-banked peripheral blood samples collected at the time of relapse were obtained and processed using the Illumina EPIC v2 array to generate DNA methylation data. Methylation data were analyzed to calculate EAA using first-generation (Horvath, Hannum) and second-generation (PhenoAge, GrimAge2) epigenetic clocks. Comparisons were performed between R/R HL patients and controls, as well as across patient subgroups stratified by clinical characteristics.

Results: Second-generation clocks demonstrated statistically significant increases in EAA in R/R HL patients compared with controls (PhenoAge: $p = 0.0009$; GrimAge2: $p = 0.035$). Additionally, R/R HL patients showed higher median EAA than control patients (median PhenoAge acceleration: 10.89 [IQR, 15.31] vs -3.17 [IQR, 5.36]; median GrimAge acceleration: 3.21 [IQR, 7.47] vs -1.84 [IQR, 3.60]). Among first-generation clocks, Horvath's clock demonstrated significant age deceleration in relapsed HL patients compared with controls (median age acceleration: -3.16 vs 0.69, $p = 0.007$) whereas Hannum's clock showed no significant difference. EAA did not differ significantly according to ethnicity, cHL status or treatment exposure ($p > 0.05$ for all comparisons).

Conclusion: In this single-center analysis, we observed that second-generation epigenetic clocks detected significantly increased biological aging in patients with R/R HL. These findings support a potential association between biological aging and R/R HL, indicating that EAA may represent a biomarker of underlying disease biology and treatment-related aging. Further studies are needed to clarify the prognostic and clinical impact of accelerated epigenetic aging in HL.

P131: Autologous Stem Cell Transplantation after Anti-PD-1 Therapy in Heavily Pretreated Patients with Relapsed/Refractory Classical Hodgkin Lymphoma: Real-World Outcomes

Iuliia Protopopova¹, Nikita Mochkin¹, Vladislav Sarzhevskiy¹, Elena Demina¹, Vladimir Melnichenko¹, Nikita Shorokhov¹, Anastasia Samoylova¹, Aisel Mamedova¹, Anna Bannikova¹, Anatoliy Rukavitsyn¹, Elena Smirnova¹, Vladimir Bogatyrev¹

¹FSBI National Medical Surgical Center n.a. N.I. Pirogov, Moscow, Russia

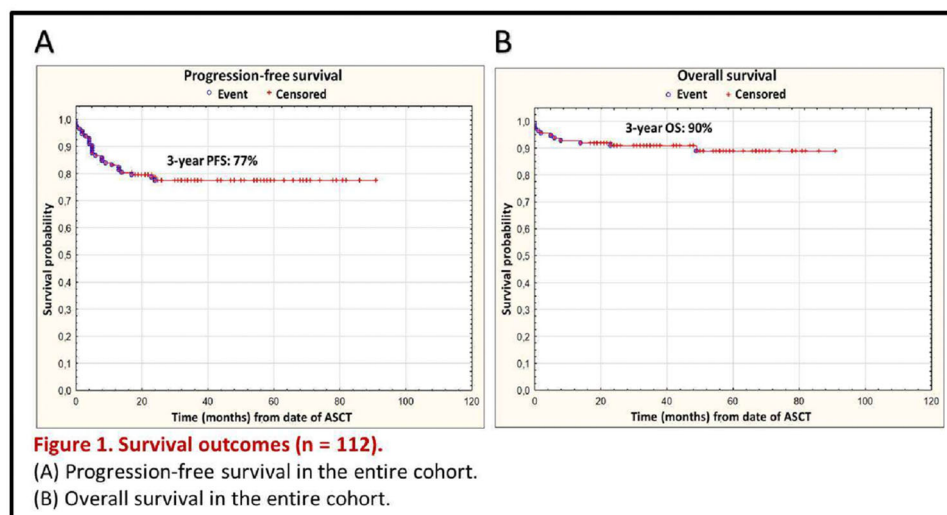


Figure 1: Survival outcomes (n = 112). (A) Progression-free survival in the entire cohort. (B) Overall survival in the entire cohort.

Background: Autologous stem cell transplantation (ASCT) after anti-PD-1 therapy is an effective option in relapsed/refractory classical Hodgkin lymphoma (cHL). However, real-world outcomes often diverge from clinical trials, as patients are heavily pretreated and frequently undergo ASCT in the ≥ 3 rd-line setting. This study provides real-world data from our clinical practice.

Aims: To evaluate ASCT outcomes after anti-PD-1-based regimens in the entire cohort and the ≥ 3 rd-line subgroup (ASCT after anti-PD-1 in the ≥ 3 rd-line setting), identify prognostic factors for PFS, and characterize relapse patterns.

