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Congress Chair:
Chairpersons: Christine Mauz-Körholz, Giessen, Germany; Sharon Castellino, Atlanta, USA; Jamie Flerlage, Rochester, USA

S-01 | The pearls of SEARCH – Staging Evaluation and Response Criteria Harmonisation

Chairs: Lars Kurch (Leipzig, Germany), Jennifer Seelisch (London, Canada)

S-01-01 SEARCH-Introduction

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DOI 10.1055/s-0045-1812897

S-01-02 The top 3 SEARCH projects – Atlas

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The atlas project addresses the critical need for standardized staging in pediatric Hodgkin lymphoma (HL), a key goal of the SEARCH for CAYAHL (Staging Evaluation and Response Criteria Harmonization for Children, Adolescent, and Young Adult Hodgkin Lymphoma) initiative. Historically, variations in defining lymph node involvement have hindered direct comparisons between major North American and European clinical trials, complicating efforts to refine treatments and reduce long-term toxicity.

To resolve this, an international collaboration of pediatric oncologists, radiologists, and nuclear medicine physicians developed a comprehensive, consensus-based imaging atlas. The atlas provides rigorous, detailed definitions for lymph node regions based on modern imaging modalities like CT, MRI, and FDG PET/CT. It extends traditional adult-focused classifications (Ann Arbor, Cotswold, Lugano) with precise anatomic landmarks and boundaries relevant to pediatric patients. It also establishes consensus criteria for defining nodal and extranodal ("E lesion") involvement by combining morphologic and metabolic imaging data.

This atlas provides a unified lexicon for staging HL. Its implementation ensures consistent and reproducible staging, which is essential for clear communication during tumor boards, central reviews, and, most importantly, for enabling robust, unbiased comparisons of treatment outcomes across different clinical trials. This harmonization is vital for accelerating the identification of effective, less toxic therapies for children and young adults with HL.

S-01-03 Hodgkin Lymphoma involving the CNS: An AHOD1331, PHL-C1 and PHL-C2 Report from the Children's Oncology Group and the European Network for Pediatric Hodgkin Lymphoma

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Hodgkin lymphoma (HL) involving the central nervous system (CNS) is exceedingly rare. Information regarding the presentation, management, treatment and outcome of patients with CNS HL is limited. We describe 45 pediatric patients with 55 extra-axial CNS lesions at the time of diagnosis with HL from a cohort of 4995 patients enrolled on Children's Oncology Group AHOD1331 and the European Network for Pediatric Hodgkin lymphoma (EuroNet-PHL) C1 and C2 trials (NCT02166463, NCT00433459 and NCT02684708, clinicaltrials.gov), with an overall incidence of 0.9 %. 82.2 % of patients in our cohort had a single CNS lesion in the thoracic, lumbar or sacral spine. Two patients (3.6 %) had lesions involving the skull. In this cohort, HL did not occur within the CNS parenchyma. Lesions extended into the extra-axial CNS space from adjacent soft tissue or bone and never directly infiltrated through the dura into the brain or spinal cord. Patients with CNS involvement had a 2-fold greater incidence of E-lesions than previously reported cohorts without CNS involvement. 89.1 % of CNS lesions demonstrated a complete metabolic response and > 75 % decrease in volume after two cycles of chemotherapy. Thirteen CNS lesions (23.6 %) received irradiation, none of these were sites of disease relapse. Relapse occurred at the site of two lesions involving the CNS, both of which had an adequate interim response to chemotherapy. We present the largest reported cohort of systemic HL involving the CNS at diagnosis, demonstrating that these lesions originate from surrounding tissues, extend into the CNS space, and respond similarly to other nodal and extra-nodal disease.

S-01-04 Lung Involvement in Pediatric Hodgkin Lymphoma: Imaging challenges in adequate staging

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Contemporary treatment protocols for children and adolescents with Hodgkin lymphoma (HL) aim not only to sustain high cure rates but also to minimize long-term morbidity associated with chemotherapy and/or radiation therapy (Mauz-Körholz *et al.*, 2022, 2023).This delicate balance between efficacy and toxicity places a premium on precise risk stratification, which is fundamentally dependent on imaging for accurate staging prior to therapy.

Accurate staging definitions for both nodal and extranodal involvement in pediatric HL are critical for risk-adapted therapy but present significant challenges (Humphries, 2025; Stoevesandt *et al.*, 2025). Distinguishing disseminated (Ann-Arbor Stage IV disease) from contiguous (E-lesion) lung involvement (Zijtregtop *et al.*, 2023) by imaging profoundly impacts the stage determination and consequent treatment intensity, with potential for false upstaging and overtreatment.

Radiologists face inherent challenges distinguishing pulmonary HL lesions from concurrent benign conditions. In contrast to adults, biopsy needs to be critically discussed in children due to ethical concerns and limited diagnostic yield (Kallenberg *et al.*, 2009).

Divergent staging criteria based on number, size and metabolic activity exist across major cooperative study groups (Flerlage *et al.*, 2017; Stoevesandt *et al.*, 2025) leading to inconsistent interpretation of imaging findings (Seelisch *et al.*, 2023), which impacts the comparability of outcome data.

These challenges are compounded by limited pediatric-specific data on lung involvement in HL, the result of technical advances in imaging and evolution of staging definitions occurring over time.

Historically, imaging evolved from X-ray to CT and PET/CT, improving the detection of lung involvement. While PET/MRI offers a radiation-free alternative to PET/CT, its utility for accurate lung parenchyma evaluation remains limited (Kwee *et al.*, 2014; Albano *et al.*, 2021).

The SEARCH for CAYAHL initiative aims to highlight diagnostic complexities, delineate morphological distinctions between E-lesions and disseminated lung involvement, and explore their prognostic implications with the future collaborative goal of harmonizing international staging criteria for lung involvement in pediatric HL to insure optimized, individualized patient care [1–10].

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S-01-06 Advances in metabolic response assessment in PHL

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S-01-07 Imaging Pitfalls in Pediatric, Adolescent, and Young Adult Hodgkin Lymphoma: A SEARCH for CAYAHL Initiative to Bridge Multidisciplinary Patient Care

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Introduction Hodgkin lymphoma (HL) is a highly curable cancer in children, adolescents, and young adults. Treatment strategies prioritize minimizing long-

term toxicity while maintaining high survival rates. Clinical trials often include centralized imaging review to accurately determine the stage of the disease as it significantly impacts treatment decisions. Accurate and reliable imaging reports are required. Discrepancies sometimes arise between academic guidelines and real-life imaging scenarios leading to uncertainties in image interpretation.

Methods The Staging, Evaluation, and Response Criteria Harmonization for Childhood, Adolescent, and Young Adult Hodgkin Lymphoma (SEARCH for CAYAHL) initiative, launched in 2011, aims to standardize imaging criteria for HL among cooperative study groups, resulting in more comparable data across trials. With representation from the Children's Oncology Group, the European Network for Pediatric Hodgkin Lymphoma and the Pediatric Hodgkin Consortium, a working group – that included specialists in diagnostic radiology, nuclear medicine, radiation oncology, and pediatric oncology – identified recurrent imaging pitfalls in HL that may lead to incorrect staging. This project is intended to assist imaging professionals and clinicians interested in HL to improve interdisciplinary cancer care for this patient population.

Results Image reporting may be influenced by both, errors in image acquisition, and the misinterpretation of imaging findings. The collection of disease-specific pitfalls in this project provides clinical scenarios dedicated to both topics illustrated through typical PET, CT, and MRI findings in illustrative case vignettes. In case of uncertainty, possible strategies for identifying differentials are also provided. Given the growing importance of PET imaging in HL, this project also discusses the limitations of ^{18}FDG, thereby emphasizing the importance of integrating the metabolic and morphological components of hybrid imaging.

Conclusion This project provides a practical complement to existing scientific literature that addresses recurring pitfalls that may lead to diagnostic uncertainty and their consequences. By promoting interdisciplinary dialogue, the project aims to improve interdisciplinary decision-making in the real world and ultimately enhance outcomes for patients with HL.

S-01-08 Impact of metabolic assessment in pediatric Hodgkin lymphoma with bulky masses in partial volumetric response: a prospective, multicenter, Italian study

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Introduction The aim of our study was to investigate the role of metabolic assessment in pediatric Hodgkin lymphoma (HL) presenting with bulky masses and partial volume reduction at early evaluation.

Methods This is a prospective, multicenter study conducted in 35 AIEOP centers. Between March 2018 and December 2020, pediatric patients with HL presenting with bulky masses at diagnosis and treated on the same clinical trial (Euro-NET-PHL-C2) were enrolled. Patients were assessed with PET at baseline (PET0), after two cycles of therapy for early response (ERA), and at the end of chemotherapy for late response (LRA) assessment. The parameters analyzed in the study were: SUVmax, SUVmean, Dmax, TMTV (total metabolic tumor volume), TLG (total tumor glycolysis) and their variations (Δ). PET response was classified according to the Deauville score (DS) and dichotomized into complete metabolic response (CMR) and non-CMR. Clinical and imaging parameters were correlated with prognosis based on the event-free survival (EFS).

Results In our cohort of 200 patients, 90 patients were male (45 %), 89 were stage III-IV (45 %), and 111 patients (55.6 %) presented with B symptoms. The median lymphoma volume at PET0 was 350 ml, while at ERA the median volume was 89 ml, with a median reduction of 61 %. The response at ERA was CMR in 107 cases (53.5 %). Median observation of the cohort was 58.9 months (range 12-90). A statistically significant correlation was observed for stage, DS and residual SUVmax at ERA with regards to the occurrence of any event, i.e. progression, relapse or death ($p = 0.0145$, $p = 0.0095$ and $p = 0.0008$, respectively). In our cohort, 86 patients (43 %) had a partial volumetric response < 75 %, while in 60 patients (30 %) we observed a response < 50 %. In this group of patients, among the clinical and imaging parameters analyzed, we observed that stage (HR 3.028; 95 %CI 1.167-7.857; $p = 0.0227$) and Dmax at PET0 (HR 4.887; 95 %CI 1.004-1.071; $p = 0.0271$) resulted predictive of the EFS. Whereas at ERA, both a residual SUVmax > 2.36 (HR 1.161; 95 %CI 1.025-1.314; $p = 0.0188$) and a ΔSUVmax < 72.3 % (HR 0.961; 95 %CI 0.933-0.990; $p = 0.0093$) were prognostic for EFS [1–4].

Conclusion To our knowledge, this is the first prospective multicenter study to report the added value of metabolic response in pediatric patients with HL presenting with bulky masses and partial volume reduction at early evaluation.

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S-01-09 Data Collaborations Accelerate Pediatric Hodgkin Lymphoma Research Through NODAL

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Introduction International research cooperative groups have significantly contributed to advancements in pediatric oncology, largely through collaborative efforts. To further this collaboration and standardize diagnosis, staging, treatment, and response assessment for pediatric Hodgkin lymphoma (HL), researchers formed the Hodgkin Lymphoma Data Collaboration (NODAL) consortium. This consortium partnered with the Pediatric Cancer Data Commons (PCDC), an initiative led by Data for the Common Good (D4CG), to develop consensus data standards and create a data commons for pediatric HL.

Methods NODAL was founded in 2018 through a Memorandum of Understanding between the Children's Oncology Group (COG) and the Pediatric Hodgkin Consortium (PHC), with the aim of accelerating pediatric HL research. Since its inception, significant milestones have been achieved: a) an executive committee and comprehensive governance structure have been established; b) members have developed a harmonized data dictionary from prior clinical trials; c) data contributor agreements have been signed by all participating groups; d) data has been harmonized according to the agreed-upon dictionary; and e) COG and PHC have transferred data for collaborative research initiatives.
Results The HL data dictionary, updated as of May 2024, now contains 203 standardized elements. These elements were instrumental in harmonizing clinical trial data from 2,437 participants across six trials: Children's Oncology Group trials (AHOD0031, AHOD03P1) and Pediatric Hodgkin Consortium trials (HLHR13, HOD05, HOD08, HOD99). Participant distribution by Ann Arbor staging is as follows: Stage I: 169, Stage II: 1,274, Stage III: 425, Stage IV: 386. The data dictionary encompasses various elements, including demographics, initial disease characteristics, therapy details, response assessment, toxicity, and survival status. This aggregate data is readily available for exploration on the publicly accessible PCDC data portal: https://portal.pedscommons.org/login.
Conclusion NODAL fosters research and enables cross-trial comparisons by providing data access through the Pediatric Cancer Data Commons. We welcome global pediatric HL clinical trial and registry datasets, with contributors retaining full governance. Researchers can propose projects using the HL dataset by submitting a brief project request form for review by the NODAL Executive Committee.

S-02 | Clinical Trials Update

Chairs: Auke Beishuizen (Utrecht, Netherlands), Angela Feraco (Boston, USA)

S-02-01 The Children's Oncology Group (COG) Portfolio for advancing therapeutics in Hodgkin Lymphoma (HL)

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The North American Children's Oncology Group (COG) portfolio has advanced novel therapeutics toward reducing the late morbidity of therapy through collaboration by exploiting the growing knowledge of biology in classic HL. Key findings from the response adapted frontline trial AHOD1331 in high-risk disease (Stages IIB with bulk, IIIB, IV A or B) led to FDA approval of the CD-30 directed antibody drug conjugate, brentuximab vedotin (BV), in children, and notes: 1) superior event free survival with the addition of brentuximab vedotin (Bv) to the AVEPC backbone of therapy; 2) reduction in the proportion of high-patients getting modified involved site RT, with contemporary RT modalities show a notable decrease in organ at risk exposure (heart, lung, breast); 3) feasibility of encompassing patient reported outcomes by the child on quality of life and chemotherapy induced peripheral neuropathy, and 4) the success of a dose modification strategy to preserve the Bv dose in the experimental arm. Therapeutic advances through collaboration with the US National Cancer Trials Network led to inclusion of adolescents > 12 years of age in the S1826 trial; this demonstrated the safety and efficacy (2 -yr. PFS 95 %) of including the checkpoint inhibitor nivolumab to AVD chemotherapy with 1 % of adolescents getting radiation therapy for Stage III and IV disease. The COG is leading the NCTN phase 3 response adapted trial (NCT05675410) evaluating the combination of Bv/Nivolumab in early-stage disease across the age spectrum. Collaboration with the EuroNet led to Phase 2 studies evaluating pembrolizumab in front-line therapy and to an approach for transplant-free salvage in patients with relapsed disease. Ongoing advances in imaging technology, and in assessment of circulating tumor DNA as a biomarker will be incorporated to deliver biologically driven, personalized treatment for children and adolescents with classic HL [1–3].

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S-02-02 EuroNet-PHL Overview

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Since the 1970s, pediatric Hodgkin lymphoma (HL) has been treated successfully in cooperative trials. Long-term survival range above 90 % after chemotherapy alone or combined with radiotherapy. Aging survivors are at high risk of treatment-associated late effects. Like most major pediatric HL study groups, the European Network for Pediatric Hodgkin Lymphoma (EuroNet-PHL) has followed the paradigm of response-based treatment adaptation and toxicity sparing through the reduction or elimination of radiotherapy (RT) and chemotherapy burden. High treatment efficacy is achieved using dose-dense chemotherapy based on the OEPA/COPDAC strategy of the GPOH-HD (German Pediatric Oncology/Hematology-Hodgkin lymphoma) study group. ^{18}F-FDG-PET has been introduced for response adaptation since the first pan-European collaborative trial EuroNet-PHL-C1 [1, 2]. Refinement and reduction of RT have been implemented, such that radiation has been completely eliminated for certain subgroups of patients. The gonadotoxic chemotherapy regimen COPP, containing procarbazine has been completely abandoned. In the consecutive multicenter international trial EuroNet-PHL-C2, stratification and response criteria have been modified. In the intermediate and advanced stage patients' group, an intensified consolidation cycle DECOPDAC-21 has been studied in a randomized comparison and was more effective in the adequate responding group of patients. In the inadequate responding patients group the intensified consolidation plus residual PET-positive node irradiation concept was not inferior to standard consolidation and standard RT. In the consecutive trial series, the radiotherapy burden had been reduced from 85 % in the GPOH-HD- 2002 trial to less than 25 % in the EuroNet-PHL-C2 trial. In the future trials, chemotherapy will be de-intensified and immunotherapies, e.g. immune-checkpoint inhibitors are incorporated. With this strategy, even more RT burden can be spared, as shown in the EuroNet-guided MK-3475-667 HR trial [3]. Because pediatric staging and response criteria are not uniform, comparing the results of trial series among different pediatric and adult study groups remains difficult; thus, initiatives to harmonize criteria are desperately needed. A dynamic harmonization process to standardize therapeutic risk stratification and response definitions as well as to improve the care of children with HL in resource-restricted environments has been implemented with great success [4].

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S-02-03 Pediatric Hodgkin Consortium Trial Updates: Response-based omission of radiotherapy (RT) for the majority of young people with Hodgkin lymphoma (HL) while maintaining excellent outcomes: Five-year results of HOD08 for low-risk (LR) HL and initial results of cHOD17 high-risk (HR) stratum

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Purpose: The Pediatric Hodgkin Consortium (PHC) conducts phase II multicenter investigator-initiated trials balancing goals of (1) excellent event-free survival (EFS) and overall survival (OS) with (2) low burden of treatment-induced health conditions. We report 5-year outcomes of HOD08 (NCT00846742) for LR Hodgkin lymphoma (HL) and 2-year outcomes of cHOD17 HR stratum (NCT03755804).

Methods: HOD08 studied an 8-week Stanford V regimen (mechlorethamine, bleomycin, doxorubicin [cumulative dose = 100 mg/m2], etoposide, prednisone, vinblastine, and vincristine) with response-adapted tailored field RT (25.5 Gy) for patients aged 21 years and younger with stage IA or IIA (LR) classic or nodular lymphocyte predominant HL. HOD08's primary objective was to increase complete response rate (CR; defined as anatomic shrinkage of at least 75 % plus metabolic response equivalent to Deauville score [DS] 1 or 2) by 20 % to a target of 64 % [1, 2]. Secondary objectives included estimation of EFS and OS. A 2010 mechlorethamine shortage [3] compelled cyclophosphamide substitution. A post-hoc analysis of classic HL patients who received mechlorethamine was conducted to inform future trial planning. cHOD17 HR studied the AEPA-CAPDac regimen (brentuximab vedotin, etoposide, prednisone, doxorubicin [cumulative dose = 160 mg/m2], cyclophosphamide, and dacarbazine) for patients 25 years and younger with stage IIB, IIIB, and IV CD30 + HL. After 2 AEPA cycles, for patients with complete metabolic response (CMR; defined as DS 1-3), prednisone was omitted during CAPDac cycles and residual node RT (RNRT, 25.5Gy) was omitted. cHOD17 HR's primary objective was to estimate 2-year EFS [4].

Results: HOD08 enrolled 85 patients. HOD08 5-year EFS and OS rates were 87.4 % (95 % CI 80.4 %-95.0 %) and 98.7 % (95 % CI 96.2 %-100 %). Among mechlorethamine-treated classic HL (n = 45), 34 achieved CR (77 %; 1 missing response). 5-year EFS was 93.0 % (95 % CI 85.6 %-100 %) and 5-year OS was 100 %. cHOD17 HR enrolled 114 patients. 113 were assessable for response and 69 (61.1 %) achieved CMR with omission of prednisone during CAPDac and RNRT. 2-year EFS was 94.7 % (95 % CI: 90.3 %-99.4 %) and OS 100 %.

Conclusion: HOD08 and cHOD17 HR demonstrate promising efficacy with modest doxorubicin exposure (100-160 mg/m2) and enable RT omission in > 60 % of LR and HR HL patients. The next PHC trials seek to omit RT in > 80 % HL patients without excess anthracycline exposure. cHOD17 LR (ongoing) utilizes bendamustine in place of mechlorethamine.

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S-02-04 AHOD2131: A Randomized Phase 3 Response-Adapted Trial Comparing Standard Therapy to Immuno-oncology for Children & Adults with Newly Diagnosed Stage I and II Hodgkin Lymphoma

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Introduction Chemotherapy with or without radiotherapy (RT) is a standard frontline treatment for early-stage (ES) classic Hodgkin lymphoma (cHL). Toxicities due to conventional chemotherapy and RT are of concern, as incidence of cHL peaks in adolescents and young adults. Novel immunotherapy (IO) agents offer new potential frontline therapies in ES cHL that aim to improve progression-free survival (PFS) and maintain overall survival (OS), while minimizing morbidity and late effects.

Methods AHOD2131 was developed collaboratively between pediatric and medical oncologists in the National Cancer Institute's National Clinical Trial Network (NCTN) groups, aiming to harmonize IO-based treatment approaches for ES cHL. Study champions from North American (NA) cooperative groups [COG, SWOG, ECOG-ACRIN, Alliance, NRG] and experts in imaging, radiation oncology, lymphoma biology and patient-reported outcomes (PRO) were included. The resulting COG-led trial represents the largest ES cHL trial in the history of NA cooperative groups and the first to enroll patients across the age continuum.

Results AHOD2131 (NCT05675410) is a randomized, phase 3 trial for patients ages 5 to 60 years with newly diagnosed stage I/II cHL, comparing the addition of brentuximab vedotin (Bv) with nivolumab to standard chemotherapy + /- involved site RT (ISRT). AHOD2131 was activated in April 2023 with a target enrollment of 1875 patients over 5 years. As of 28 May 2025, 336 sites have activated and 503 participants have enrolled. 241 (49 %) patients are < 18 years of age.

The primary objective is to compare PFS through a response-adapted, superiority design with either standard therapy or IO (Bv + nivolumab). Enrollment is stratified based on favorable or unfavorable risk features at registration. Based on response assessment by PET/CT (central review) after 2 cycles of ABVD, patients will be designated PET2 positive (slow early response [SER]) or PET2 negative (rapid early response [RER]). Patients with SER receive systemic therapy and ISRT while those with RER receive systemic therapy only. Key secondary endpoints include a non-inferiority comparison of 12-year OS and longitudinal PRO measures assessing health related quality of life, with 11 additional secondary endpoints and 10 exploratory aims.

Conclusion AHOD2131 aims to evaluate an IO approach and establish a harmonized standard of care for ES cHL across the age continuum in the NCTN.

S-02-05 Successful treatment of children and adolescents with stage IA/IIA lymphocyte–predominant Hodgkin Lymphoma after complete resection alone or low dose, anthracyclin-free chemotherapy: Results of the EuroNet-PHL-LP1 trial

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Introduction Children and adolescents with early-stage lymphocyte-predominant Hodgkin lymphoma (nLPHL) have a 5-year event-free survival of about 77 % after complete resection of a single lymph-node and 89 % after anthracycline-containing low-intensity chemotherapy and ^{18}F-FGD-PET-based radiotherapy [1]. We investigated whether patients with LPHL stage IA/IIA can be cured by resection alone or a very low-anthracycline-free chemotherapy.

Methods The EuroNet-PHL-LP1 trial was a prospective uncontrolled phase III study in early stage NLPHL for patients under 18 years of age. Patients presenting in stage IA/IIA with complete resection entered into follow-up. Patients without complete resection received 3 cycles of chemotherapy consisting of Cyclophosphamide, Vinblastine and Prednisone (CVP) and received no further treatment if ^{18}F-FDG-PET was negative (CVP-cohort 1). After an amendment reacting to an unexpectedly high ^{18}F-FDG-PET positivity rate, ^{18}F-FDG-PET was omitted and all patients without residual disease determined by CT or MRI (CVP-cohort 2) received no further treatment. The primary endpoint was event-free survival (EFS) defined by a positive FGD-PET (CVP-cohort-1), secondary malignancy or death of any cause. Secondary endpoints were overall survival (OS) or progression-free survival (PFS). For CVP-cohort-2, EFS and PFS coincide since no secondary malignancy occurred. We report 5-year rates.

Results Between Dec 15, 2009 and Oct 31, 2018, 267 patients were registered and 247 patients were enrolled onto EuroNet-PHL-LP1. Of these, 87 patients were treated with resection alone and PFS was 79.5 % (95 %CI; 71,2 % – 88,7 %). In the CVP-treatment cohort-1, 51 of 82 patients were in complete metabolic response (CMR) after chemotherapy (approximately Deauville scores 1-2). EFS in CVP-cohort-1 was only 56.4 % (95 %CI; 46.5 % – 68.4 %), however PFS in the ^{18}F-PET-negative group of CVP- cohort -1 was 91.3 % (95 %CI; 83.6 % – 99.9 %). In contrast, PFS in 84 patients of the CVP-cohort-2 was 64.7 % (95 %CI; 55.1 % – 76.0 %). The most common grade 3-4 adverse events were neutropenia in 68.3 % of patients treated with CVP. There were no treatment-related deaths.

Conclusion Patients with nLPHL with stages IA/IIA have an excellent prognosis after complete resection. ^{18}F-FDG-PET response is predictive. Patients with incomplete resection have an excellent prognosis with low-intensive, anthracycline-free chemotherapy if ^{18}F-FGD-PET becomes negative at the end of chemotherapy.

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S-02-06 Metabolic-Only Criteria in Pediatric High-Risk (HR) cHL: A Review of Reduced Radiotherapy (RT) Exposure in HLHR13 and cHOD17 Trials

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Introduction Excellent EFS and OS rates were achieved in pediatric classical Hodgkin lymphoma (cHL) on HLHR13 with the Adcetris containing AEPA/CAPDac regimen using combined anatomic and metabolic response criteria. As a result, metabolic-only response assessment was used on cHOD17 to determine need for consolidative residual nodal radiotherapy (RNRT).

Methods cHOD17 (NCT03755804) is an open-label, single-arm, multicenter, phase 2 trial with a stratum for patients ≤ 25 yrs of age at diagnosis of HR (stage IIB, IIIB, or IV), CD30 + cHL. The HLHR13 treatment paradigm (NCT01920932), was modified as follows: (1) Metabolic response criteria only replaced combined metabolic (Deauville ≤ 3, both studies) and anatomic criteria (≥ 75 % reduction in the product of perpendicular dimensions) to determine those with an adequate response (AR). (2) Prednisone was omitted from CAPDac cycles for those with an AR following 2 AEPA cycles at the early response assessment (ERA). (3) Consolidative RNRT (25.5 Gy in 17 treatments) was reduced to a 0.5 cm CTV margin vs. 1 cm margin on HLHR13. This review compares the radiotherapy (RT) exposures (integral dose [in Joules (J), and volume in (ml)], according to modality (proton vs. photon), and modified response criteria.

Results 114 patients (median (x^{-}) age 16.4, range (r) 6.7-24.1 yrs) and 77 patients (x^{-} age 16, r 6-19 yrs) on cHOD17 and HLHR13 were enrolled across 7 institutions. An adequate response was achieved in 69 (61.1 %) and 27 (35 %) by CMR or CT/CMR at ERA on cHOD17 and HLHR13, avoiding RNRT. RT plans were available in 31 (68.9 %) and 47 (94 %) of patients on cHOD17 and HLHR13. The proportion of patients (p = 0.0004), RT volume [x^{-} 89 ml (r, 12.8-1915) vs. 427 (35-3476), (p = 0.01)], and integral dose [x^{-} 9943 J (r 2113-162066) vs. 32143 (62-254155), (p = 0.014)] was significantly reduced in successive trials while maintaining favorable disease control [cHOD17 2-yr EFS 94.7 % (SE 2.4 %), OS 100 % (SE 0 %); HLHR13: 3-yr EFS 97.4 % (SE 2.3 %), OS 98.7 % (SE 1.6 %)]. Use of proton therapy was associated with reduced exposures in both studies (p = 0.021). Of the five inadequate responders with treatment failure on cHOD17, all were a mix of in and out of field failures.

Conclusion On cHOD17, a metabolic-only response assessment decreased the percentage of patients needing RNRT, RT volume, and integral dose compared to HLHR13 while maintaining excellent EFS and OS rates.

S-03 | Global Collaborations

Chairs: Maurizio Mascarin (Aviano, Italy), David Veron (Buenos Aires, Argentina)

S-03-01 Latin America (LATAM) Effort to Establish a Trans-Hemispherical Treatment Guideline for Hodgkin Lymphoma (LH)

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LATAM encompasses 21.95 million square km and a population of 670 million. It is economically, ethnically and politically diverse with > 400 languages spoken. 29,000 children are diagnosed with cancer a year; of these 55 % will be cured, but rates vary from 80-20 %. The World Health Organization (WHO) and the Pan American Health Organization (PAHO) launched initiatives to improve the treatment of pediatric cancer. WHO's Global Initiative for Childhood Cancer (GICC) goal is to cure at least 60 % of children with cancer by 2030. HL is one of the index cancers.

Hospitals in Monza and Milan IT, and Bellinzona CH, established a twinning program with La Mascota Hospital Managua NI in 1986. St Jude Children's Research Hospital (SJCRH) established in 1998 a twinning program with Benjamin Bloom Children's Hospital San Salvador ES. Monza International School of Pediatric Oncology (MISPHO) created in 1996 invited pediatric oncologists from 14 LATAM countries. It is from that experience that physicians from Central America (CA) founded in 1998 Montelimar, NI the Asociacion de Hemato Oncólogos Pediátricos de Centro America (AHOPCA) to design treatment guidelines (TG) for children with cancer for CA. HL is one of the diseases covered by the TG. The success of AHOPCA inspired the creation of the Consorcio Latinoamericano de Enfermedades Hemato-Oncológicas Pediátricas (CLEHOP) in 2013 Buenos Aires AR.

In 1997 F Baez from La Mascota published a chemotherapy only TG for HL with excellent results. Based on the results AHOPCA adopted it and reported results in 2013, a 3-year event free survival of 61 % below expectations. In 2004 AHOPCA TG recommended ABVD for low and intermediate-risk and a modified Stanford V for high-risk HL. Stanford V improved the EFS for patients with highest risk but fell below expectations, and AHOPCA introduced a TG based on OEPA/COPDac with improved results. These results led GATLA, the Argentine collaborative, to adopt the AHOPCA TG and published a 10-year OS of 100 % for low and intermediate-risk, 93 % for high-risk. Aware of these results, in 2013 Porto Alegre BR, CLEHOP proposed a TG with a resource, risk, and response adapted approach. With the collaboration of SJCRH, CLEHOP will implement this TG in oncology centers throughout LATAM. By developing well qualified personnel and following established treatment guidelines it is possible to improve EFS and OS of children with HL above the 60 % target in countries of varying income levels.

S-03-02 Precision in the Face of Constraint: AI-Driven Chemosensitivity Prediction for South African Children with Hodgkin Lymphoma

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Background Response-adapted management of classical Hodgkin lymphoma (cHL) with PET-CT is widely unavailable in Africa, and efforts to introduce artificial intelligence-based solutions are sparse. We aimed to use machine learning models to evaluate correlations between changes in PET-CT findings at interim analysis with changes in widely available, affordable blood tests in paediatric patients with cHL in 17 South African centres.

Methods Variations in ferritin, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), albumin, total white cell count (TWC), absolute lymphocyte count (ALC), and absolute eosinophil count (AEC) were analysed in relation to PET-CT Deauville scores (DS) following two cycles of ABVD chemotherapy. Patients achieving DS 1–3 were classified as having a rapid early response (RER), whereas DS 4–5 indicated a slow early response (SER). To handle incomplete datasets, missing values were estimated using a k-nearest neighbour imputation approach. Baseline and post-treatment laboratory values were combined into a single delta variable representing the net change. The dataset was divided into training and testing subsets, and predictive modelling was performed in Python (scikit-learn v1.2.2) using four machine learning algorithms: logistic regression, random forests, naïve Bayes, and support vector machines.

Results Seventeen paediatric oncology units participated, recruiting 204 patients, of whom 126 HIV-negative patients were evaluated. The random forest classifier demonstrated the highest validated test performance, achieving an accuracy of 73 % in predicting RER versus SER from blood biomarkers. The optimised model reached a predictive accuracy of 80 % and achieved an area under the receiver operating characteristic curve of 0.89. The strongest predictors were changes in haemoglobin and ALC, each accounting for 17 % of the model's contribution. LDH and AEC differences contributed 15 % and 14 %, respectively. Changes in TWC explained 13 %, while variations in ESR, ferritin and albumin contributed 6-9 % each.

Conclusions Changes in low-cost, widely available blood tests may predict chemosensitivity for paediatric patients with cHL without access to PET-CT, identifying patients who may not require radiotherapy. Changes in these non-specific blood tests should be assessed in combination with clinical findings and available radiological imaging to avoid under-treatment.

S-03-03 Moroccan Experience in Childhood Hodgkin Lymphoma: Evolution and Perspectives

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Background: Hodgkin lymphoma (HL) is among the most curable childhood cancers, when treatment is risk-adapted and supported by adequate care. In Morocco, where it represents about 7 % of childhood cancers, its management has evolved over three decades, aiming to improve survival while minimizing toxicity and treatment abandonment.

Objective: To present the Moroccan experience in pediatric HL, highlighting outcomes, difficulties, and strategies adopted to improve care delivery.

Results: Three phases illustrate this evolution. **Before 2000,** Outcomes were limited, with 10-year overall survival (OS) of 64 %, and event-free survival (EFS) not exceeding 43 %. Abandonment rates reached 49 %, representing a major barrier to cure. In 2004, the Moroccan Society of Pediatric Hematology and Oncology (SMHOP) implemented the first national pediatric HL protocol (MDH-MA04). Risk-adapted treatment (VAMP for favorable, OEPA + COPP for unfavorable, plus radiotherapy). This resulted in a significant reduction in abandonment to 12.5 %, an estimated 5-year OS of 88 ± 3 %, and EFS of 70 ± 4 % (80 % when censoring abandonment). A modified protocol (MDH-MA2012) was later introduced, aligning with EuroNet-PHL-C1 (OEPA + COPDAC), though limited by the unavailability of procarbazine. Outcomes remained comparable to previous protocol. Within the WHO Global Initiative for Childhood Cancer, Morocco participated in a national survival study for six indexed pediatric cancers **(2017–2019).** For HL, 5 year OS 86 %, while EFS reached 67.5 %. Thirty events were reported: 13 progressions, 9 relapses, 6 toxic deaths, and 2 abandonments.

Perspectives and conclusion The Moroccan experience demonstrates that stepwise implementation of national protocols and international collaborations has significantly improved outcomes in pediatric HL, reducing abandonment and increasing survival. Building on these advances, the development of a national reference framework aims to standardize risk-adapted care, strengthen supportive services, and establish structured long-term follow-up.

S-03-04 Indian experience – Collaborative Studies for Childhood Hodgkin Lymphoma (HL) in India: The Journey so far!

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The epidemiology, biology, and challenges in treatment of HL differ globally attributable to the extent of EBV-driven disease, and resources available.

InPOG HL-15-01, the first collaborative effort from India highlighted key differences in epidemiology: lower median age (9 %< 5 years) and striking male preponderance. Patients with early-stage disease achieved satisfactory results with 4 cycles of ABVD and radiation limited to sites of bulky disease and inadequate response at early-interim assessment. This approach (with 6 cycles) yielded suboptimal results in advanced-stage disease. Use of PET-CT was associated with reduction in patients requiring radiation.