Methods: We retrospectively analyzed patients with cHL who underwent ASCT after anti-PD-1-based regimens (2018–2024). Patients receiving salvage therapy between anti-PD-1 and ASCT were excluded. Survival was estimated using Kaplan-Meier method. Prognostic factors included: number of prior lines of therapy, time interval from anti-PD-1 to ASCT (< 60 vs ≥ 60 days), and refractory status to the pre-anti-PD-1 line.

Results: A total of 112 patients were analyzed (median age 35 years, range 19–56). The median number of prior lines of therapy was 2 (range, 2–7). Prior to anti-PD-1, 58%, 34%, and 15% of patients were refractory to 1, 2, and 3 consecutive lines, respectively. Anti-PD-1 was administered as monotherapy (37.5%) or with chemotherapy (62.5%). The median number of anti-PD-1 cycles was 6 (range, 2–52).

Pre-ASCT Responses: complete response (CR) (83%), partial response (PR) (12.5%), progressive disease (0.9%) and indeterminate response (3.6%). Conditioning regimens: BEAM (20%) and BeEAC (80%). Post-ASCT maintenance: brentuximab vedotin (13.4%) and anti-PD-1 (15.1%).

At a median follow-up of 37 months (range, 1–91), 3-year OS and PFS were 90% and 77% for the entire cohort (Figure 1). In the ≥ 3 rd-line subgroup, 3-year OS and PFS were 90% and 78%. No prognostic factors significantly impacted PFS in the entire cohort. However, in the ≥ 3 rd-line subgroup, refractory status to the pre-anti-PD-1 line was associated with shorter PFS (3-year PFS 64% vs 85%; $p = 0.02$). A total of 14 relapses occurred, with 13 within 18 months of ASCT (range, 4–24 months). All relapsing patients had pre-ASCT CR or PR.

Conclusion: ASCT after anti-PD-1 demonstrates high effectiveness for heavily pretreated patients in routine practice. In the ≥ 3 rd-line subgroup, refractory status to the pre-anti-PD-1 line was associated with shorter PFS. Most relapses occurred within 18 months post-ASCT.

P132: Allogeneic Hematopoietic Stem Cell Transplantation for Relapsed/Refractory Classical Hodgkin Lymphoma in the Brentuximab Era: Updated Single-Center Experience

Natalya Milanovich¹, Alena Dziuba¹, Oksana Marozava¹, Yury Strongin¹, Oksana Nechay¹, Tatsiana Talako¹, Natalia Volkovets¹, Aliaksandr Avadok¹, Anatoly Uss¹

¹Bone Marrow Transplantation Unit No. 3, Minsk Scientific and Practical Center for Surgery, Transplantation and Hematology, Minsk, Belarus.

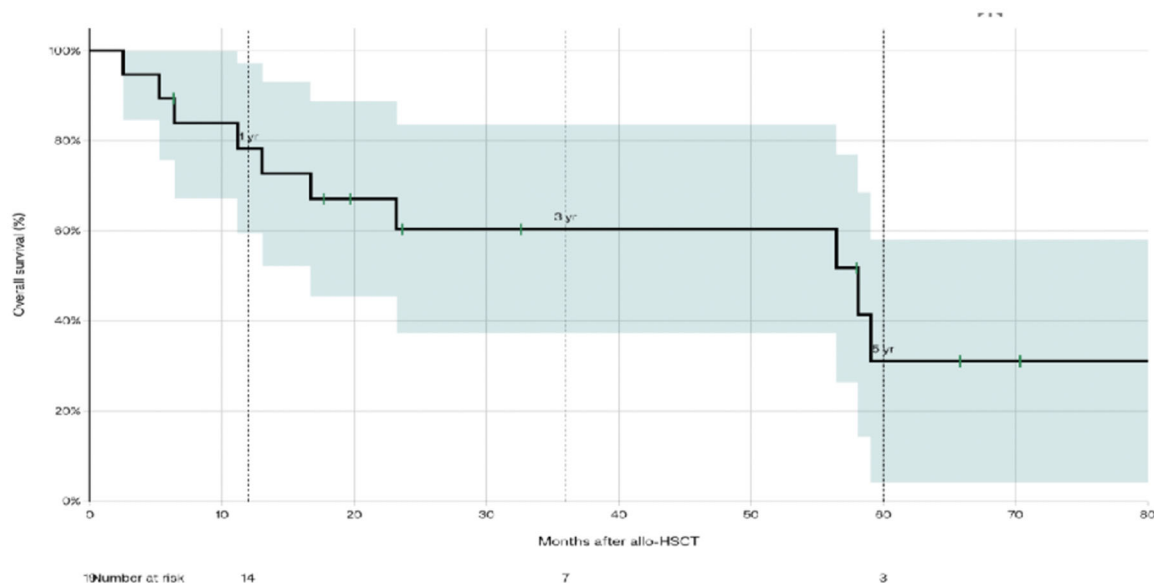


Figure 1: Overall survival after allo-HSCT in patients with R/R cHL.

Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a potentially curative option for patients with relapsed/refractory classical Hodgkin lymphoma (R/R cHL) after failure of salvage therapy and high-dose chemotherapy. PD-1 inhibitor-based salvage regimens have shown high response rates in clinical trials and real-world cohorts, but their use is constrained by limited regulatory approval and restricted reimbursement in many real-world settings. Consequently, many patients still proceed to allo-HSCT after brentuximab vedotin (BV)-based therapy with limited exposure to PD-1 inhibitors.

Methods: This retrospective single-center study included 19 consecutive patients with R/R cHL who underwent allo-HSCT. Demographic characteristics, time from diagnosis to allo-HSCT, prior therapies, and survival outcomes were updated as of June 15, 2026. Prior treatment exposure included autologous HSCT (auto-HSCT), BV-containing therapy, and BV plus nivolumab before allo-HSCT. Overall survival (OS) was estimated using the Kaplan-Meier method.

Results: The median age at allo-HSCT was 29.6 years (range, 20.3–42.9), and the median time from diagnosis to allo-HSCT was 4.9 years (range, 0.7–11.8). Prior auto-HSCT had been performed in 16 patients (84.2%). BV-based therapy before allo-HSCT was administered in 10 patients (52.6%), including 8 treated with BV alone and 2 with BV plus nivolumab. With a median follow-up of 23.2 months, the estimated 1-, 3-, and 5-year OS rates were 78.3% (95% CI, 59.4–97.2), 60.4% (95% CI, 37.3–83.5), and 31.1% (95% CI, 4.2–58.0), respectively (Figure 1). Ten deaths were recorded: 6 were associated with disease relapse/progression and 4 with graft-versus-host disease (GvHD)-related complications.

Conclusions: In this updated single-center cohort, allo-HSCT provided meaningful survival despite extensive exposure to auto-HSCT and BV-based regimens, with only limited pre-transplant use of PD-1 inhibitors reflecting real-world access barriers. Long-term OS remained modest, with mortality driven by both relapse and GvHD-related complications, underscoring the need to optimize disease control before transplant and reduce post-transplant toxicity.

P133: Recurrent Hemophagocytic Lymphohistiocytosis and Hepatic Failure in EBV-Associated Hodgkin Lymphoma

Ignacio Tobarra¹, Marc Bosch^{1,2}, M Laura Fox^{1,2}, Josep Castellví¹, Cristina García^{1,2}, Pau Abrisqueta^{1,2}, Cecilia Carpio^{1,2}, Jhon Kevin Fuentes¹

¹Department of Hematology, University Hospital Vall d'Hebron, Barcelona, Spain, ²Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

Episode (Date)	Clinical Context	EBV Viremia	Ferritin (ng/mL)	Triglycerides (mg/dL)	AST / ALT (IU/L)	Total Bilirubin (mg/dL)	Primary Salvage Treatment
1. Onset (June 2024)	Multorgan failure at diagnosis.	51,725 IU/mL (Log 4.71)	3,785	302	40 / 111	24.4	Methylprednisolone (1 mg/kg/d) and ABVD
2. Relapse (Feb-March 2025)	Initiation of 2L (Br-ESHAP). Encephalopathy and anasarca.	3,981 IU/mL (Log 3.6)	7,432	252	31 / 77	25.1	Br-ESHAP + Dexamethasone
3. Flare-up (March 2025)	Intra-treatment refractoriness.	1,152 IU/mL (Log 3.06)	16,148	405	20 / 123	0.0	Anakinra + Methylprednisolone pulses (1 g/d)
4. Pre-3L Progression (May 2025)	Lymphoma progression prior to nivolumab.	5,226 IU/mL (Log 3.72)	5,058	N/A	Normal	Normal	Nivolumab

ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; Br-ESHAP, Brentuximab vedotin, Etoposide, Methylprednisolone, Cytarabine, and Cisplatin; ABVD, Doxorubicin, Bleomycin, vinblastine, Dacarbazine; EBV, Epstein-Barr Virus; N/A, Not Available; 2L, Second-line; 3L, Third-line.

Note: Table formatting generated with the assistance of artificial intelligence (Gemini AI).

Table 1: Clinical evolution and treatment.

Introduction: Classic Hodgkin lymphoma (cHL) is a highly curable neoplasm. However, <30% of patients have a relapse/refractory disease. The concurrence of cHL and hemophagocytic lymphohistiocytosis (HLH) is a rare and life-threatening event usually mediated by Epstein-Barr virus (EBV) with a dismal prognosis. We report a clinical case of 42 year-old male that debuted with HLH related to EBV (+) cHL.

Case presentation: A 42-year-old male was admitted with B symptoms and cytopenias. Positron emission tomography-computed tomography (PET/CT) showed nodal and extranodal hypermetabolic activity. A high plasma EBV viral load was detected. The patient experienced a rapid clinical deterioration with multiorgan failure (renal and hepatic failure).