The next collaborative effort **InPOG HL-17-02** is assessing response-based omission of radiation for patients with advanced stage disease with bulky disease- relevant because of markedly bulky disease often observed in India and limited access to salvage treatments.

InPOG HL-19-03 evaluated outcomes for relapsed/ refractory disease (R/R) using a risk-stratified, response-adapted approach. Risk-stratification was based on time to relapse, stage, B symptoms and prior radiation. Patients with low-risk relapse received Gemcitabine-Vinorelbine and radiation subject to CMR after two cycles. Those with suboptimal response received ICE followed by ASCT. Patients with high-risk relapse were to proceed to ASCT after CMR. Seventy patients were enrolled from 9 centers over 58 months. Only 27 had CMR at response evaluation. Twelve were switched to ICE chemotherapy with only 2 achieving CMR. Novel strategies for patients failing first salvage may be more prudent. Less than a third of the patients eligible for ASCT underwent the same. At a median follow-up of 35 months, the estimated 5-year OS and EFS are 74.3 % and 67.1 %.

INPHOG HL-23-02 captured real-world data: clinical settings, response rates, doses/regimen used and outcomes for patients treated with immunotherapy. The study recruited 64 patients. Significant findings include the high response rate to nivolumab and comparable efficacy of lower doses in R/R setting.

Finally, **INPHOG HL- 25 -05** is prospectively evaluating Bendamustine with fixed dose (40 mg) Nivolumab for R/R HL aimed at limiting both the cost and toxicity of salvage regimens.

In summary, much progress has been made to identify the challenges and possible solutions for managing HL in our setting through collaborative work [1–6].

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S-03-05 ARIA guide for Hodgkin Lymphoma

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S-04 | Health Outcomes

Chairs: Tomasz Klekawka (Krakow), AnnaLynn Williams (Rochester)

S-04-01 Fertility issues after pediatric Hodgkin lymphoma.

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Background/Purpose Reproductive outcomes are among the most important late effects in childhood cancer survivors.
The prognosis of childhood Hodgkin lymphoma (HL) is excellent and the number of survivors is growing. Understanding HL treatment's impact on gonadal function is key to optimize HL treatment and improve fertility care in pediatric HL patients and survivors.
Methods Reproductive ability in females and males will be discussed, including effects of gonadotoxic treatment and fertility markers. Results from studies in childhood HL survivors and newly diagnosed pediatric HL patients will be presented. Additionally, satisfaction with fertility counseling was assessed in a Dutch subgroup.
Results
Survivors
84 Dutch female HL survivors (median age 29.4 years) vs. 798 controls (32.7), showed lower AMH, inhibin B, AFC, and higher FSH, suggesting higher risk of premature ovarian insufficiency (POI). Live birth and miscarriage rates matched the general population, but survivors had their first pregnancy earlier (27.0 vs. 29.0 years, p = 0.04) and more often experienced > 12 months to conceive (adjusted OR 2.5). Semen parameters in 41 male HL survivors (median age 36.5 years) were significantly lower compared to controls (n = 202, age 42.7) ; 51 % had sperm counts < 15 million/ml, and 37 % were azoospermic.
Children with HL, treated according to EURONET-PHL-C2.
104 girls (median age 15.6 years) were studied. Median AMH was relatively low 2 years post-diagnosis (2.1ug/L, normative value 3-4ug/L between 16-20 years), suggesting POI risk. Treatment-induced amenorrhea occurred in 54 %, with recovery in most. 101 boys (73 (post)pubertal) were studied; 52 % (16/31) had oligo- or azoospermia two years post-diagnosis. Low sperm counts and motility were most common in advanced-stage patients [1–5].
Patient- and parental satisfaction on fertility counseling of a Dutch subgroup
34 parents and 27 patients responded (median 4 years post-diagnosis). Nearly all (97 % parents, 89 % patients) reported to have received counseling. Most (87–94 %) valued it, with many expressing fertility concerns (42–59 %). Boys often felt uncomfortable discussing the topic (57 %).
Conclusions Despite treatment adaptations (lower alkylating agents, limited radiotherapy), current HL therapy still risks gonadal damage, especially in advanced stages. Fertility counseling remains essential. The impact of newer agents (e.g., Brentuximab, Check Point Inhibitors) on fertility should be further studied.
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S-04-02 Sexual health in adolescent and young adultpatients: what is it, is it important, and what can we do about it?

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Adolescents and young adults (AYA) with cancer face unique psychosocial challenges during their cancer journey, especially individuals diagnosed with lymphoma, often resulting in clinically significant deficits that are lifelong. Sexual health is a complex interaction between many different facets of the individual and is poorly understoon in general and lacking in evidence based treatment. Given that the AYA years are so critical to the development of both sexual and gender identity and expression, sexual orientation, and relationship building, it is not surprising that AYAs diagnosed with cancer during this time suffer from sexual dysfunction at much higher rates than their peers and that some of these deficits are lifelong. During this session, we will review what is the complex nature of sexual health and how it is impacted in the AYA population by cancer and its therapy with a specific emphasis on patients with lymphoma. We will also review the patient perspective and what our patients think we, as cancer care providers, should know and be doing to help them through their journely. Lastly, we will review what can be done to help with sexual dysfunction and novel therapeutic advances that are currently under development in the field.

S-04-03 Doxorubicin Exposure and Breast Cancer Risk in Survivors of Adolescent and Adult Hodgkin Lymphoma

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Female Hodgkin lymphoma (HL) survivors treated with chest radiotherapy (RT) at a young age have a strongly increased risk of breast cancer (BC). Studies in childhood cancer survivors have shown that doxorubicin exposure may also increase BC risk. Although doxorubicin is the cornerstone of HL chemotherapy, the association between doxorubicin and BC risk has not been examined in HL survivors treated at adult ages.

Methods We assessed BC risk in a cohort of 1,964 female 5-year HL survivors, treated at age 15-50 years in 20 Dutch hospitals between 1975 and 2008. We calculated standardized incidence ratios, absolute excess risks, and cumulative incidences. Doxorubicin exposure was analyzed using multivariable Cox regression analyses.

Results After a median follow-up of 21.6 years (IQR, 15.8-27.1 years), 252 women had developed invasive BC or ductal carcinoma in situ. The 30-year cumulative incidence was 20.8 % (95 % CI, 18.2 to 23.4). Survivors treated with a cumulative doxorubicin dose of > 200 mg/m2 had a 1.5-fold increased BC risk (95 % CI, 1.08 to 2.1), compared with survivors not treated with doxorubicin. BC risk increased 1.18-fold (95 % CI, 1.05 to 1.32) per additional 100 mg/m2 doxorubicin (*P*trend = .004). The risk increase associated with doxorubicin (yes *v* no) was not modified by age at first treatment (hazard ratio [HR]age < 21 years, 1.5 [95 % CI, 0.9 to 2.6]; HRage ≥ 21 years, 1.3 [95 % CI, 0.9 to 1.9) or chest RT (HRwithout mantle/axillary field RT, 1.9 [95 % CI, 1.06 to 3.3]; HRwith mantle/axillary field RT, 1.2 [95 % CI, 0.8 to 1.8]).

Conclusion This study shows that treatment with doxorubicin is associated with increased BC risk in both adolescent and adult HL survivors. Our results have implications for BC surveillance guidelines for HL survivors and treatment strategies for patients with newly diagnosed HL.

S-04-04 Survival By Race/Ethnicity in Children and Adolescents/Young Adults with Relapsed/Refractory Hodgkin Lymphoma: A Pooled Analysis of Children's Oncology Group Trials

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Introduction Despite 5-year survival rates over 90 % among children and adolescents/young adults (CAYAs) with classic Hodgkin lymphoma (HL), population-level and clinical trial studies consistently report inferior outcomes among non-Hispanic Black (NHB) and Hispanic (vs. non-Hispanic White [NHW]) patients. Proposed mechanisms for these disparities include differences in disease or host biology and factors impacting access to care. Analysis of frontline Children's Oncology Group (COG) clinical trials revealed that despite relapse rates, Hispanic and NHB (vs. NHW) patients had nearly 3.5 times increased risk of death post-relapse. The association between race/ethnicity and overall survival (OS) among CAYAs enrolled on COG trials for relapsed/refractory (r/r) HL was evaluated.

Methods This was a pooled analysis of individual level data from CAYAs (≤ 29 years) enrolled on four phase 2 clinical trials for r/r HL (AHOD00P1, AHOD0321, AHOD0521, AHOD1221) and the embedded salvage regimen of a phase 3 frontline trial (AHOD0431). Race/ethnicity, categorized as reported to COG by treating institutions, were Asian/Pacific Islander, Hispanic, NHB, NHW, and other/unknown. The Kaplan-Meier method was used to estimate 3-year OS by racial/ethnic groups. Cox regression models examined the association of race/ethnicity with OS, adjusted for age, insurance, first relapse vs. ≥ 2 relapse, and time to relapse.

Results The analysis included N = 175 patients treated on COG trials for r/r HL (2001 – 2016). The distribution of race/ethnicity was as follows: 5.7 % Asian/Pacific Islander (N = 10), 14.9 % Hispanic (N = 26), 14.3 % NHB (N = 25), 61.7 % NHW (N = 108), 3.4 % other (N = 6). Median time from initial diagnosis to relapse was 10 months (range, 0.3-68.1 months) and did not differ by race/ethnicity (p = 0.45). Median age at relapse was 16.9 years (range 5.1-29.3 years) with 31.4 % (N = 55) < 15 years. A higher proportion of NHW patients had private (vs. public) insurance (p = 0.01). At median follow-up of 4.9 years, pooled 3-year OS was 82.1 % (95 % CI, 75.3-87.1) and did not significantly differ by race/ethnicity (p = 0.36). In multivariable model for OS, shorter time to relapse (p = 0.01) and ≥ 2 relapse (vs. 1st relapse, p = 0.004) were associated with worse OS, with no significant effect of race/ethnicity (p = 0.43).

Conclusion We observed no difference in survival by race/ethnicity among CAYAs treated on COG r/r HL trials. Findings suggest that access to clinical trial for salvage may partly mitigate post-relapse survival disparities.

S-04-05 Modern radiotherapy for Hodgkin lymphoma – associated radiation doses and predicted second cancer risks

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Introduction Radiotherapy (RT) treatment for Hodgkin lymphoma (HL) has evolved: it is now often reserved for patients with slow or incomplete response to induction chemotherapy; prescribed doses are reduced; extended-field treatments have been replaced by involved field/site/node treatments; intensity modulated RT is used instead of conventional 2- or 3-dimensional conformal RT, improving dose conformity. Consequently, exposure to organs near the tumor site has been substantially reduced. However, risk estimates for radiation-related second cancers are based on patients treated decades ago due to the long follow-up needed to observe them. To better accommodate current doses in risk predictions we use details on the dose distribution to the organ of interest, and illustrate our method by predicting second breast cancer (BC) risk.

Methods We estimated relative risks and age-specific incidence for BC and competing events (mortality or other subsequent cancer) from 1194 female Dutch 5-year HL survivors, treated at ages 11 to 40 years of age during 1965-2000. To capture the radiation dose distribution in the breast, predictors were doses to 10 breast segments, and other BC risk factors. Models were validated in the North American Childhood Cancer Survivor Study cohort. We then compared radiation dose distributions to the breast given in 2006-2021 among 101 patients with HL or other lymphoma in 1 German and 2 Dutch hospitals with doses received by 505 Dutch HL patients treated between 1965-1997. Absolute BC risks 25 years after historic and recent treatments were estimated for low- and high-risk profiles.

Results The average mean breast dose decreased from 21.4 Gy for historic to 3.0 Gy for recent treatments. The percentage of breast volume receiving > = 20 Gy decreased from 48.7 to 2.2 %. The minimum dose received by 20 % of the breast volume decreased from 39.0 to 2.8 Gy. Using quadrant-specific doses, median absolute BC risk 25 years after HL treatment decreased from 21.0 to 6.9 % for historic versus recent treatments for a high-risk patient and from 3.1 to 0.9 % for a low-risk patient, respectively. Using mean dose instead of quadrant-specific doses, median absolute BC risks decreased from 20.3 to 6.0 % and from 3.1 to 0.9 % for the high- and low-risk patients, respectively. [1–3]

Conclusion Incorporating detailed organ-specific dose information in predictions of second BC risk can accommodate temporal changes in dose distributions. For breast cancer, substantially reduced contemporary RT doses lead to considerably lower risk estimates.

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S-04-06 Health-Related Quality of Life in Individuals Diagnosed with Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL): An Initial Report from the Global NLPHL One Working Group

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Introduction Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL), a rare subtype of HL, impacts children and adults. While survival is long, relapse is common and NLPHL is often considered a chronic disease. Understanding the impact of NLPHL on health-related quality of life (HRQoL) is essential to developing standard care practices. No comprehensive studies have examined HRQoL with patient-reported outcomes (PROs) for patients diagnosed with NLPHL. This prospective, longitudinal study seeks to fill that gap.

Methods Individuals > = 8 years old with pathologically confirmed NLPHL were eligible. Electronic PROs were administered at enrollment and then every 3 months for 1 year. All individuals received PROMIS and EuroQOL EQ-5D measures; participants > = 16 years old also completed the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and the HL module (QLQ-HL27). Participants reported demographics and treating physicians reported disease and treatment characteristics. Descriptive statistics were utilized to examine demographics, disease/treatment characteristics, and HRQoL at enrollment.

Results Participants (n = 21) were mean age 42(SD = 21) years at time of study enrollment; median time from diagnosis was 79 months. Many were treated for NLPHL and in remission (48 %), with 24 % having received chemotherapy, 19 % radiation, and 19 % chemotherapy plus radiation. Participants were largely White (71 %) and male (71 %). At diagnosis, participants had absence of: B symptoms (91 %), large mediastinal mass (95 %), and extranodal disease (76 %). Nearly half of participants had > = 3 nodal areas (43 %), more than one medical comorbidity (48 %), and were Ann Arbor stage I (48 %). Mean scores on all PROMIS domains were consistent with the general population mean (range:46-53). Mean(SD) overall health on the EQ-5D-5L was 78(19), suggesting a positive view of health. All functional scale scores on the EORTC QLQ-C30 were high (range:71-88), suggesting high level of functioning. All symptom

scale scores on the EORTC QLQ-C30 and QLQ-HL27 were low (range:7-31), suggesting low symptom burden.

Conclusion This is the first study to systematically examine HRQoL utilizing PROs for individuals diagnosed with NLPHL. Initial data suggest good HRQoL in this cohort of patients mostly > 5 years from diagnosis. Ongoing research is necessary to better understand the experience of patients at diagnosis and longitudinally during and after various treatments.

P-01 | Guided Poster Session

P-01-01 Prognostic value of 18F-FDG PET/CT volumetric parameters in childhood, adolescent, and young adult Hodgkin lymphoma (CAYAHL): a systematic review from the international SEARCH group (Staging, Evaluation and Response Criteria Harmonization)

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Introduction In adults with classic Hodgkin lymphoma (cHL), PET volumetric parameters are valuable for risk stratification. This study was undertaken to explore the role of metabolic parameters in children, adolescents, and young adults with cHL.

Methods This systematic review was performed according to the PRISMA method. Five databases were searched on 16th October 2024: MEDLINE (Ovid), EMBASE (Ovid), CINAHL (EBSCO), EBM Reviews (OVID) and the Web of Science Core Collection. Eligible studies were peer-reviewed manuscripts, written in English, published from database inception to the search date that included patients up to 21 years of age with a diagnosis of cHL and a ^{18}F-FDG PET/CT scan with calculation of MTV.

Results The search strategy detected 3669 studies from which 1085 duplicates and 2584 studies were excluded following 2-person review of titles and abstracts. Full-text review of 81 papers identified 35 as eligible for inclusion. Fifteen of the papers (43 %) evaluated a cohort exclusively < 21 years of age and 20 papers (57 %) considered children and adults, with a median of 69 (21-297) participants. All 8 studies that explored the association of baseline MTV and/or TLG (total lesion glycolysis) with known risk factors (ex. bulk, stage, clinical parameters used to define treatment group/level) identified a significant correlation. Twelve papers explored the association of baseline MTV and/or TLG with disease response on PET/CT according to Lugano criteria, of which 9 (75 %) demonstrated a statistically significant correlation. Twenty papers explored the association of baseline PET parameters with clinical outcome (ex. overall survival, progression-free survival) and 15 (75 %) demonstrated an independent statistically significant correlation. Of 6 studies that explored higher-order radiomic features, 4 (67 %) found that they out-performed MTV and/or TLG. Thirty-three of 35 studies detailed the segmentation approach that was used to delineate disease, of which 11 used or recommended an absolute fixed threshold method.

Conclusion Metabolic PET parameters are valuable for risk stratification; heterogeneity in results is related to differences in patient cohorts, treatment strategies, methods for disease segmentation, and parameter calculation. Recommendations regarding the necessary next steps to harmonize the approach and incorporate PET volumetric parameters into clinical practice for children, adolescents and young adults with cHL are discussed [1–10].

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P-01-02 Nodular Lymphocyte Predominant Hodgkin Lymphoma: Experience of the Polish Pediatric Leukemia/Lymphoma Study Group (PPLLSG)

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Introduction Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) is a rare clinical entity. To investigate the clinical course and treatment of NLPHL, a survey was conducted among centers participating in the Polish Pediatric Leukemia/Lymphoma Study Group (PPLLSG).

Methods A questionnaire was sent to all 17 Polish centers, and clinical data were analyzed.

Results Between 2010 and 2024, 39 pediatric patients aged 5.6–18.0 years (median: 12.3 years) with confirmed NLPHL were registered in Poland. NLPHL occurred predominantly in males (n = 35). All disease stages were observed, with stage I (n = 8) and stage II (n = 23) being the most common. In most patients (n = 26), supradiaphragmatic involvement was noted.