The clinical presentation was consistent with HLH confirmed by bone marrow aspirate. The lymph node biopsy demonstrated EBV(+) cHL. Thus, treatment with ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) for 6 cycles was started. At the end of treatment evaluation, patient had a second event of HLH in the context of lymphoma progression. Then, Br-ESHAP (Brentuximab vedotin, etoposide, methylprednisolone, cytarabine and cisplatin) was initiated with transient improvement. Due to persistent HLH event, anakinra and high dose of steroids was added to therapy.

After a fourth HLH episode, third-line treatment with nivolumab was started. Remarkable clinical improvement and resolution of EBV reactivation were observed with this treatment.

The HLH recurrences linked to EBV reactivation prompted evaluation by a multidisciplinary team due to suspicion of an underlying primary immunodeficiency. Although the genetic panel (NGS) did not identify known causal mutations, the committee dismissed autologous transplantation and ruled out the use of an HLA-identical familial donor to avoid the potential transmission of an unknown genetic defect. Finally, the patient underwent allogeneic hematopoietic stem cell transplantation from an unrelated donor (9/10). Last evaluation, confirmed complete remission with full donor chimerism.

Conclusion: In this patient, relapsed EBV(+) cHL associated with HLH, nivolumab offered a targeted and highly effective treatment which allowed HLH resolution and cleared viremia, serving as a bridge to allogeneic transplantation. Beyond suspicion of immunodeficiency and in absence of molecular genetic characterization, selection of an unrelated donor is recommended to avoid familial susceptibility.

P134: Impact of Pre-transplant Brentuximab Vedotin on Toxicities and Outcomes of Autologous Stem Cell Transplantation in Patients With Relapsed/Refractory Hodgkin Lymphoma

Clara Sanches¹, Miguel Neto¹, Filipa Osório¹, Ana Isabel Brito¹, Margarida Badior¹, Inês Carvalhais¹, Ana Carneiro¹, Pedro Medeiros¹, Filipa Moita¹, Ana Luísa Pinto¹, Ricardo Pinto¹, Fernanda Trigo¹

¹Hematology-Oncology and Transplant Unit, Unidade Local de Saúde São João, Porto, Portugal

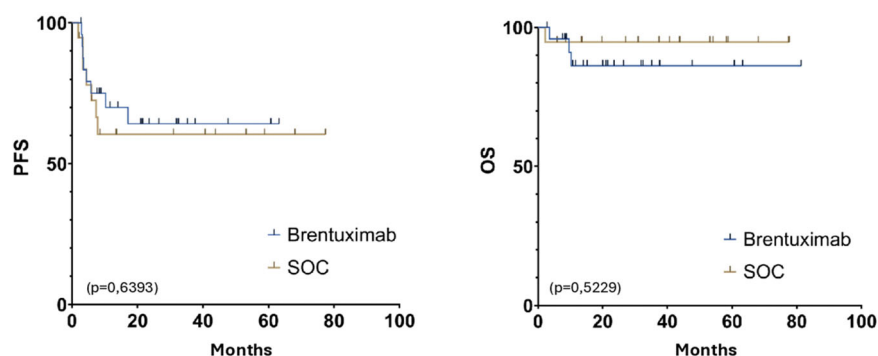


Figure 1: Progression-free survival (PFS) and overall survival (OS) according to pre-transplant brentuximab vedotin (BV) exposure.

Background: Up to 30% of patients with Hodgkin lymphoma (HL) will relapse or are refractory to front-line therapy. Salvage chemotherapy followed by autologous stem cell transplantation (ASCT) remains the standard of care in this setting. Brentuximab vedotin (BV) is increasingly used as salvage therapy prior to ASCT in relapsed/refractory (R/R) HL. However, its impact on transplant-related toxicities and outcomes remains unclear.

Methods: We performed a retrospective single-center study including 44 adult patients with R/R HL who underwent ASCT between January 2019 and January 2026. Patients were stratified according to pre-transplant exposure to BV (BV group, n = 25) or standard salvage chemotherapy (SOC group, n = 19). Mobilization efficacy, engraftment kinetics, toxicities, and post-transplant outcomes were compared.

Results: Median age at transplantation was 35 years (18–62), 54.5% were male. At diagnosis, most patients presented with advanced-stage disease (Lugano stage III–IV, 75.0%), 47.7% with B symptoms and 27.3% with bulky disease. Primary refractory disease following first-line therapy (ABVD) was significantly more frequent in the BV group (80.0% vs 47.4%). Patients in the BV group more frequently received ≥ 3 regimens prior to ASCT, including BV combined with ESHAP, DHAP, ICE, bendamustine, or anti-PD-1-based therapies. BV-related adverse events were predominantly mild and manageable: $\leq G2$ peripheral neuropathy (n = 2), $\geq G3$ infections (n = 3), and transient $\leq G2$ hepatic toxicity (n = 1). Most patients underwent BEAM conditioning (97.7%). Median infused CD34+ cell dose was comparable between groups, although poor mobilization occurred more frequently among BV-treated patients (16.0%). Median neutrophil and platelet engraftment times were similar between groups. No significant differences were observed regarding infectious complications, hospitalization duration, or transplant-related mortality. CR rates at day +100 post-ASCT were comparable between the BV and SOC groups (72.0% vs 73.7%). No statistically significant differences were observed in PFS or OS between the two groups (Figure 1).