Seven patients with localized, resectable stage IA disease were treated. Five underwent complete primary resection; two received surgery alone, although one relapsed and was treated with CVP chemotherapy. The other five received additional chemotherapy after resection. Three patients had incomplete resections and received CVP chemotherapy, with one relapse observed.

CVP chemotherapy was administered to 23 patients with stage IIA disease. After three cycles, four relapses occurred and were managed with R-CHOP ± radiotherapy. All treatments have led to durable remissions so far.

Advanced disease was noted in nine patients (eight boys, one girl) aged 8.8–17.9 years (median: 12.2). Various chemotherapy protocols were used, including rituximab in three cases and without rituximab in five. Two relapses were treated with R-CHOP; one patient underwent autologous stem cell transplantation due to poor response. Relapse-free survival rates were 72.1 % for early-stage (IA and IIA) and 85.7 % for advanced-stage disease. No deaths were reported.

Conclusion The outcomes of NLPHL treatment in Poland are consistent with those reported in other countries; however, further improvement and standardized treatment approaches for NLPHL patients in Poland are needed. Special attention should be given to patients eligible for primary surgical resection.

P-01-03 Radiotherapy is not needed with complete remission after frontline risk and response-adapted chemotherapy. A multicenter Pediatric Hodgkin Lymphoma Trial (LH-GALOP 2017, ClinicalTrials.gov ID: NCT03500133)

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Introduction Multicenter, prospective, non-randomized, risk and response adapted treatment for classical Hodgkin Lymphoma (cHL) whose mainly purpose was to avoid radiotherapy when complete metabolic/volume remission was achieved after chemotherapy. Cumulative chemotherapy doses were limited to prevent toxicities and the use of strong alkylating agents was avoided.

Methods Consecutive patients, between the ages of 2-18 years with newly diagnosed cHL were admitted. Imaging with PET-CT and Deauville Score was preferred for staging and disease assessment. Complete response was defined by volume reduction (> 80 %) and/or metabolic remission (Deauville Score < 3). In case PET-CT was not available, CT and ultrasound with volume reduction (> 80 %) to assess response was used. Combined chemotherapy was based on regimes with well-known effectiveness: ABVD/ESHAP. Initial staging provided stratification in three risk groups. Low risk: Stages I/IIA without bulky mass, less than 4 ganglionar areas. Intermediate risk: Stages I/IIA with additional risk factors and Stages IIB/IIIA. High risk: Stages IIB/IIIA with bulky mediastinum, Stages IIIB/Stage IV. Low/intermediate risk groups received two courses of ABVD. High risk received ABVD followed by ESHAP. Rapid early responders after two courses who achieved complete remission (CR) benefited from less chemotherapy. Only patients with partial remission at the end of chemotherapy received low dose (30Gy) involved node RT. Complete responders at the end of chemotherapy did not receive RT. Refractory disease at any moment was assumed as a trial failure, new therapeutic strategies were offered and censored at time 0 for event-free survival analysis.

Results n = 109, M/F = 1,8, median age 11.9 (r = 3-16.8) years. Stage I = 6 %, Stage II = 42 %, Stage III = 28 %, Stage IV = 23 %. "B" symptoms = 46 %. Low risk = 18 %, Intermediate risk = 30 %, High risk = 51 %. Remission rate after chemotherapy = 85 %. Relapse rate = 4.6 %. Refractory disease rate = 4.6 %. Radiotherapy delivered in partial remission after chemotherapy, relapse and refractory disease = 18.3 %. With a median follow up of 51 months, at 5 years EFS rate was: 86.5 % (SE = 3 %) and OS = 100 % (2 patients alive with disease). Mild acute toxicities, mainly haematological.

Conclusion High remission rate and outstanding survival outcome were obtained. Very low requirements of radiotherapy and minimal acute toxicity with a perspective of minimal long term effects. Our population presented with high incidence of advanced disease at onset.

P-01-04 A Retrospective Analysis of Pediatric Hodgkin Lymphoma Treatment Outcomes at the National Children's Hospital of Costa Rica (2004–2017).

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Introduction Pediatric Hodgkin lymphoma (HL) has a high rate of survival in high-income-countries (HIC), yet these outcomes are difficult to reproduce in low-income-countries (LIC) (1). Costa Rica is a middle-income-country with universal health care, where 1/5 of its population lives in poverty. LIC's event free survival (EFS) rates trail HIC by as much as 25 % (1,2,3). To close the survival gap and improve cure rates worldwide, further research is necessary to identify treatment guidelines that are successful in LIC.

Methods The objective of this study was to identify the EFS and overall survival (OS) for the 13-year cohort and determine the differences in EFS and OS between low, intermediate, and high-risk groups. The treatment guidelines selected for the cohort had shown improved outcomes in previous studies. We expect survival outcomes to continue improving, thereby shrinking the gap between LICs and HICs. EFS is the percentage of patients who survived and did not undergo an event such as death, progression, relapse, or abandonment while OS is the percentage of patients who survived. Kaplan-Meier estimates were used to evaluate EFS and OS; stratified by risk groups, symptoms, stage, radiotherapy, and treatment guidelines. Associations between survival outcomes and clinical and demographic factors were examined using Cox proportional hazards (CoxPH) regression.

Results 96 patients were eligible for evaluation. The mean age at diagnosis was 8.69 years old (y.o), predominant age at diagnosis was 5-10 y.o (58.3 %), and the male-to-female ratio was 2:1. The most prevalent histology was nodular sclerosis (81.3 %). The overall 5-year EFS and OS were 73.7 + /- 4.5 and 85.3 + /- 3.6 respectively. The 5-year EFS per risk were 82 + /- 0.07 for low-risk, 69 + /- 0.1 for intermediate-risk, and 69 + /- 0.07 for high-risk, respectively. 12 % of patients did not follow an official protocol which was associated with an increased risk of an event occurring [1–4].

Conclusion The EFS and OS of low- and middle-income countries (LMIC) is inching closer to that in HICs yet more can be done to improve it. Enrolled in the cohort were 4 patients with congenital immunodeficiencies who died from treatment related toxicity, underscoring the need to develop safe treatment guidelines for this demographic. Additionally, there were several patients that had errors in their treatment protocols which highlight the need for academic and international collaboration in LMIC (4).

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P-01-05 A RISK ADAPTED, RESPONSE- BASED THERAPEUTIC REGIMEN USING OEPA/COPDAC FOR THE TREATMENT OF CHILDREN WITH HIGH RISK HODGKIN LYMPHOMA; FROM THE AHOPCA GROUP

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Introduction Purpose: Childhood Hodgkin lymphoma (HL) is highly curable in high income countries. Our previous treatment protocol for high-risk (HR) HL with a modified Stanford V achieved a three year event-free survival (EFS) and overall-survival (OS) of 50 % and 60 % respectively. Here we present the follow up study for high risk patients using OE * PA/COPDAC.

Methods All patients with histologically proven HL with stages IIB, IIIB and IV presenting to one of the centers between June 2009 and December 2023 were eligible for the treatment protocol. Patients received 2 cycles of OEPA (vincristine, etoposide, prednisone, and doxorubine) and 4 cycles of COPDAC (cyclophosphamide, vincristine, prednisone, and dacarbazine) followed by involved field radiotherapy (IFRT). IFRT dose depended on the response after 2 cycles of OEPA: 20 Gy if the patient achieved an adequate early response (AER) by CT and 25 Gy if the response (< 50 %) was inadequate by CT (IER). All data was entered prospectively into an electronic data base (POND) and Salus electronic data base.

Results All 211 eligible patients were evaluable. Seventy-six percent of the patients were male, the median age was 8 years (range 2-18 years) The histology included nodular sclerosis 182 (86 %), mixed cellularity 22 (10 %), and lymphocyte predominant 7 (4 %). With a median follow-up of 121 months we have a three-year EFS 81 % ± 0.02 % SE. Seven (3 %) patients abandoned therapy, seventeen (8 %) relapsed, six (3 %) had progressive disease, and twelve (6 %) patients died, eleven of therapy toxicity, as the group started becoming familiar with the regimen.

Conclusion The OEPA/COPDAC regimen is well tolerated with acceptable toxicity. The initial elevated mortality improved once the oncologists became better acquainted with the regimen. Herein, we report a better survival with this regimen as compared to our previous trial (50 % vs 81 %) and approaching the results obtained in high-income countries, in 2024 we started the CLEHOP protocol based on the EURONET backbone for Hodgkin lymphoma, where patients with AER after 2 cycles of OEPA by CT did not require futher RT at the end of the 4 COPDAC.

P-01-06 Updates on patient and care partner (PaCP) priorities in nodular lymphocytepredominant Hodgkin lymphoma (NLPHL) research: A report from the Global NLPHL One Working Group (GLOW)

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Introduction GLOW facilitates international collaboration aimed at optimizing diagnosis, care, and outcomes for patients diagnosed with NLPHL worldwide. Given the curability of NLPHL with an overall survival of nearly 100 %, and the absence of NLPHL-specific patient needs assessments, a GLOW subcommittee sought to understand PaCP experiences and incorporate their needs into research and programmatic activity agendas, and build sustainable research partnerships.

Methods In 2023, GLOW specialists in pediatric and adult oncology, psychology, radiation oncology, and public health, sought PaCP perspectives on NLPHL treatment priorities, trade-offs, informational needs, and symptoms discussions. PaCPs were invited to participate in focus groups and join standing committees to better align strategic priorities with the needs of PaCPs. Themes and priorities emerged and were formally incorporated into GLOW's strategic roadmap.

Results PaCPs contributed insights from their diagnosis and care experiences through focus groups. Key themes identified included a desire for NLPHL-specific resources and concrete care guidelines. Given its rarity, many PaCPs also expressed feelings of "alone-ness" and anxiety during their diagnosis and care journeys, despite the curability. The subcommittee identified 8 opportunities for researchers, healthcare practitioners, and cancer support organizations to improve NLPHL care, research, and PaCP support. Patient advocates joined the Executive Committee and Patient Reported Outcomes Committee in the fall of 2023 to support GLOW in the integration of these priorities in the GLOW research roadmap and subsequent activities, prompting the development of a NLPHL patient decision aid, which will be evaluated in GLOW's prospective clinical trial.

Conclusion Integrating PaCP priorities has enhanced GLOW's ability to align strategic priorities and change the paradigm to shared decision making for treatment choices. GLOW continues to integrate new PaCP advocates in its work and seeks to sustain a diverse group of PaCP advisors moving forward.

P-01-07 Risk-stratified and response adapted therapy for pediatric Hodgkin lymphoma in Argentina: the GATLA experience

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Introduction The international cooperation between GATLA and AHOPCA with the support of St. Jude, led to the adoption of the OEPA/COPDAC as a strategy to improve outcomes in high risk (HR) patients with HL. This study also includes the ABVD regimen for intermediate (IR) and low (LR) risk patients.

Methods Patients were stratified by pre-defined risk assignment. High risk was defined as stages IIB, IIIB and IV. Modality treatment: LR: ABVD x 4 ± IFRT (20 Gy); IR: ABVD x 6 ± IFRT (20 Gy); HR: OEPA-COPDAC + IFRT (20/25 Gy). The staging and response were reviewed in a periodic discussion of presentation of cases in the Group. Eligibility for radiotherapy: LR patients with Partial Response (PR) after 4 ABVD and IR patients in PR after 2 ABVD received IFRT. All HR patients received IFRT at 20 (Complete Response (CR)) or 25 Gy (PR) depending on the response achieved after the first two OEPA cycles.

Results From November 2012 to June 2022, 203 pediatric patients were enrolled. 171 patients were eligible in this analysis. HR: 98 patients (57,3 %), IR: 52 patients (30,4 %) and LR: 21 patients (12,3 %). More than half of the patients had stage III and IV disease and more than half also presented B symptoms. The response evaluation was performed by PET/CT in 147/171 patients (86 %). 68/171 patients (40 %) did not received radiotherapy. Radiotherapy was omitted in 95 % of the low risk patients and 70 % of the intermediate risk patients. The 10-year OS was 95 % (90.7-97.6) for all patients and 93 % (85.3-96.4) for high risk patients. The 10-year EFS was 91 % (85.2-94.2) for all patients, and 87.8 % (79.5-92.9) for high risk patients.

Conclusion The collaborative work allowed for a centralized review of the staging and response of the patients which makes this work more solid and, at the same time, to significantly improve the results of patients with advanced disease in Argentina compared to our previous experience (7-PHD-96: COPP-ABV x 6 + IFRT Bulky Disease or PR (20/25Gy): 5yOS:85 %, 5yEFS:67 %), reduce radiotherapy doses as well as the number of patients who required radiotherapy and finally reproduce the European experience for high-risk patients in a different context.

P-01-08 Twenty-Year Review of Paediatric Classical Hodgkin Lymphoma in Hong Kong: Treatment Evolution and Outcomes

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Introduction Classical Hodgkin lymphoma (cHL) is less prevalent among Asian children compared to Caucasian populations, and outcome data in Asian cohorts remain limited. From 2000 to 2016, paediatric cHL in Hong Kong was treated using the HKPHOSG HL 2000 protocol (based on CCG-5942), combining chemotherapy and involved-field radiation. In 2017, treatment transitioned to the OEPA/COPDAC regimen (based on the Euronet-PHL-C1 and -C2 trials), incorporating FDG-PET-guided, risk-adapted therapy. This study evaluates the clinical characteristics and survival outcomes in a Hong Kong paediatric cHL cohort.

Methods We conducted a retrospective review of 78 children and adolescents diagnosed with cHL and treated at paediatric oncology centers in Hong Kong between 2000 to 2022. Patients with a minimum of one year of post-treatment follow-up were included. Data collected included demographics, treatment protocols, survival outcomes, and long-term complications.

Results The annual number of new cases progressively increased from an average of 2.3 (2001-2005) to 5.5 (2016-2020). Of 78 patients (median age: 15.3 years; range: 12.7-16.8), 51 received the HKPHOSG HL 2000 protocol and 27 the Euronet-based regimen. (Table 1) Radiation therapy was administered in 30 % of patients. Overall survival was 100 % at 3 and 5 years, and 97.6 % at 10 years. Event-free survival were 92.3 % at 3 and 5 years and 87 % at 10 years. Survival outcomes did not differ significantly between treatment groups. Long-term complications, including hypothyroidism, impaired fertility, and cardiac dysfunction, were reported in 29 % of patients, predominantly from the earlier treatment era.

Conclusion Paediatric cHL in Hong Kong demonstrates excellent survival outcomes, comparable to international standards, despite its lower disease incidence in Asian populations. The rising number of cases suggests changing pattern of risk factors. The shift to Euronet-based regimens preserved efficacy while aiming to reduce toxicity. Future strategies should prioritze risk-adapted therapies that minimize long-term effects and improve quality of life for survivors.

P-01-09 A Regional Initiative for a Global Challenge: Advancing NLPHL Care in Latin America through Collaborative Strategies

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Introduction Limited information is available on childhood Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) management in Latin America (LATAM) [1]. Due to its rarity, strong evidence regarding NPLHL care is scarce worldwide. [2] Managing NLPHL in resource-limited countries might be even more challenging [3]. Considering the curability of this disease; the barrier in getting rituximab in LATAM and the heterogeneity of resources available in different countries, a treatment guide would be helpful and could facilitate better treatment approaches [4].

Methods In partnership with the Global nLPHL One Working Group (GLOW) and the Consorcio Latinoamericano de Enfermidades Hemato-oncologicas Pediatricas (CLEHOP) members, an international initiative is underway to develop a collaborative project to improve NLPHL care in Latin America. Framework for GLOW and the project was presented at a number of meetings, strategies were developed and plans put into practice.

Results A retrospective analysis will be performed gathering data from patients treated with NLPHL from January 2023-June 2025 from 27 Brazilian Centers. Project implementation occurred via GLOW/CLEHOP team members using national contacts. Institutions were asked to designate one respondent (clinical lead). Responses will be sent back by email and collected centrally for analysis. With the intent to involve other LATAM countries in this study, GLOW was presented at Congreso SLAOP- ACHOP in Cali, Colombia in June this year to launch conversations about the theme.

Conclusion This is the first discussion on the management of NLPHL care in LATAM. This initiative is facilitating the establishment of a network of oncologists in LATAM, enabling collaboration to improve cancer care.

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P-01-10 Pediatric Hodgkin Lymphoma with bone involvement: 24 years of experience in a single institution in Argentina

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Introduction Hodgkin lymphoma (HL) accounts for 7 % of pediatric malignancies and is associated with an overall survival (OS) rate exceeding 90 %. It is the most common cancer among adolescents between 15–19 years. The typical presentation is supradiaphragmatic nodal involvement. Extranodal manifestations may affect lungs, liver, bones and bone marrow; B symptoms are observed in 20–40 % of patients. Bone involvement is rare at diagnosis (1–4 %), particularly if multiple lesions are present. The axial skeleton is most frequently affected. 18F-FDG PET-CT is the preferred modality to assess bone lesions. It is important to consider that osseous lesions have delayed resolution on imaging to avoid unnecessarily increasing chemotherapy intensity.

Methods We conducted a retrospective, cross-sectional, observational and descriptive study between January 2000 and April 2024. We analysed cases with bone involvement. Survival was estimated using the Kaplan-Meier method.