Conclusion: These findings support the use of BV-containing regimens as an effective and well-tolerated pre-transplant salvage strategy in R/R HL. BV may reduce exposure to intensive multiagent salvage chemotherapy, although further studies with larger cohorts and longer follow-up are needed to better define its impact on long-term survival outcomes and toxicities.

P135: Immunophenotyping of CD8+ T cells from classical Hodgkin Lymphoma patients treated with PD-1 blockade

Matthew Salaciak^{1,2,3}, Tho-Alfakar Al-Aubodah⁴, Samantha Worme^{1,2}, Laura Widawski⁴, Claudia L. Kleinman^{1,5}, Ioannis Ragoussis⁶, Ryan Rys¹, Madelyn Abraham^{1,2}, Angelo Rizzolo¹, Paige McCallum¹, Christophe Goncalves¹, Gerben Duns⁷, Christian Steidl^{7,8}, Sonia Del Rincon^{1,2}, Koren K. Mann^{1,2,9}, Ciriaco Piccirillo⁴, Francois E. Mercier^{1,2,3}, Nathalie Johnson^{1,2,3}

¹Lady Davis Institute, Jewish General Hospital, Montreal, Quebec, ²Division of Clinical and Translational Research, McGill University, Montreal, Quebec, Canada, ³Department of Medicine, McGill University, Montreal, Quebec, Canada, ⁴Department of Microbiology and Immunology, McGill University, Montreal, Quebec, Canada, ⁵Department of Human Genetics, McGill University, Montreal, Quebec, Canada, ⁶McGill Genome Center, ⁷Centre for Lymphoid Cancer, BC Cancer, Vancouver, Canada, ⁸Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada, ⁹Department of Pharmacology and Therapeutics, McGill University, Montreal, Quebec, Canada

Introduction: Classical Hodgkin lymphoma (cHL) features rare Hodgkin-Reed-Sternberg (HRS) cells within a dense, dysfunctional immune infiltrate. While PD-1 blockade helps some relapsed cHL patients, durable responses are uncommon. In solid tumors, progression from intermediate to terminal T-cell exhaustion drives resistance to PD-1 blockade. We evaluated T-cell exhaustion states in relapsed cHL.

Methods: We performed longitudinal single-cell RNA sequencing (scRNA-seq) of PBMCs from one patient during PD-1 inhibitor (PD1i) therapy. T-cell clones in blood and tissue were tracked by TCR sequencing. Gene expression was analyzed using Seurat and assessed for memory stem-like and terminal effector-like signatures. Findings were validated at the protein level by flow cytometry in 11 relapsed HL patients (pre- and post-PD1i) and 6 healthy age-matched controls, and by PhenoCycler imaging of 24 tissue biopsies (13 diagnostic, 11 post-PD1i).

Results: scRNA-seq identified 25,268 cells, 10,593 were T cells. Markers defined nine PBMC clusters, with key transcriptional changes in T cells. TCR analysis detected clonotypes in 39.5% of T cells, with overlap between scRNA-seq, bulk PBMCs, and tumor tissue. At relapse, CD8 + T cells expanded, inverting the CD4 + /CD8+ ratio. Longitudinal analysis of gene expression networks showed a shift from TCF1+ precursor to CX3CR1 + T-bet+ intermediate exhausted states, coinciding with relapse and expansion of a dominant CD8+ clonotype. Flow cytometry of PBMC confirmed enrichment of CD8 + CX3CR1 + T-bet+ cells in relapsed cHL, mainly PD1i non-responders, compared to controls ($p = 7.3 \times 10^{-3}$). Healthy controls had more CD8 + TCF1 + CD127+ stem-like cells compared to relapse cHL patients ($p = 1.07 \times 10^{-2}$). Spatial imaging of cHL tissue post PD1i had increased CX3CR1, PD-1, and T-bet expression in CD8 + T cells, while diagnostic cHL tissue had lower CX3CR1 and higher TCF7 ($p = 2.44 \times 10^{-4}$). Thus, diagnostic cHL T cells, in blood and tissue, are mainly stem-like, while relapsed HL contains more intermediate/terminally exhausted T cells, likely contributing to poor PD1i responses.

Conclusions: Multiomic analyses show CD8 + T-cell states change dynamically during PD1i in cHL. Durable responses likely depend on maintaining progenitor-exhausted T cells, while relapse involves the accumulation of intermediate-exhausted CD8 + T cells. This may explain better PD-1 inhibitor responses in frontline versus later lines of therapy.