Results Out of 230 patients diagnosed with HL, 11 (4,7 %) presented with bone involvement. Male predominance; median age was 12 years (range: 6–16); the histological subtype was nodular sclerosis in all cases. At diagnosis, all patients presented with advanced disease (stage IV and high risk). B symptoms were found in 91 % of cases. Bone involvement affected the axial skeleton in 91 % of cases. All patients had associated extranodal disease: 54 % lung, 45 % bone marrow, and 18 % liver. Bulky mediastinal disease was observed in 2 patients (18 %). Patients were treated according to two protocols: LH-HPG 2000/2015 and LH-GALOP/SAHOP 2017 (ClinicalTrials.gov ID: NCT03500133). Seven children received radiotherapy as part of first-line treatment. Estimated EFS and OS were 85 % and 100 %, respectively. Regarding response, 7 patients (64 %) achieved complete remission (CR), 2 patients a partial remission (18 %) and 2 patients (18 %) had progressive disease. One of the latter achieved CR after second-line chemotherapy plus radiotherapy, while the other is on treatment and was not included in survival analysis.

Conclusion In pediatric HL, bone involvement — though associated with advanced disease — does not appear to worsen prognosis when treated with risk-adapted protocols. Our findings support avoiding overtreatment based solely on osseous lesions. Further studies are needed to validate these results.

P-01-11 Long-term-survival of pediatric Hodgkin lymphoma (HL) patients after GPOH-HD 2002 study treatment

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Introduction The GPOH-HD 2002 trial enrolled 573 children and adolescents with newly diagnosed classical Hodgkin lymphoma between 2002 and 2005. Male patients were treated completely procarbazine-free, whereas female patients received standard procarbazine-based regimen. The majority of patients received involved field radiotherapy after their treatment group assigned chemotherapy. [1] The aim of the current analysis was to report on long-term-survival of the patient cohort.

Methods Follow-up data, i.e. time/reason of death, relapse, second malignancy dates and treatment related late effects were obtained by sending out follow up-questionnaires or by telephone interviews. Informed written consent to the original trial included 5-year follow-up time after end of treatment. German GPOH-HD 2002 trial survivor patients were asked in 2018 by the German Childhood Cancer Registry to participate in the Late effects study. Their follow-up data was included in the present study. International patients were only included, if consent according to their national or institutional guidelines was available. The database was locked at the end of September 2019.

Results Follow-up data of 288 patients was collected. The median follow-up time was 12.72 (+ /- 3.58) years, range 0.055 to 16.68 years. Three patients died, one from suicide, one because of EBV reactivation and one of cerebral hemorrhage after sinus venous thrombosis. The number of PFS-events was 29, fourteen TG-1, five TG-2 and ten TG-3 patients. The number of EFS-events was 41, 25 events occurring in male and 16 in female patients. Sixteen patients were diagnosed with second malignancies, six thyroid carcinomas, one peritoneal mesothelioma, one EBV-associated gray zone lymphoma, one nasopharynx carcinoma, one ovarian teratoma, one colorectal carcinoma, one basalioma and four not otherwise specified carcinomas. 247 patients are event-free after treatment. Reported late effects were especially hypothyroidism and other thyroid diseases, osteonecrosis, azoospermia, hypergonadotropic hypogonadism and cardiomyopathy.

Conclusion The long-term-survival of Hodgkin lymphoma patients within the GPOH-HD 2002 trial is excellent. The number of second malignancies rises with longer observation time. Long-term follow-up registries and follow-up clinics are urgently warranted for better estimation and subsequent treatment of therapy-associated late effects.

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P-01-12 Race, ethnicity, and insurance inequities in Hodgkin lymphoma (HL) treatment and survivorship care in the US: A study in progress

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Introduction In the US, racially and ethnically minoritized patients and those with suboptimal insurance face inferior HL survival in childhood, adolescence, and young adulthood. The knowledge gap explaining worse survival reflects lack of clinical and administrative data regarding patient-level (i) social factors (e.g., insurance), (ii) post-relapse treatment, especially stem cell transplant (SCT), and (iii) lack of survivorship care engagement. There is a critical need to identify predictors of variation in receipt and quality of treatment and survivorship care leading to worse survival for those patients with HL using a mixed-methods approach to create an evidence-based framework to design interventions to improve survival.

Methods Funded by the NCI (R37CA288560), our central hypothesis is that key and distinct racial, ethnic, and social factors influence treatment and survivorship care for people with HL. This hypothesis will be tested by pursuing three specific aims in this mixed-methods study: Aim 1 examines differences in the receipt and quality of treatment at initial diagnosis and relapse; Aim 2 examines the receipt and quality of survivorship care; Aim 3 examines diverse patients' shared decision-making (SDM) experiences with initial, relapse, and survivorship care using in-depth interviews. Aims 1 and 2 leverage a novel linkage of two comprehensive databases: the Patient-Centered Outcomes Research Network (providing longitudinal patient-level electronic health record and administrative claims data) and the Center for International Blood and Marrow Transplantation Research (providing SCT data). For Aim 3, a minimum of 90 semi-structured, in-depth interviews of HL survivors and caregivers enriched in minority and insurance type representation will be conducted to understand SDM for patients and caregivers through their lived experiences.

Results For Aims 1 and 2, a cohort ≥ 26,000 patients diagnosed 2010-2024, representative of the US by race, ethnicity, social factors, and age will be evaluated for differences in (i) treatment and (ii) survivorship care. For Aim 3, 90 semi-structured interviews with survivors and caregivers will provide necessary information to understand gaps in SDM across the cancer continuum.

Conclusion At the completion of this mixed-methods study, we will move the field forward by defining targetable areas for intervention and inform policy to reduce survival disparities for minoritized HL survivors.

P-01-13 Late sequelae of Hodgkin Lymphoma treatment in Polish childhood cancer survivors.

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Introduction Survivorship of childhood cancer has become a crucial aspect of long-term healthcare. Hodgkin lymphoma (HL) is a highly curable cancer, with a survival rate of approximately 90 %, which largely depends on the stage of the disease at the time of diagnosis. However, treatments administered during childhood are associated with an increased risk of long-term complications. In this multicenter study, we assessed the frequency of late effects in a group of Polish survivors of childhood HL.

Methods The study group included 390 childhood cancer survivors (CCS) (female—159; male—231) treated for HL in Poland between 1987 and 2017. Participants were selected from the Polish National Childhood Cancer Survivors Database (n = 2244).The mean age at diagnosis was 12.54 ± 4.10 years, and the follow-up was 18.17 ± 3.63 years. All patients were treated according to international protocols approved by the Polish Pediatric Leukemia and Lymphoma Group.

Results Normal function of all organs was presented by 220 (56.4 %) participants. Abnormalities in one organ or system were developed by 24 (6.2 %) children, in two organs or systems by 34 (8.7 %), in three organs or systems by 31 (7.9 %), and at least four by 81 (20.8 %) participants of the study. In the entire study group, the most frequent (> 15 % of cases) dysfunctions concerned the following organs/systems: skin (22.8 %), circulatory (17.7 %), thyroid (16.9 %), immune (15.9 %).

In comparison to the stage of the disease at diagnosis, HL survivors treated for stage III or IV had a higher incidence of thyroid gland dysfunction (p = 0.022)

than those treated for stage I or II. Participants who experienced a recurrence of the disease showed a higher incidence of gastrointestinal (p = 0.006), respiratory (p = 0.048), and immune (p = 0.005) system abnormalities. Among subjects with longer follow-up (> 5 years), more frequent thyroid gland (p = 0.035) and musculoskeletal system (p = 0.012) dysfunctions were observed. In participants who received radiotherapy, a greater prevalence of vision deterioration was noted (p = 0.031). Moreover, subjects who underwent bone marrow transplantation presented a higher incidence of gastrointestinal (p = 0.008) and immune system (p = 0.004) abnormalities.

Conclusion The incidence of late effects following HL treatment is high, and most patients experience more than one complication. This study confirms the need for continuous monitoring and long-term care of childhood cancer survivors of HL.

P-01-14 Second neoplasms after treatment of Hodgkin lymphoma in young adult patients – Slovenian results from the long-term follow-up clinic at the Institute of Oncology Ljubljana

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Introduction A long-term follow-up clinic for childhood and adolescent cancer survivors in Slovenia was established in 1986. In the year 2007, we also included young adult cancer survivors. Hodgkin lymphoma has high survival rates, though aggressive treatment in the past had a high level of toxicity. The first reports about second neoplasms after oncological treatment were published as early as the 1970s.

Methods We analyzed the data from all patients treated in Slovenia for Hodgkin lymphoma between 1983 and 2010, who were young adults at the time of diagnosis, up to the age of 30. Data were collected from the Slovenian Cancer registry and patients' health records. We performed a Kaplan-Meier survival analysis to estimate the cumulative probability of developing a second neoplasm following treatment for Hodgkin lymphoma.

Results Data from 413 patients were analyzed. Second neoplasms were identified in 79 patients (19 %), and seven patients had multiple neoplasms. The most common were skin malignancies, followed by breast and thyroid cancers. Hematolymphoid neoplasms were found in 10 patients, and mesenchymal tumors were found in 3. Five patients had gastrointestinal/hepatobiliary cancer, and six patients had lung carcinoma. Urinary tract tumors were found in 3 patients, and gynecological neoplasms were found in 11 patients. The complete list is presented in Table 1. Kaplan-Meier analysis to estimate the cumulative incidence of second malignant neoplasms in our patient cohort is shown in. We acknowledge that not all second neoplasms are treatment related [1, 2].

Conclusion With the centralized treatment of Hodgkin Lymphoma in Ljubljana, a centralized long-term follow-up clinic, and the established Slovenian Cancer registry, we were able to perform a population-based analysis of data on second malignant neoplasm in young adult Hodgkin Lymphoma survivors. It shows the second neoplasm burden and helps guide additional research on survivorship care and screening plans. Survival of primary disease should not be our only concern, as patients are now long-term survivors, and we should be taking care of the long-term side effects of cancer treatment. Our analysis also has its limitations. Death without a second malignancy is a potential competing risk; while Kaplan-Meier provides a useful estimate, it may overestimate the true cumulative incidence in such settings. Furthermore, treatment plans are evolving and becoming less toxic, and side effects differ from older ones.

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P-01-15 Response-Adapted Omission of Radiotherapy in Pediatric Patients with Intermediate- and High-Risk Hodgkin Lymphoma Treated per EuroNet-PHL-C1: A Single Institution Analysis of Outcomes and Patterns of Failure

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Introduction EuroNet-PHL-C1 demonstrated that 40 % of intermediate- and high-risk pediatric Hodgkin lymphoma (HL) patients treated with OEPA-COPDAC chemotherapy achieved adequate response (AR) at early response assessment (ERA), and thus were able to omit radiotherapy (RT). Patterns of failure with this treatment paradigm, and specifically, whether or not all initial sites of disease require RT for those with inadequate response (IR) at ERA are unknown. The purpose of our study is to examine outcomes and patterns of failure for those treated per EuroNet-PHL-C1 at a single institution. We hypothesized that limiting RT to only sites of IR at ERA does not result in increased failures.

Methods Pediatric patients with intermediate- and high-risk classical HL treated at a single institution in Texas per EuroNet-PHL-C1 between 2015 and 2021 were included in this IRB approved retrospective study. Patients were treated per protocol with radiation omitted for those with AR (Deauville 1-2 and > 75 % tumor shrinkage) at ERA (PET after 2 cycles of chemo). For those with IR who required RT, only sites of IR (Deauville 3-5) at ERA were treated using involved site radiation treatment (ISRT), instead of all initial sites of disease as on EuroNet-PHL-C1. Outcomes including overall survival (OS) and progression free survival (PFS) were calculated using Kaplan-Meier curves and patterns of failure were classified as either initial site only, new site only, or initial and new sites.

Results 35 patients were identified, of which 33 had evaluable follow up with median follow up of 33 months. The median age at diagnosis was 14 years, 48 % were female. Only 7 (21 %) had IR at ERA and thus required RT. In the group who received RT, 4/7 (57 %) had initial B-symptoms and 4/7 (57 %) had initial bulky disease, compared to 9/26 (35 %) and 20/26 (77 %), respectively, in those who did not receive RT. For the entire cohort, 2-year PFS and OS were 91 % and 100 %, respectively. For those who had RT, 2-year PFS was 83 % compared to 92 % in those who did not need RT. There were a total of 3 relapses (9 %) at last follow up with 1/7 (14 %) in those who had RT vs. 2/26 (8 %) in those without RT.

Conclusion At a single institution, the majority of patients treated per EuroNet-PHL-C1 avoided RT with excellent outcomes. For those requiring RT, limiting RT to only sites of IR at ERA does not appear to adversely affect outcomes, though analysis is limited by the low number of failures.

P-01-16 Pretreatment Serum Cytokine and PD-1 Profiles Predict Relapse Risk in Pediatric Hodgkin Lymphoma: A Retrospective Analysis of Seven Cases

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Introduction In pediatric Hodgkin lymphoma, risk stratification based on pretreatment biomarkers may refine individualized therapy beyond conventional stage and histology. We investigated whether pretreatment serum levels of IL-10, TARC, and PD-1 correlate with relapse risk and survival outcomes.

Methods We retrospectively analyzed seven children (age 5–20 years, median 12) diagnosed with Hodgkin lymphoma between 2014 and 2024, all of whom had stored pretreatment serum samples. One patient received an ABVD-based regimen; the other six were treated according to GPOH-HD protocols. Cases were classified as high-risk (n = 2) or low-risk (n = 5). Three patients relapsed (including one fatality), and four remained in sustained remission. Serum IL-10 and TARC were quantified by Luminex multiplex assay and PD-1 by ELISA. Group means were compared using one-tailed Mann–Whitney U tests (exact), supplemented by permutation p-values, bootstrap 95 % confidence intervals (CI) for mean differences, and effect sizes (Cliff's δ).

Results Mean IL-10 was 18 pg/mL in the relapse group versus 3 pg/mL in the remission group ($p \approx 0.11$; bootstrap 95 % CI 0.11–29.55; Cliff's $\delta = 0.67$). Mean TARC was 28,900 pg/mL versus 203 pg/mL ($p \approx 0.12$; CI excludes 0; $\delta = 0.75$). Mean PD-1 was 220 pg/mL versus 74 pg/mL ($p \approx 0.14$; CI 30–270 pg/mL; $\delta = 0.67$). Although permutation tests did not reach conventional significance, all bootstrap CIs excluded zero and effect sizes were large, supporting true group differences [1–3].

Conclusion Pretreatment elevations of IL-10, TARC, and PD-1 are associated with relapse and poor outcome in pediatric Hodgkin lymphoma. Particularly, high PD-1 distinguished all relapsed cases. These biomarkers warrant validation in larger, prospective cohorts to guide risk-adapted therapy.

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P-01-17 Hodgkin Lymphoma-like posttransplant lymphoproliferative disorder after pediatric kidney transplant.

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Introduction Posttransplantation lymphoproliferative disorders (PTLD) are a heterogeneous group of lymphoproliferative lesions that occur in immunosuppressed transplant recipients, including 4 categories: (1) early lesions, (2) polymorphic PTLD, (3) monomorphic PTLD and (4) Hodgkin lymphoma (HL) and HL-like PTLD, this last group is the least common and the few treatment recommendations are directed at conventional chemotherapy for HL. The current available literature data indicate the presence of important immunophenotypic and clinical differences between HL PTLD and HL-like PTLD, suggesting that HL-like PTLD is in fact most often a form of B-cell PTLD.

Methods Case report and systematic review of the literature.

Results A 19-year-old woman with a renal transplant at age 13 due to focal segmental glomerulosclerosis and ulcerative colitis diagnosed at 16 y.o, managed with tacrolimus, azathioprine, and prednisone. Six years post-transplant, she developed Hodgkin-like PTLD, the aypical cells where CD30 + and co-expressing CD20, CD79, PAX5, were negative for CD15 and EBV. The disease involved nodal regions above and below the diaphragm, with rapid growth. She was treated with Brentuximab vedotin (BV) and rituximab, adjusted for renal function. After 2 doses of Brentuximab and 4 of rituximab, she achieved complete morphological remission and an excellent partial metabolic response. Four more doses of Brentuximab are planned.

Conclusion Although HL-like PTLD has been grouped with classic HL PTLD, controversy remains as to whether it is truly a form of HL or whether it should be more appropriately considered as a form of B-cell PTLD benefiting from less toxic therapies including monoclonal antibodies as first-line of treatment [1–3].

References

[1] Posttransplantation lymphoproliferative disorders (PTLD) are a heterogeneous group of lymphoproliferative lesions that occur in immunosuppressed transplant recipients, including 4 categories: (1) early lesions, (2) polymorphic PTLD, (3) monomorphic PTLD and (4) Hodgkin lymphoma (HL) and HL-like PTLD, this last group is the least common and the few treatment recommendations are directed at conventional chemotherapy for HL.(Semakuka, B., 2006) (Sean D Pitman 2006)

[2] The current available literature data indicate the presence of important immunophenotypic and clinical differences between HL PTLD and HL-like PTLD, suggesting that HL-like PTLD is in fact most often a form of B-cell PTLD(Krishnamurthy, S., 2010)

[3] Conclusions: Although HL-like PTLD has been grouped with classic HL PTLD, controversy remains as to whether it is truly a form of HL or whether it should be more appropriately considered as a form of B-cell PTLD benefiting from less toxic therapies including monoclonal antibodies as first-line of treatment.(Twist, C.J., 2019)(Johanna Kampers 2017)(Rosanna Fulchiero2022)

P-01-18 EBV encoded miRNAs fascilitating immune evasion in Hodgkin lymphoma

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Introduction Epstein–Barr virus (EBV) constitutes a very common pathogen and is implicated in multiple malignancies including Hodgkin lymphoma (HL), a malignancy which mainly affects adolescents and young adults. Latent EBV infection includes distinct gene expression patterns (I, IIa, IIb and III), each associated with different EBV-associated malignancies. Latency IIa, which is associated with HL, is characterized by the expression of latent membrane proteins 1 and 2A (LMP1and LMP2A), Epstein-Barr nuclear antigen 1 (EBNA1) and the expression of EBV encoded RNAs (EBER RNAs) and BamHI A rightward transcript (BART) microRNAs (miRNAs). MiRNAs play a significant role in the maintenance of the few neoplastic cells by facilitating escape from anti-tumor immune control.

Methods We conducted a literature search and provide an overview of the role of miRNAs in immune evasion in HL [1–10].

Results Several viral miRNAs target pattern-recognition receptors, namely Retinoic Acid-Inducible Gene I (RIG-1) and NLR Family Pyrin Domain Containing 3 (NLRP3), interfere with interferon (IFN) and other proinflammatory cytokine-mediated signaling including IL-1α, IL-1β and IL-6, as well as block the recognition of malignant cells by natural killer cells. Regarding adaptive immunity, EBV miRNAs 1) target LMP1 and limit its expression and therefore the antigenic stimulus, 2) interfere with the release of proinflammatory cytokines and thus with the differentiation of CD4 + to Th1 T-cells, and finally 3) hinder peptide transport and loading to major histocompatibility complex (MHC) class I molecules while at the same time targeting lysosomal enzymes involved in antigen processing and MHC class II mediated presentation. MiRNAs also take

advantage of the immunosuppressant effect of immune checkpoints, specifically by finetuning the LMP1-associated induction of Programmed Cell Death 1 Ligand 1 (PD-L1).

Conclusion Novel immunotherapies have revolutionized the field of oncology initially by offering effective treatment approaches for relapsed/refractory cases and are gradually being used as first or second line regimens. miRNAs have recently emerged not only as valuable biomarkers but also as therapeutic targets. We therefore propose the quantification of the expression levels of these immune related miRNAs, which could serve as prognostic biomarkers in children and adolescents with HL.

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P-01-19 Post-transplant lymphoproliferative disease type Hodgkin lymphoma: limiting toxicity while maximizing efficacy with personalized treatment approach in a rare entity. Experience in a case series.

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Introduction Post-transplant lymphoproliferative disorder (PTLD) is a heterogeneous group of lymphoproliferative diseases that occur following immunosuppression in patients treated with solid organ or bone marrow transplantation, often related to infection by Epstein-Barr virus (EBV).

According to the most recent World Health Organization classification, the following histologic subtypes are distinguished: 1) hyperplastic lesions, 2) polymorphic lymphoproliferative disorders, and 3) lymphomas. Rare are PTLD-Hodgkin lymphoma (LH) forms (16 % of PTLDs), classical Hodgkin type (histologically CD30 + CD20-) or Hodgkin-like (CD30 ± ; CD20 +). Classical chemotherapy and radiation therapy regimens have been used as treatment, albeit with frequent dose reductions for high toxicity, in some cases life-threatening [1, 2]. Extremely rare and limited to adult patients is the experience with immunotherapy, such as the monoclonal antibody brentuximab vedotin anti-CD30 conjugate with monomethyl auristatin A (BV).

Methods We report the experience of 2 centers from the Italian Pediatric Hematology and Oncology Association (AIEOP) on 4 pediatric cases of PTLD-LH treated with BV ± chemotherapy.

Results Patients were 2 males and 2 females, of 10, 13, 17, and 20 years old, in which PTLD arose at 4, 8, 2, and 5 yrs after kidney (3 patients) or heart (1 patient) transplantation, presented classic PTLD-LH, stage IIA, IIB one patient each and IIIB 2 patients, with mean EBV viremia of 53138 gv/ml (range 749-178797gv/ml). Patients were treated with reduction of immunosuppressive therapy + BV as monotherapy (1 case) or BV associated with chemotherapy according to AVD scheme (doxorubicin, vinblastine, deticene) (3 cases). Treatment changes were required in 2 patients: in 1 case liposomal doxorubicin was used and in 1 case omission of multiple doses of chemotherapy with radiotherapy on residual sites (25.5 Gy right supraclavicular reg). Patients achieved complete remission of disease (mean FUP of 15.5 months).

Conclusion Treatment of PTLD-LH requires an individualized and patient-calibrated treatment approach to spare toxicity and preserve the function of the transplanted organ. In our experience, we aimed at modulating treatment to the patients' comorbidities and toxicities to optimize efficacy. Immunotherapy was well tolerated, achieving adequate remission of disease.

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S-05 | Translational Biology

Chairs: Sylvia Hartmann (Essen, Germany), Wolfram Klapper (Kiel, Germany)

S-05-01 Molecular biology of Hodgkin lymphoma

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Introduction The biology of Hodgkin lymphoma is still enigmatic in many aspects (Küppers, 2025). A special situation are composite lymphomas, which often are represented by a Hodgkin lymphoma and another B cell lymphoma in the same patient. In such cases, it is highly interesting to clarify whether the combined lymphomas have a comon origin or derive from independent B cells.

Methods To gain further insights into the molecular pathogenesis of classic Hodgkin lymphoma, we are performing a whole exome sequencing (WES) and whole genome sequencing (WGS) study of isolated Hodgkin and Reed-Sternberg cells from 27 cases of classic Hodgkin lymphoma. We also studied four cases of composite lymphomas by WES of microdissected lymphoma cells.

Results The WES and WGS studies of the classic Hodgkin lymphomas confirmed many known recurrent genetic alterations, but revealed also previously unrecognized recurrent gene mutations. An overview of this study will be provided. The molecular analysis of the composite lymphomas revealed patterns of the stepwise transformation process in such lymphomas (Berg et al., 2025).

Conclusion The genetic analysis of Hodgkin and Reed-Sternberg cells and of composite lymphomas revealed numerous novel insights into the complex transformation process of classic Hodgkin lymphoma [1, 2].

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S-05-02 Translation of Genomic Findings in Pediatric cHL

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Classic Hodgkin lymphoma (cHL) is defined by rare malignant Hodgkin and Reed-Sternberg (HRS) cells within an immune-rich tumor microenvironment (TME). Advances in single-cell sequencing, spatial imaging, and HRS purification now permit detailed genomic and microenvironmental profiling, revealing age-related differences that distinguish cHL in children, adolescents, and young adults (CAYAs). Genome-wide studies show recurrent alterations in JAK/STAT and NF-κB regulators (SOCS1, TNFAIP3, STAT6), immune evasion genes (B2M, CIITA), and 9p24.1 amplification driving PD-L1/PD-L2. Pediatric and AYA patients exhibit an accelerated rate of mutations, higher mutational burden, and a distinct TME compared with older adults. Transcriptomic profiling of cHL has demonstrated features that are distinct from non-Hodkin lymphoma including an unfolded protein response, escape from NK-cell recognition, and profound B-cell program disruption and cytoskeletal remodeling. Circulating tumor DNA (ctDNA) may capture some of these features and provides a noninvasive marker of residual disease. Here we will present emerging data on the cHL genome, transcriptome, and TME with a focus on how this may help guide precision biomarkers and identify novel therapeutic targets for CAYAs with cHL.

S-05-03 Insights into the tumor microenvironment of Hodgkin lymphoma by single cell analysis

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The tumor microenvironment of lymphoma reflects the complex interaction of malignant and non-malignant cells co-developing as cellular ecosystems in various anatomical niches. Understanding the composition and function of these ecosystems is critical for improved molecular taxonomies of lymphomas and development of immunotherapies that can ideally be deployed with precision. Modern technologies, enabling measurements of cellular ecosystems at single cell resolution, have catalyzed research efforts that describe compositional heterogeneity of tumor microenvironments and cellular crosstalk mechanisms in defined lymphoma entities. In this invited presentation, Dr. Steidl will present an integrative, multilayered characterization of cellular ecosystems in classic Hodgkin lymphoma as a framework for molecularly defined disease classifications. The comprehensive genomic and spatially resolved profiling revealed paradigmatic links between somatic gene mutations, and TME composition and function paving the way for therapeutic interventions interfering with oncogenic signaling and cellular ecosystems in lymphoma.

S-05-04 Epigenetic Age Acceleration Before and After Treatment for Young Adult Hodgkin Lymphoma: A Pilot Study from URCC10055

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Introduction Decades after treatment, survivors of Hodgkin lymphoma (HL) exhibit accelerated epigenetic aging compared to age-matched controls. However, the temporal onset of this acceleration remains unclear. To address this gap, we assessed epigenetic aging before and after chemotherapy treatment for HL.

Methods 51 patients with HL and 49 age- and sex-matched controls provided peripheral blood pre- and post-chemotherapy. Luminex multiplex assayed inflammatory markers. DNA methylation data from Illumina EPIC V2 Arrays were used to generate Horvath, Hannum, and PhenoAge epigenetic clocks. Epigenetic age acceleration (EAA) was derived by calculating the residual from regressing epigenetic age against age at blood draw. Linear regression examined mean EAA differences between survivors and controls at each time point adjusting for sex. Analyses were stratified by age < 40 (n = 27 HL and 27 controls). Spearman correlations examined associations between EAA and inflammatory biomarkers.

Results Most patients were treated with ABVD chemotherapy (87 %); 46 % were stage III/IV. Prior to any therapy for HL, patients exhibited significant EAA versus controls. HL patients experienced, on average, 7.25 more years of DNAmPhenoAge EAA (B[95 %CI] 7.25[4.40, 10.11]; p < 0.001) and 3.75 more years of Hannum EAA compared to controls (B = 3.75 [1.69, 5.82]; p < 0.001). HL did not experience a significant change in EAA from pre- to post-chemotherapy. Differences in EAA between HL and controls were more pronounced among < 40 years for Horvath and Hannum clocks.

Those with classical HL (n = 37) had a higher mean PhenoAge EAA compared to those with mixed cellularity (n = 7) or lymphocyte predominant (n = 3; mean[SD] 4.4[6.8] vs 1.3 [7.8] vs -1.5[0.7]). Those with stage 3/4 classical HL had higher PhenoAge EAA (3.4 [5.8] vs 2.6 [6.9]). Those that received RCHOP had greater PhenoAge EAA post-treatment (3.9[15.7] vs ABVD 2.4[9.5]). Among HL patients, pre-treatment, hsCRP, TNF-R1, S100b, and Glutathione were significantly correlated with higher PhenoAge EAA while TNFR1 and S100b were correlated with higher Horvath and Hannum EAA (p's < 0.05). Post-Treatment, S100b and TNFRI correlated with higher PhenoAge and Horvath EAA (p's < 0.05).

Conclusion Patients with HL experience EAA prior to treatment potentially linked to disease type, burden, inflammation, or genetics. Future research is needed to validate these findings and understand their trajectory into survivorship.

S-05-05 Towards characterization of the DNA methylome of classic Hodgkin lymphoma

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Introduction DNA methylation, where cytosines typically in CpG sites gain a methyl group, can affect gene expression, particularly when in regulatory elements. Thus, it serves as marker for cell lineage and differentiation, adds to the understanding of the pathogenesis and is a cancer biomarker. Over a decade ago, low resolution DNA methylation profiling proved a correlation between loss of B-cell identity in classic Hodgkin lymphoma (cHL) and altered DNA methylation. We initiated studies on genome-wide DNA methylation in cHL and report here first results for widely used cHL cell lines (cHLs).

Methods 10 cHLs, 45 B-cell lymphoma cell lines (BCL) and 110 normal B-cell populations (BC) were screened with HumanMethylation450K and/or EPIC BeadChips. CHLs were analysed for differentially methylated CpGs (DMCs) compared to BCL and BC (FDR ≤ 0.001, Δβmean ≥ 0.4), and between cHLs of B- and T-cell origin (FDR < 0.05). DMC-validation was realised by Oxford Nanopore (ONT) sequencing of 6 cHLs and 10 BCL. An EBV-classifier, derived from the analysis of Burkitt lymphoma (BL; Glaser et al., 2025) was applied. With strand-specific mRNA sequencing of 8 cHLs and 22 BCL (Illumina NovaSeq PE150), differentially expressed genes (DEGs) were identified (FDR < 0.05, |log-2FC| > 1).

Results We identified 4,493 hyper- and 264 hypomethylated DMCs in cHLs, compared to BCL and BC. ONT sequencing verified 79-90 % of DMCs, with cHLs hypermethylation enriched in promoters. The 2,966 DEGs in cHL compared to BCL were linked to mechanisms of B-cell activity, extracellular matrix structures and cell migration properties. A total of 34.9 % array-identified hypermethylated DMCs were associated with DEGs downregulated in cHLs, affecting transcription start sites in 18.3 %. Comparing cHLs derived from B- vs. T-cells, the 207 DMCs were remarkably not enriched for B- or T-cell developmental or differentiating genes. Using a set of DMCs in EBV positive vs negative BL, all cHLs clustered with EBV-positive BL, independent of their EBV status.

Conclusion Differential DNA methylation in cHLs is characterized by a strong hypermethylation at promoter regions, compared to BCL and BC. Gene expression differences in cHLs can be linked to this and likely contribute to B-cell identity loss and other cHL characteristics. The presence of a DNA methylation signature characteristic for EBV positive vs EBV negative BL further fosters speculation on a hit-and-run mechanism for EBV in cHL.

S-05-06 Expression of HLA on Hodgkin-Reed-Sternberg Cells and B-cells in the microenvironment of pediatric and adolescent classical Hodgkin Lymphoma

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Introduction Expression of HLA-molecules on Hodgkin-Reed-Sternberg-cells (HRSC) is lost in a considerable number of classical Hodgkin Lymphoma (HL) (Nijland et al., 2017). We have previously demonstrated that HLA-expression on HRSC is associated with the composition of the tumor microenvironment independent of EBV (Müller-Meinhard et al., 2024). However, the afore-mentioned studies have been conducted in adult patients only. Similarly, the content of benign B-cells in the tumor microenvironment is one the best established prognostic bio-markers in adult HL (Grund et al., 2023, Jachimowicz et al., 2020).

Methods We analyzed biopsies obtained at the time of diagnosis of patients treated in the EuroNet-PHL-C1 trial (Mauz-Körholz et al., 2023). To identify an association with aggressiveness of the disease, we correlated with the early response to chemotherapy after the second cycle of OEPA defined as adequate response (AR) and inadequate response (IR) (Mauz-Körholz et al., 2023). HLA on HRSC was evaluated by visual inspection for b2M (HLA-I) and HLA-DR (HLA-II), respectively. B-cell content in the tumnor microenvironment (TME) was analyzed on digitalized whole slide images (WSI) stained for CD20 using QPath software.

Results EBV was present in HRSC in 10/39 (25 %) of cases with complete information. EBV was detected equally in lymphomas with AR and IR, respectively. Expression of HLA-I was detectable on HRSC in 20/50 (40 %) cases which is substantially higher than in adult patients in Germany (11 %)(Reinke et al., 2020, Müller-Meinhard et al., 2024). Expression of HLA-II was detected at similar frequencies in the current pediatric/adolescent cohort (27/56, 48 %) and adult patients (56 %)(Müller-Meinhard et al., 2024), respectively. Interestingly, expression of HLA-I was less frequent in lymphomas with AR (7/23, 30 %) compared to lymphomas with IR (9/19, 47 %) but the difference was not statistically significant. As expected, B-cell content in the TME was highly variable (mean 29.6 % of all cells of the TME). However, in this small cohort B-cell content in the TME was not different between lymphomas with AR and IR (29 %, n = 9 and 33 %, n = 10, respectively).

Conclusion This preliminary analysis suggests that the associations between HLA expression of HRSC, composition of the TME and response to therapy described in adults may differ in pediatric/adolescent patients.

S-05-07 Targeting immune evasion mediated by LOX-1$^+$ neutrophils in Hodgkin Lymphoma via nanobodies antagonistic for CD39 enzymatic activity

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Introduction Hodgkin Lymphoma is one of the most common malignancies in children and adolescent and a classic example of tumour-mediated immune evasion. Here, we interrogated the role of neutrophilic granulocytes in Hodgkin Lymphoma

Methods We combined clinical data analysis, in vitro functional assays, flow cytometry, and transcriptomic profiling to investigate the systemic role and immunomodulatory potential of neutrophils in pediatric Hodgkin Lymphoma.

Results We observed pronounced dysregulation at initial diagnosis, including elevated absolute neutrophil counts and significantly increased initial neutrophil to lymphocyte ratio in those with relapse. Further, we identified dysregulation of neutrophil-related cytokines in pediatric Hodgkin Lymphoma patients,

implicating neutrophils in disease progression. In vitro exposure of healthy neutrophils to HL cell line supernatants induced morphological and phenotypic changes, including upregulation of LOX-1, a marker of immunosuppressive neutrophils. Functionally, these HL-primed neutrophils suppressed T-cell proliferation and cytokine secretion. Transcriptomic profiling confirmed a distinct program in HL-primed neutrophils, with upregulated genes related to ROS generation and innate immunity. Immunosuppression was partially reversed by ROS inhibition and substantially reversed by a biparatopic nanobody targeting CD39 enzymatic activity, identifying extracellular ATP degradation as a key suppressive mechanism. While neutrophils were scarce in tumour tissues, patient-derived serum induced similar immunosuppressive phenotypes in healthy neutrophils, confirming systemic modulatory effects.

Conclusion These findings reveal that neutrophils are reprogrammed by HL to support immune evasion on a systemic level with CD39 as potential therapeutic target.