P136: Post-ASCT Brentuximab Vedotin (BV) maintenance in high-risk relapsed/refractory Hodgkin lymphoma in the era of novel salvage therapies: a bias-adjusted analysis of 4 LYSA real-world cohorts

Amira Marouf¹, Tesla Murari Mirimo², Jean Galtier^{3,4}, Gaétan Basile³, Pilar Dutari⁵, Cédric Rossi^{6,7}, Fanny Cherblanc⁸, Loïc Chartier², Krime Bouabdallah³, Robin Noel⁵, Hervé Ghesquière⁹, Bénédicte Deau-Fischer¹

¹Groupe hospitalier privé Ambroise Paré-Hartmann, Neuilly Sur Seine, France, ²Department of Biostatistics, Lymphoma Academic Research Organisation (LYSARC), Lyon, France, ³CHU de Bordeaux, Service d'hématologie Clinique et de thérapie cellulaire, F-33000 Bordeaux France, ⁴BRIC (BoRdeaux Institute of onCology), UMR1312, INSERM, Univ. Bordeaux, F-33000, Bordeaux., ⁵Department of Hematology, Institut Paoli Calmettes, Marseille, France, ⁶Department of Hematology, CHU Dijon Bourgogne, ⁷INSER1231 Equipe EPI2THM, Université Bourgogne Europe, Dijon, France., ⁸Lymphoma Academic Research Organisation, Lyon, France, ⁹Department of Hematology, Centre Hospitalier Lyon-Sud, Hospices Civils de Lyon, Université Claude Bernard Lyon 1, Lyon, France

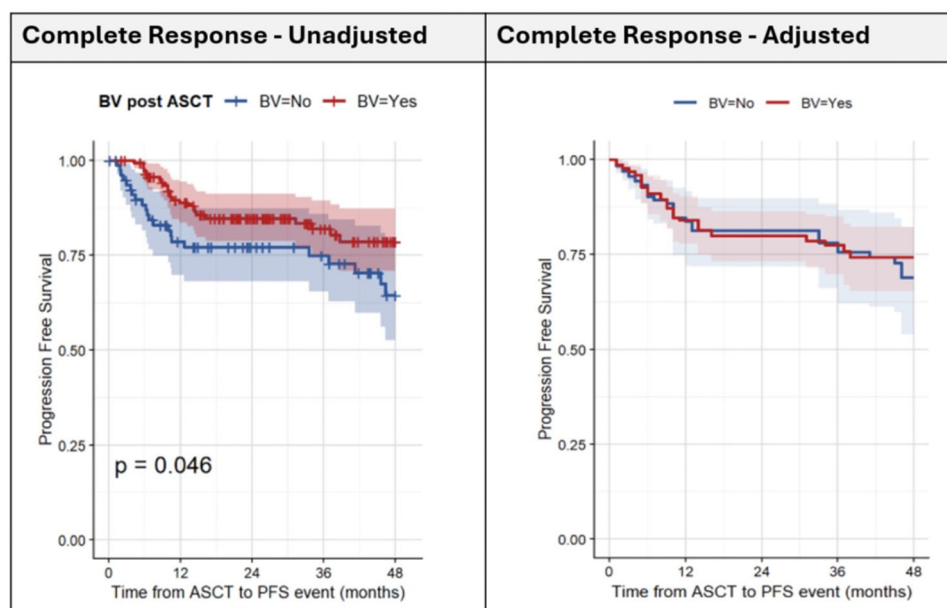


Figure 1: Impact of BV maintenance on PFS among patients in complete response before ASCT. PFS is shown by Kaplan-Meier analysis using the log-rank test (left), and after adjustment using propensity-score weighting and a time-varying Cox model (right).

Introduction: AETHERA showed that Brentuximab Vedotin (BV) maintenance after autologous stem-cell transplantation (ASCT) improved PFS in BV-naïve high-risk relapsed/refractory classical Hodgkin lymphoma (R/R cHL). However, BV and PD-1 inhibitors before ASCT may reduce its added value. To address this question, we analyzed 4 French LYSA cohorts using methods accounting for treatment-selection confounding and immortal time bias.