S-06 | Novel Therapeutics & Cellular Therapies

Chairs: Matthias Braun (Giessen, Germany), Marius Rohde (Giessen, Germany)

S-06-01 Antigen-specific/TCR-based T cell Therapies for Lymphoma

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Immunotherapy with antigen-specific/TCR-based T cells is a promising, targeted therapeutic option for patients with lymphoma including for immunocompromised patients with post transplant lymphoproliferative disease. In this presentation, we will evaluate the various antigen specific /TCR- based T cell products that target viral and non-viral tumor-associated antigens specific for lymphoma. During this presentation we will discuss: (1) the different methodologies to expand virus-specific T cell and non-viral tumor-associated antigen-specific T cell products and (2) an overview of the immunological principles involved when developing such manufacturing protocols, and (3) the next generation T cell therapies including combining with gene engineering. Ex vivo expanded antigen-specific cells have now been safely administered to treat over 1000 patients with virus and non-virus -associated lymphomas. Hence, we will provide a comprehensive review of the clinical trial results evaluating the safety, feasibility, and efficacy of these products in the clinic. In summary, this presentation seeks to provide new insights regarding antigen-specific T cell technology to benefit a rapidly expanding T cell therapy field for lymphomas.

S-06-02 CAR-T Cells in Hodgkin Lymphoma

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CAR-T cell therapy has transformed the treatment landscape for several hematologic malignancies, and its application in Hodgkin lymphoma (HL) is an area of growing interest. Despite the unique challenges posed by HL's immunosuppressive tumor microenvironment (TME), adoptive cell therapies targeting HL-specific antigens have shown promise. Among these, CD30-directed CAR-T cells have demonstrated encouraging antitumor activity in patients with relapsed or refractory (r/r) disease, including those who have failed standard treatments such as chemotherapy, brentuximab vedotin, and checkpoint inhibitors.

However, while initial responses to CD30 CAR-T therapy can be robust, durable remissions remain limited, likely due to poor T cell persistence within the hostile TME. Strategies aimed at improving CAR-T cell efficacy in HL by shifting the local immune balance toward effector activity will be discussed. In particular, the presentation will focus on enhancing CAR-T cell trafficking to the tumor, based on the rationale that increased infiltration into the TME may improve the likelihood of tumor elimination before suppressive mechanisms prevail.

The presentation will highlight the rationale, design, and early outcomes of an ongoing clinical trial testing a modified CAR-T product with enhanced tumor homing, alongside biomarker-based response monitoring. Insights from this study will inform the design of future CAR-T cell therapies and broader efforts to overcome immunosuppressive barriers in HL and related malignancies.

S-06-03 NK Cell Engagers in Hodgkin Lymphoma

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There remains a significant unmet need for effective therapies in patients with classical Hodgkin lymphoma (HL) whose disease is refractory to both brentuximab vedotin and checkpoint inhibitors. Hodgkin Reed-Sternberg (HRS) cells universally express CD30, making it a compelling therapeutic target. AFM13 is a bispecific antibody designed to engage CD30 on HRS cells and CD16A on natural killer (NK) cells, thereby directing NK cell-mediated cytotoxicity against the tumor.

However, AFM13 demonstrated limited efficacy as a monotherapy in relapsed/refractory HL, likely due to the immunosuppressive tumor microenvironment and a deficiency of functional NK cells in these patients. To address this, combination strategies have been explored – particularly the use of AFM13 with off-the-shelf allogeneic NK cell therapies – to overcome resistance associated with impaired endogenous NK cell function.

Clinical studies combining AFM13 with allogeneic NK cells have shown encouraging results, including high response rates and a favorable safety profile in heavily pretreated relapsed/refractory HL patients. This presentation will review the rationale for NK cell engagers in HL, highlight emerging clinical data—including findings from the LuminICE trial, and discuss future directions and potential applications of this promising therapeutic approach.

S-06-04 Tumor-Specific Immune Responses and Biomarkers in pediatric High-Risk Hodgkin Lymphoma Patients

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Introduction Integrating immunotherapy into pediatric classical Hodgkin lymphoma (cHL) requires understanding treatment-driven immune responses and predictive biomarkers. The Children's Oncology Group AHOD1331 trial (NCT02166463) randomized patients (ages 2–21) with newly diagnosed high-risk cHL to receive either standard ABVE-PC chemotherapy or brentuximab vedotin (Bv) + AVE-PC with response-adapted radiation. We evaluated peripheral blood T cell responses and soluble immune markers—including sCD30, sCD163, and TARC—in relation to event-free survival (EFS). Our goals were to (i) assess whether Bv enhanced tumor antigen-specific T cell recognition and (ii) identify potential biomarkers of treatment response.

Methods Peripheral blood was collected at diagnosis and post-treatment. Plasma and PBMCs were isolated for batch testing of cytokines (Th1/Th2), sCD30, sCD163, and TARC via Luminex. T cell responses to tumor-associated antigens (PRAME, MAGEA4, survivin) were measured using IFN-γ ELISPOT after ex vivo expansion. T cell specificity was reported as spot-forming cells (SFC/10^5 T cells). Statistical analyses included paired Wilcoxon signed-rank tests and Cox proportional hazards models.

Results Among 216 patients analyzed (from 587 enrolled), 184 had paired cytokine data, 147 had sCD30/sCD163, 146 had TARC, and 71 had T cell response data. Proinflammatory cytokines (IFN-γ, IL-17a, MCP-1) significantly increased post-treatment; immunosuppressive IL-13 decreased. sCD30, sCD163, and TARC levels were significantly lower post-treatment ($p < 0.0001$) in both arms. Lower pre-treatment sCD30 correlated with fewer EFS events across both arms with non-linear effect (Figure 2). T cell responses to PRAME significantly increased post-treatment ($p = 0.04$).

Conclusion Treatment increased T cell responses to PRAME and reduced immunosuppressive cytokines, indicating an immune environment favorable to T cell activation. Although cytokine shifts were similar across arms, our findings support further studies of immune biomarkers and tumor antigen-specific T cells to optimize immunotherapy strategies in cHL.

S-06-05 Age- and Sex-Related Treatment Response in Pediatric/Adolescent Hodgkin Lymphoma: Insights from the EuroNet-PHL-C2 Italian Cohort

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Introduction This study investigates the influence of sex and age on treatment response in pediatric Hodgkin lymphoma (HL) patients enrolled in the EuroNet-PHL-C2 trial, integrating clinical, metabolic, and immunoprofiling data.

Methods In this prospective multicenter study, 68 HL patients treated across 35 Italian AIEOP centers (2018–2020) were analyzed. FDG-PET was performed at baseline (PET0), after two chemotherapy cycles (early response assessment, ERA), and post-chemotherapy (late response assessment, LRA). Responses were classified as Adequate (AR; Deauville 1–3) or Inadequate (IR; Deauville 4–5). Baseline PET parameters (SUVmax, SUVmean, TMTV, TLG) were available for 50 patients. Event-free survival (EFS) was evaluated by age and sex. Tumor mRNA expression of 678 immune-related genes (NanoString) was analyzed in diagnostic samples.

Results The cohort included 37 males (54.4 %) and 53 patients aged > 12 years (77.9 %). Disease stages: TL1 (5.9 %), TL2 (29.4 %), TL3 (64.7 %). AR rates were 51.5 % (ERA) and 29.4 % (LRA). Older age correlated with higher IR risk, particularly in males (IR increase: 10 % → 35 %) vs. females (3 % → 12 %). LASSO regression identified 14 immune-related genes (e.g., IL22RA1, $p = 0.019$) as potential IR predictors at LRA, adjusted for sex and age, with pathway analysis linking them to inflammatory/chemokine signaling. A significant association was found between PET SUVmean and IL22RA1 expression in IR patients ($p = 0.03$).

Conclusion Age and sex significantly impact late metabolic response in pediatric HL, with older males at highest risk of poor outcomes. IL22RA1 emerges as a predictive biomarker, highlighting the role of tumor immune microenvironment and inflammation in treatment resistance.

S-06-06 Impaired T Cell Immunity in Children and Adolescents with Hodgkin Lymphoma (HL)

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Introduction HL contains only 1 % of characteristic Hodgkin-Sternberg-Reed cells, while other immune cells make up most of the microenvironment [1]. With a favorable prognosis after standard radio-chemotherapy, late effects are a major concern for aging HL survivors [2].

Methods To better understand disease biology, we examined lymphocyte populations (n = 29 pts) and cytokine levels (n = 22 pts) in the peripheral blood (PB) before (TP1), at six weeks (TP2), three (TP3), and six months (TP4) after treatment using flow cytometry analysis. In addition, global gene expression profiles of purified PB $CD4^+$ and $CD8^+$ T cells from HL patients before and after therapy (n = 9) were compared with those from healthy donors (n = 11) using 3´-mRNA sequencing. All patients were prospectively enrolled in the EuroNet-PHL-C2 trial (clinicaltrials.gov ID NCT02684708) or subsequent registry and treated with a risk-/response-adapted regimen.

Results Our data indicate elevated leukocyte and granulocyte counts in pediatric HL patients at diagnosis, while lymphocyte counts return to pre-therapy levels at TP4. Flow cytometry analysis showed recovery of naïve $CD19^+$ B and a significant decrease in $CD3^+$ T cell counts at TP4 compared to diagnosis, with notably lower numbers of naïve and Th9 $CD4^+$ T cells ($p = 0.02$). These findings may highlight a predominant role of inactive $CD4^+$ T cells in pediatric HL and suggest their effective elimination by treatment. While plasma cytokine levels were reduced at diagnosis, significantly higher levels of GM-CSF, IL10, IL17A, TNFα, MCP1, and perforin were observed at TP4. Gene expression analysis in T cells of newly diagnosed HL patients compared to healthy controls revealed 133 genes significantly downregulated and 44 genes upregulated in $CD8^+$ T cells, as well as 104 genes downregulated and 73 genes upregulated in $CD4^+$ T cells (FDR = 0.05). Of note, downregulated genes were involved in signaling pathways related to immune activation, cytokine response, and receptor signaling.

Conclusion Overall, these data suggest a predominance of naïve $CD4^+$ T cells in the PB of pediatric HL patients at diagnosis, which is linked to lower cytokine levels and gene expression patterns indicating impaired immune activation and cytokine response. This points to a slightly different disease pathology in children compared to adults.

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S-07 | Advances in Radiotherapy

Chairs: Brad Hoppe (Jacksonville, USA),
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S-07-01 Radiation Therapy versus High Dose Chemotherapy and Autologous Stem Cell Transplant Consolidation Treatment in Relapsed Hodgkin Lymphoma

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Historically, high-dose chemotherapy followed by autologous stem cell transplantation (HDT/ASCT) has been the standard consolidative approach for patients with relapsed or refractory Hodgkin lymphoma. However, this intensive strategy carries significant acute and late toxicities, and evolving evidence suggests that select patients—particularly those with favorable biology and excellent response to salvage therapy—may achieve long-term disease control with less intensive approaches.

This session will review and compare consolidative radiotherapy (RT) versus HDT/ASCT in the management of relapsed Hodgkin lymphoma, focusing on emerging risk-adapted strategies from key cooperative group trials. We will examine data from the European EuroNet-PHL studies, the Children's Oncology Group (COG) relapsed Hodgkin lymphoma protocols, and the international collaborative study combining EuroNet, COG, and Bristol Myers Squibb (BMS). Through this discussion, we will explore how disease control rates and toxicity profiles differ between patients treated with RT versus HDT/ASCT, with an emphasis on the increasing recognition that a subset of patients—such as those with low-risk, relapsed disease and excellent response to salvage therapy—can be successfully salvaged with RT alone, avoiding the long-term morbidity of transplant. The session will also highlight how radiation therapy is being strategically used in combination with or instead of transplant in modern trials, and how these data are shaping clinical decision-making and trial design [1–3]. Attendees will gain a clear understanding of evolving risk-adapted paradigms and the rationale for individualized treatment pathways for patients with relapsed Hodgkin lymphoma, particularly those in pediatric, adolescent, and young adult populations.

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S-07-02 Current Radiotherapy Applications for Pediatric and Young Adult Hodgkin Lymphoma: Beyond Involved-Site Radiotherapy

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Radiotherapy for Hodgkin lymphoma has evolved significantly, with target volumes decreasing from historical large fields (e.g., total lymphoid irradiation at 40-50 Gy) to modern, smaller fields (20-30 Gy) due to advancements in systemic therapy and diagnostic imaging, particularly ^{18}F-fluorodeoxyglucose-PET-CT. This reduction has led to decreased toxicity without compromising efficacy. For pediatric patients, contemporary trials like AHOD1331 and cHOD17 have embraced response based PET imaging to inform radiotherapy target volumes, moving beyond traditional involved-site radiotherapy (ISRT) that primarily relies on pre-treatment imaging.

New standardized nomenclature for PET-directed radiotherapy (PDRT) volumes has been developed, which is crucial for trials involving pediatric patients. PDRT specifically targets PET-positive disease. For example, in AHOD1331, pediatric high-risk Hodgkin lymphoma patients with a slow early response received pISRT (PET-directed involved-site radiotherapy) targeting PET-positive lymph node regions. Other PDRT types, such as pRSRT (PET-directed residual-site radiotherapy) and pRPRT (PET-directed residual-PET radiotherapy), are also being used in pediatric and young adult trials (e.g., HLHR13, cHOD17, AHOD2131, ANHL1931, AHOD1822) as boosts or for consolidation/salvage of residual disease. While ISRT remains standard, these nuanced PET-directed approaches allow for more refined targeting and potentially lower doses to healthy tissues, particularly important in the pediatric population.

S-07-03 Combination of novel therapeutics & RT among Hodgkin lymphoma patients

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S-07-04 Multi-modality Artificial Intelligence for Involved-Site Radiation Therapy: Clinical Target Volume Delineation in High-Risk Pediatric Hodgkin Lymphoma

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Introduction Clinical target volume (CTV) delineation for involved-site radiation therapy (ISRT) in Hodgkin lymphoma (HL) is time-consuming due to the need to analyze multi-time-point PET/CT scans co-registered to the planning

CT. Deep learning (DL) has the potential to streamline this task, but its feasibility remains unexplored. Our goal was to develop automated CTV segmentation algorithms that integrated multi-modality imaging to facilitate ISRT planning.

Methods This study included planning CT, baseline PET/CT (PET1), and interim PET/CT (PET2) scans from 288 pediatric patients with high-risk HL in the Children's Oncology Group AHOD 1331 trial. Data from 58 patients across 24 institutions were held out for external testing, while the remaining 230 cases from 95 institutions were used for model development. We investigated three DL architectures (SegResNet, ResUNet, and SwinUNETR) and evaluated the impact of incorporating PET1 and PET2 images alongside the planning CT. Performance was assessed using the 95th percentile Hausdorff distance (HD95) and Dice similarity coefficient (DSC). Inter-observer variability (IOV) was estimated by comparing original institutional CTVs with those newly delineated by four board-certified radiation oncologists on a subset of 10 cases. The quality of CTVs generated by the top-performing model and those from original institutions was independently assessed on 40 other cases by four radiation oncologists, who were blinded to the source of the CTVs.

Results On the external cohort, a SwinUNETR model incorporating planning CT, PET1, and PET2 images achieved the highest performance, with an HD95 of 34.43 mm, and DSC of 0.72. In comparison, the best planning CT-only model attained an HD95 of 58.94 mm and DSC of 0.68. All models incorporating PET/CT images were significantly better ($P < 0.01$) than CT-only models. IOV analysis yielded a DSC of 0.70 and HD95 of 30.14 mm. In clinical evaluation, DL-generated CTVs received a mean quality score of 3.38 out of 5, comparable to physician-delineated CTVs (3.13; $P = 0.13$).

Conclusion This study explored a novel application of DL in radiation oncology by developing algorithms for automated CTV segmentation in ISRT for high-risk pediatric HL. Clinical evaluation showed that the DL model was able to generate clinically useful CTVs with quality comparable to manually delineated CTVs, suggesting its potential to enhance contouring consistency and improve physician efficiency in ISRT planning.

S-07-05 Enhancing Radiotherapy Quality Assurance in Lymphoma: A Rigorous Real-Time Central Review Process in AHOD2131

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Introduction Radiation therapy quality assurance (RTQA) is essential in clinical trials to ensure protocol-compliant treatment. As lymphoma radiotherapy (RT) has evolved to use smaller volumes and more conformal techniques, treatment planning has become increasingly complex, requiring a rigorous RTQA process. We report early experiences with centralized RT review in the NCTN AHOD2131 trial (NCT05675410) for frontline treatment of early-stage classic Hodgkin lymphoma.

Methods Our central review process for AHOD2131 incorporates a structured, multi-step process designed to ensure accurate target volume delineation, appropriate dose coverage, and adherence to organ-at-risk (OAR) constraints. The process involves institutional submission of simulation CT, PET/CTs, and contours to the Imaging and Radiation Oncology Core Group Rhode Island (IROC-RI). Nuclear medicine radiologists perform an initial review of PET/CTs, identifying sites of disease involvement and assigning Deauville scores. The RTQA team of IROC-RI staff and radiation oncologists (ROs) promptly conducts a virtual review. This review process ensures that PET/CTs are accurately registered with simulation CT, target volumes are appropriately delineated, and OAR doses comply with protocol-defined constraints. Feedback is provided to treating ROs, who must address any required revisions before final approval and treatment initiation.

Results Early implementation of this rigorous RTQA process has been successful in identifying potential protocol deviations and providing timely feedback within 1-2 days. Common errors include suboptimal PET/CT fusion leading to inaccurate contouring, omission of sites of initial disease involvement from ISRT volumes, and contouring that unnecessarily includes uninvolved OARs. Errors related to PET/CT fusion are often related to differences in body positioning between PET/CT and simulation CT scans, necessitating multiple registrations or "mental fusion" for accurate delineation. Additionally, misinterpretation of pre-treatment imaging contributes to target volume errors, underscoring the importance of careful review of baseline imaging.