Methods: Adult R/R cHL patients eligible for BV maintenance after ASCT were analyzed. BV maintenance was compared with observation. Propensity scores included demographic and relapse-risk factors; inverse probability weighting was applied. Immortal time bias from delayed BV initiation was addressed using a weighted Cox model with BV as a time-varying exposure and a clone-censor-weight analysis comparing BV initiation within 4 months versus no maintenance. Outcomes were PFS and OS from ASCT

Results: Among 304 patients, 256 with complete propensity-score covariates were analyzed. Median age was 31 years; 60% were male. At relapse, 65% had disseminated disease, 49% primary refractory disease, and 25% early relapse. Most had received BV before ASCT (n = 216, 84%) and achieved CR before ASCT (n = 217, 85%). Post-ASCT management was BV maintenance (n = 165, 64%) or observation (n = 91, 35%). After a median follow-up of 39 months, 2-year PFS/OS were 81%/96% with BV and 76%/95% with observation (p = 0.086/0.98). After weighting, BV maintenance was not associated with improved outcomes. In the time-varying Cox model, BV was not associated with PFS (HR 0.80, 95% CI 0.46–1.41; p = 0.45) or OS (HR 1.71, 95% CI 0.50–6.02; p = 0.40). Among BV-exposed patients, PFS did not differ by maintenance use (p = 0.34), whereas BV maintenance was associated with improved PFS in the small BV-naïve subgroup (n = 38; p < 0.001). In patients in CR before ASCT, the apparent unadjusted PFS benefit of BV maintenance (p = 0.046) disappeared after adjustment and immortal-time bias correction (HR 0.77, 95% CI 0.42–1.42; p = 0.41).

Conclusion: In 4 LYSA cohorts, the added value of post-ASCT BV maintenance appeared limited after prior exposure to novel agents when robust causal methods were applied. A potential benefit was mainly observed in the small BV-naïve subgroup, whereas no clear benefit was evident after BV-based salvage, particularly in patients achieving CR before ASCT. These findings support refinement of post-ASCT consolidation strategies beyond historical AETHERA criteria.

P137: Anti PD1 containing salvage regimen is highly effective in chemorefractory HL patients

Francesca Pierdomenico^{1,2}, Carolina Freitas^{3,2}, Diana Viegas^{1,2}, Inês Coelho^{1,2}, Maria Inês Barbosa^{1,2}, Alina Ionita^{1,2}, Susana Carvalho^{1,2}, Maria Gomes Da Silva^{1,2}

¹Hematology Department, ²Instituto Portugues de Oncologia de Lisboa Francisco Gentil, ³Transplant Unit

Despite the introduction of new drugs, relapsed/refractory Hodgkin Lymphoma (R/R HL) remains challenging. Pembro-GVD (pembrolizumab, gemcitabine, vinorelbine and liposomal doxorubicine) has emerged as an effective salvage regimen before consolidation with high dose chemotherapy and autologous stem cell transplantation (ASCT). However, there are limited real life data regarding its efficacy and safety in 3rd line.

We present a retrospective, unicentric analysis of 10 R/R HL who received pembro-GVD in 3rd line (2nd salvage) between 7/2023 and 9/2025. We evaluated overall response rate (ORR) and complete response rate (CRR) by PET-CT scan according to Lugano criteria, as well as transplant rate. Refractory disease was defined as progression at end of treatment in PET/CT. Toxicity and treatment discontinuation was assessed per cycle.

Median age at diagnosis was 34,9 (20–56) years and 7/10 patients were males. At diagnosis, 8/10 presented with advanced disease (6 in stage III-IV), 8/10 with B symptoms and 3/10 with bulky disease. They were all treated with a PET-guided strategy, starting with 2 cycles of ABVD, and 4/10 intensified to escBEACOPDAC. Six patients had refractory disease, 2 an early relapse (<6 months) and 2 a late relapse. As 1st salvage, all patients received a platinum-based regimen associated to brentuximab vedotin; 8 were refractory.

Median number of pembro-GVD cycles was 3 (2–4). Response was assessed after 2 cycles in 8 patients and after 3 cycles in 2: ORR was 100% and CR rate 80%. Six patients continued pembro monotherapy until ASCT (median: 2 cycles). All but one patient proceeded to ASCT in response. After ASCT, all patients achieved CR. After a median follow-up of 18,5 months all patients but one maintained CR.

Adverse events occurred in 8/10 patients at any time during treatment: 7 immuno-related (four G3-4) and 7 haematological toxicities (one G2 and 6 G3-4; two febrile neutropenia). Dose reduction or treatment delays occurred in 5 patients; treatment was discontinued due to toxicity after 3rd cycle in 4 patients. No deaths occurred.

In this small series of patients with adverse prognosis, pembro-GVD in 3rd line was effective as salvage regimen and allowed consolidation with ASCT with continuous CR in most patients. The incidence of adverse events was higher than in other series. Considering the early response to pembro-GVD, patients should quickly proceed to ASCT consolidation after cycle 2 to minimize toxicity.

Resource constrained setting

P139: Implementation of BrECADD According to HD21 Standards in a Middle-Income Country: Barriers and Feasibility in Mexican Public Hospitals

Laura Nayeli Tecayehuatl Negrete¹, Luis Felipe Rubalcava Lara², Gerardo Santiago Jiménez³, Alonso Hernández Company³, Perla Rocío Colunga Pedraza⁴, Bogar Pineda Terreros¹, Martín Jacobo Pacheco¹, María Eugenia Mejía Chávez¹, Karina Angelica Arzate Ramírez¹, María Catalina López Aparicio¹, Ramón Alberto Barreda González¹, Ana Xochitl Muñoz Gutierrez¹, Juan Rangel Patiño⁵

¹Centro Médico Nacional La Raza, IMSS, Ciudad de México, México., ²Instituto Nacional de Cancerología, Ciudad de México, México., ³Hospital General de México "Dr. Eduardo Liceaga", Ciudad de México, México., ⁴Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., ⁵Instituto Nacional de Ciencias Médicas y Nutrición "Dr. Salvador Zubirán", Ciudad de México, México.

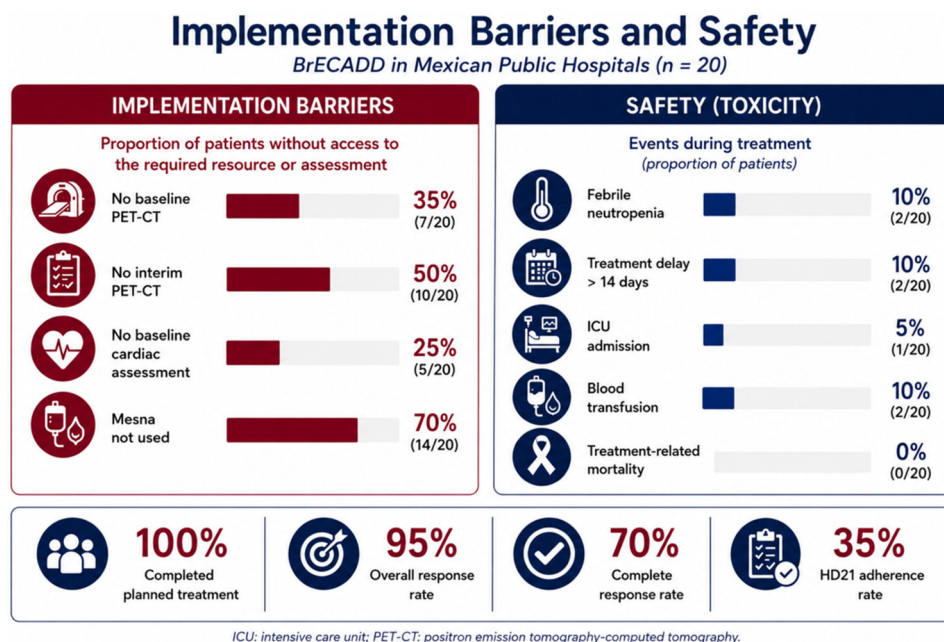


Figure 1: Despite a 100% treatment completion rate, full HD21 adherence was achieved in only 35% of patients. The main barriers were identified within the diagnostic infrastructure domain, particularly limited access to baseline and interim PET-CT.

Background: BrECADD has emerged as a new standard of care for advanced-stage classical Hodgkin lymphoma (cHL). However, little is known about its implementation outside clinical trials. We evaluated the feasibility of delivering BrECADD in Mexico.

Methods: We conducted a multicenter retrospective study of consecutive patients with newly diagnosed cHL treated with BrECADD across four Mexican public institutions. Feasibility was assessed using a predefined HD21-inspired adherence measure, defined by the availability of baseline and interim PET-CT, completion of planned treatment, and the absence of dose reductions or treatment delays >14 days. Potential implementation barriers were evaluated across four predefined domains: diagnostic infrastructure, treatment delivery, supportive care, and safety.

Results: Twenty patients were included. Median age was 33 years (IQR 22–42); 65% had nodular sclerosis subtype and 90% advanced-stage disease. B symptoms were present in 90%, bulky disease in 55%, and ECOG 0–1 in 75%.

Baseline and interim PET-CT assessments were available in 65% and 50% of patients, respectively. Treatment was administered in the outpatient setting in 75% of cases, while mesna was used in 30%.

Thirty percent received four cycles and 70% six cycles of BrECADD. Ninety percent completed treatment without dose modifications and only 10% experienced delays >14 days due to toxicity or logistical reasons. All patients received primary G-CSF prophylaxis; 70% received Pneumocystis and antifungal prophylaxis.

Febrile neutropenia occurred in 10%, intensive care admission in 5%, and transfusion support in 10%. No treatment-related deaths were observed.

The overall response rate was 95%, including 70% complete responses. Radiotherapy consolidation was administered in 30%. Four patients (20%) required subsequent systemic therapy; 12-month progression-free survival was 74.5%, and overall survival was 100%.

All patients completed planned treatment; however, full HD21 adherence was achieved in only 7 of 20 patients (35%).

Conclusions: BrECADD can be safely delivered in Mexican public hospitals, with low rates of severe toxicity. Despite a 100% treatment completion rate, full implementation of the HD21 strategy was achieved in only 35% of patients. Barriers were predominantly identified within the diagnostic infrastructure domain, particularly limited access to baseline and interim PET-CT.