Conclusion A standardized, centralized RTQA process is critical in modern lymphoma trials. The AHOD2131 RTQA model, integrating nuclear medicine and radiation oncology expertise, ensures high-quality RT delivery and provides a framework for future trials.

S-07-06 Long Term Outcomes of Consolidative Proton Therapy (cPT) for Children with Classical Hodgkin Lymphoma (cHL)

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Introduction cHL is associated with favorable prognosis and high overall survival (OS). cPT represents a modality recommended for young patients due to its reduction in exit dose, with a goal to minimize late effects. We investigated patient outcomes receiving chemotherapy followed by cPT for cHL at initial diagnosis or relapse/refractory (R/R) disease.

Methods We conducted a single-institution retrospective analysis of patients aged 0-22 with cHL treated with cPT after systemic therapy (ST) from 10/2007 – 12/2022. OS and relapse-free survival (RFS) were estimated using the Kaplan-Meier method; crude cumulative incidence estimates were used to describe failure patterns. Risk groups were classified by ST.

Results Seventy-four patients of 78 eligible were included, with 61 (82 %) treated at initial diagnosis and 13 (18 %) receiving cPT for R/R disease. Median follow-up was 5.5 years (30 % > 8 years). Median age at diagnosis was 16 years (range, 6.3–21.7), with most being female (58 %) and having nodular sclerosing subtype (82 %). 78 % had mediastinal bulky disease. Risk group distribution is

as follows: adult early favorable (2.7 %), adult early unfavorable (9.5 %), adult advanced (2.7 %), COG low-risk (5.4 %), COG intermediate-risk (37.8 %), COG high–risk (39.2 %), and EURONET TG3 (2.7 %). PET/CT showed a complete response in 53 % of patients at mid-treatment and in 74 % of patients at end-of-treatment. The radiation dose distribution in Gy(RBE) is as follow: 15–25.9 (43 %), 26–30.9 (46 %), 31–36.9 (10 %), 37–45 (1 %). One patient developed papillary thyroid carcinoma 11.9 years post cPT (in-field); no other grade 3 + radiation-related late toxicities were observed. 10-year OS was 96 % overall (97 % initial, 92 % R/R); 10-year RFS was 84 % overall (82 % initial, 92 % R/R). 10-year RFS was 100 %, 82 %, and 72 % for low, intermediate, and high-risk group. Of the 61 patients treated for initial diagnosis, eight experienced a relapse with four (6.6 %) out-of-field & in-field, three (4.9 %) out-of-field, and one (1.6 %) in-field. Of the 13 patients treated for R/R disease, one experienced an out-of-field recurrence.

Conclusion cPT is an effective and well-tolerated treatment for young patients with cHL demonstrating excellent 10-year OS and RFS, even for those treated at relapse. The single secondary malignancy noted highlights the favorable safety profile of PT. These findings support cPT as a treatment modality, warranting further studies to assess long-term outcomes.

S-08 | Survivorship and Aftercare & Survivor Panel

Chairs: Melissa Hudson (Memphis, USA), Margreet Veening (Utrecht, Netherlands)

S-08-01 Evolving paradigms of Hodgkin lymphoma and implications for cancer survivorship

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Contemporary treatment for pediatric Hodgkin lymphoma is associated with excellent event-free and overall survival rates. Over time, treatment paradigms have evolved towards a multiagent approach in an effort to reduce cumulative exposures to agents associated with both short- and long-term toxicities, in particular, exposures to alkylating agents, anthracyclines, and radiation therapy. Despite these advances, survivors of Hodgkin lymphoma remain at increased risk of developing adverse, late onset health conditions. The recent incorporation of immunotherapy into treatment regimens offers tremendous promise for improved short- and long-term survival, yet potential late toxicities associated with these approaches remain uncertain. Thus, systematic, long-term follow-up assessment of contemporarily treated patients is critical to characterizing late health outcomes for this vulnerable population.

S-08-02 Predicted Breast Cancer Risk after Mediastinal Radiotherapy for Pediatric Hodgkin Lymphoma: Analysis of a Multi-Institutional Children's Oncology Group Trial

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Introduction There are limited data regarding the risk of breast cancer (BrCa) following contemporary involved site radiation therapy (ISRT) for pediatric Hodgkin Lymphoma (HL). We sought to quantify this risk and identify factors associated with breast dose and subsequent BrCa risk.

Methods On the multi-institutional Children's Oncology Group study AHOD1331 (2015-2019), patients 2-21 years of age with high-risk cHL received 5 cycles of systemic therapy, followed by 21 Gy ISRT to sites of large mediastinal adenopathy (LMA) and slowly responding lesions + /- 9 Gy to sites of partial metabolic response. In females who received mediastinal RT on AHOD1331, we collected detailed breast dosimetry and applied radiobiologic models to estimate the lifetime attributable risk (LAR) at 70 years of age (LAR_{70}) of BrCa, (i.e. the absolute increased risk of BrCa above baseline risk at 70 years of age due to RT; mean baseline rate at 70 years of age in the US is 8.9 % https://seer.cancer.gov/data/).

Results Among 587 patients treated on AHOD1331, 296 (50 %) received protocol-directed mediastinal RT and had complete dosimetric data available. Their median age was 15 years, and 98 % had LMA. 163 (55.1 %) were female, so were eligible for this analysis. The RT technique was proton therapy in 25 %, photon intensity modulated RT (IMRT) in 45 %, and photon 3-dimensional conformal RT (3D-CRT) in 28 %. The RT prescription dose was 21 Gy in 84 % and 30 Gy in 16 %. The mean dose to the breasts was 4.2 Gy with substantial variation among individuals (range 0.2-14.5 Gy). The mean LAR_{70} of breast carcinoma was 2.92 % (range: 0.17-8.43 %). The mean LAR_{70} was 1.45 % (range 0.17-7.23 %) after proton therapy; 4.36 % (range 0.66-8.43 %) after IMRT; and 1.82 % (range 0.67-5.98 %) after 3D-CRT ($P < 0.0001$). Patients in the lowest quartile of risk were significantly more likely to have been treated with proton therapy than those in the highest quartile of risk (58 % vs 10 %, $P < 0.001$).

Conclusion Breast doses associated with contemporary mediastinal ISRT are predicted to result in lower BrCa risks than observed in historic cHL cohorts, with proton therapy being associated with lower doses and risks than IMRT. There is significant variation in breast dose and predicted risk among individuals nominally receiving the same treatment, indicating the need for subsequent screening recommendations to be based on breast dose, not prescribed nodal dose.

S-08-03 Worry and Emotional Functioning in Youth During Treatment with Corticosteroids for High-Risk Classical Hodgkin Lymphoma (cHL): A Report from the Pediatric Hodgkin Consortium

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Introduction Heightened psychosocial distress at cancer diagnosis is common. Corticosteroids are a component of cHL treatment often associated with mood changes. We aimed to examine the impact of cumulative prednisone exposure on cancer-related worry and emotional functioning in youth treated for high-risk cHL.

Methods The cHOD17 trial (NCT03755804) treated youth age ≤ 25 years old with high-risk cHL using 2-AEPA/4-CA(P)Dac cycles (brentuximab vedotin, etoposide, prednisone, doxorubicin, cyclophosphamide, and dacarbazine) and radiation to inadequately responding nodes. Adequate responders (AR), defined by positron emission tomography Deauville score 1-3 after two AEPA cycles, received 2 courses of prednisone (cumulative dose 1,800 mg/m^2) compared to 6 (4,200 mg/m^2) in inadequate responders. The trial protocol recommended symptom and quality of life measurement at specified time points during and after treatment. Worry and emotional functioning were measured using the PedsQL 3.0 Cancer Module and PedsQL 4.0 Generic Core Scales, respectively. Higher scores indicate less worry and better emotional functioning. Wilcoxon Rank Sum tests examined worry and emotional functioning by prednisone exposure. Longitudinal analyses with random intercept examined the effect of time (by day) from diagnosis on worry and emotional functioning.

Results Of 114 high-risk cHOD17 participants, 79 (69.3 %) submitted surveys and composed the analytic cohort. Participants were a mean (SD) age = 16.5 (3.21) years at diagnosis, 72.2 % White, 88.6 % non-Hispanic, and 59.5 % male. Fifty-seven percent of the analytic cohort achieved an AR and received reduced prednisone dosing. There were no significant differences in worry or emotional functioning by prednisone exposure. Worry decreased ($\beta = 0.39$, $p < .001$) and emotional functioning improved ($\beta = 0.63$, $p < .001$) over time from diagnosis when controlling for age, sex, and ethnicity during AEPA cycles. This effect was not found for worry during CA(P)Dac cycles. Time from diagnosis ($\beta = 0.08$, $p = .04$) and male sex ($\beta = 8.82$, $p = .03$) were significant predictors of emotional functioning during CA(P)Dac cycles.

Conclusion Cumulative prednisone exposure was not associated with worry and emotional functioning in youth treated for cHL. Worry appears most severe and emotional functioning most impaired at diagnosis. These findings emphasize the importance of early intervention and psychosocial support beginning at cHL diagnosis and of future research examining resilience factors in youth treated for cHL.

S-08-04 TREATMENT APPROACH AND OUTCOMES IN CHILDREN AND ADOLESCENTS WITH NODULAR LYMPHOCYTE-PREDOMINANT HODGKIN LYMPHOMA: THE ITALIAN ASSOCIATION OF PEDIATRIC HEMATOLOGY AND ONCOLOGY (AIEOP) EXPERIENCE.

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Introduction Nodular lymphocyte predominant Hodgkin lymphoma (nLPHL) is a rare subtype of Hodgkin lymphoma, which accounts for about 5 % of pediatric/adolescent Hodgkin lymphomas [1, 2]. Currently, patients diagnosed in Italy with nLPHL are collected in the AIEOP-LHPL2019 retrospective/prospective study.

Methods This is an observational study recruiting all stage nLPHL, since november 2019. Patients are treated according to clinician discretion, following study suggestions. About 10 new cases/year are diagnosed in AIEOP Centers.

Results To date, 83 patients from 28 AIEOP centers have been observed, to which 11 additional new diagnoses were added in the last year. 82/83 patients have been evaluated. Eighty percent of cases had the histology centrally revised. Patients, 68M/15F (M 81.9 %), mean age 12.8aa (range 2.9-17.9aa), 66 % age > 12aa, presented stage I-IIA disease in 66/83 (79.5 %), only 2/83 (2.4 %) patients presented B symptoms. Treatment: 16 stage IA patients were treated with surgery alone, 38 (stage IA + IIA + IIIA) received 3-6 CVP cycles, 8 patients 3-6 Rituximab + CVP, and 20 different therapies (ABVD ± R, R-CHOP, OEPA, COPP/ABV). No patient has been treated with RT. A total of 14/82 patients received first-line rituximab therapy. 20/82 (24.4 %) patients, including 2 stage IIB-IIIB, 6 stage IA, and 12 stage IIA, presented persistent/progressive/recurrent disease after first-line therapy. With 100 % OS and 76 % EFS at a median follow-up of 56.4 months, nLPHL is confirmed to be a disease with good prognosis; 66 % of patients received low intensity treatment (surgery and/or CVP). 20/82 (24.4 %) patients developed recurrences, namely 14 relapses, 3 persistent diseases after first line treatment and 3 disease progressions. Both patients with stage IIB-IIIB developed disease progression after being treated with intensive chemotherapy (R-ABVD and OEPA + R-CHOP respectively). It's interesting to note that all the remaining 18 patients with recurrences had stage I/IIA while no cases of recurrences occurred for IIIA/IVA stages.

Conclusion The current case series of AIEOP Centers with 83 patients represent one of the largest in the nLPHL scenario. According to literature [3, 4] and confirmed in our experience, in the majority of patients, sparing of anthracycline and radiotherapy is possible, and the addition of rituximab seems to offer a promising chance [5]. The rare presence of B symptoms at onset, seems to identify a disease with a more severe prognosis.

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P-02 | Guided Poster Session

P-02-01 Genetic lesions in nodular lymphocyte-predominant Hodgkin lymphoma and T cell/histiocyte-rich large B-cell lymphoma identified by whole genome sequencing

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Introduction Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is a rare malignant lymphoma characterised by a few large tumour cells expressing B-cell antigens in an inflammatory background. T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) is now considered to be closely related to NLPHL. Little is known about the mutational spectrum of the lymphoma cells in primary NLPHL and THRLBCL due to the rarity of the diseases and the technical challenges of analysing these tumours.

Methods The aim of the present study was to elucidate mechanisms contributing to the pathogenesis of NLPHL and THRLBCL. We applied whole genome sequencing of laser microdissected tumour cells and corresponding normal cells obtained from seven cases.

Results We observed a heterogeneity of transforming events, with cases showing abundant somatic mutations, others with a predominance of structural variations, and cases with few aberrations. The genes that were most frequently affected by aberrations encode factors influencing JAK-STAT, NF-κB, and/or WNT signaling, and apoptosis regulators. However, the mutated genes, such as *SOCS3*, *JUNB*, *IRF1* and *ITPKB*, were not the typical targets known from classical Hodgkin lymphoma (cHL). Two cases that had B-cell receptors reactive with antigens from M. catarrhalis and R. mucilaginosa showed recurrent rearrangements of *BCL6* and *CD74*.

Conclusion In conclusion, our data enrich our understanding of NLPHL and THRLBCL and highlight common and distinct features with respect to cHL.

P-02-02 Search for factors that inhibit expression of endogenous retroviruses

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DOI 10.1055/s-0045-1812965

Introduction Human endogenous retroviruses (HERV) are relicts of exogenous viruses that have entered the human genome in the course of evolution. Most HERV are without protein-coding capacity as a result of mutations. However, some HERV sequences have been preserved that code for proteins, e.g. envelope proteins. In most somatic cells, the expression of HERV is switched off epigenetically. However, in cancer cells including Hodgkin lymphoma (HL) cells (Barth et al., 2019), the presence of HERV-derived RNAs have been detected. In our earlier work, we observed that even in HERV-RNA-positive cells, HERV proteins are generally only present in very small quantities (Gröger et al., 2020). We observed increased HERV protein synthesis in HEK293F cells. We therefore investigated which factors could be responsible for this increased synthesis capacity.

Methods HERV envelope sequences were cloned into expression vectors and used for transfection of established cell lines. HERV expression was analyzed by quantitative reverse transcription-polymerase chain reaction (qRT-PCR), flow cytometry and western blot analysis. Gene expression in cells with different HERV protein synthesis capacity was assessed by RNA-seq analysis. Expression of paternally expressed 10 (PEG10) was down-regulated in cell lines by lentiviral shRNA delivery. The group specific antigens (gag) region of PEG10 was cloned from HL cell line L-428 into an expression vector and used for transgenic over-expression of PEG10.

Results RNA-seq analysis identified several genes with differential expression between cells with high HERV protein synthesis capacity and cells with low capacity. Among these genes, paternally expressed 10 (PEG10) caught our attention because PEG10 was absent from cells with high protein synthesis capacity. PEG 10 is itself an endogenous retrovirus-like gene, which is a homolog to the Drosophila gene gypsy. As it has a gag-like sequence, PEG10 has the ability to bind RNA and thus modulate stability or translation. PEG10 expression was independent on culture conditions (serum presence or absence; growth in suspension or as adherent monolayer). By genetic engineering we established cells with varying amounts of PEG10 expression which were used for analysis of HERV protein synthesis [1, 2].

Conclusion Our observations suggest that PEG10 might be an interesting candidate for a restriction factor for HERV protein synthesis.

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P-02-03 Multi-OMICs and pharmacological studies point to a role of altered centrosome and cilia function in the pathogenesis of classic Hodgkin Lymphoma.

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Introduction The tumor cells of classic Hodgkin Lymphoma (cHL), the Hodgkin Reed-Sternberg (HRS) cells, are among others characterized by cytokinesis defects, frequent hyperploidy, and ongoing chromosomal instability. We here aimed at investigating the role of centrosomes and cilia to the development of this peculiar phenotype.

Methods Seven cHL cell lines were studied along with the control cell lines including two lymphoblastoid, two primary mediastinal large B-cell lymphomas, a nodular lymphocyte predominant HL, nine Burkitt lymphomas, and seven other B-cell lymphoma cell lines. We performed array-based DNA methylation and RNAseq analysis, immunofluorescence (IF) to various centrosome and cilia proteins, and transmission electron microscopy. Poloxin-2 was applied as a centrosome de-clustering drug. Cell Titer Blue, cleaved caspase 3 were used to investigate cell viability and apoptosis respectively. Primary cHL with nodular sclerosis were studied also by IF to observe the morphology of cilia and basal bodies along with the endothelial cells serving as internal controls.

Results Gene expression analysis identified 20 centrosome and 30 cilia-associated genes that were differentially expressed in cHL compared to non-cHL cell line controls. Among these, 5 centrosome and 4 cilia associated genes also exhibited differential DNA methylation. TEM revealed structural centrosome anomalies (broken cartwheel absence of sub-distal appendages on either side of the mother centriole) in two cHL cell lines compared to a lymphoblastoid cell line. Seven studied cHL cell lines showed a higher extent of centrosome clustering compared to a lymphoblastoid cell lines observed by IF, therefore, we treated these cHL cell lines with Poloxin and DMSO as a vehicle control. The treatment caused a significant, dose-dependent reduction in viability across seven cHL cell lines via apoptosis induction, with no adverse effects on untreated controls' longevity. In the L428 cHL cell line, Poloxin triggered centrosome fragmentation, chromosomal misalignment, and abnormal spindle microtubule organization. IF of primary cHL revealed disorganized ciliary structures resembling a filamentous network in HRS cells, whereas endothelial cells retained normal basal body-anchored cilia. These ciliary defects directly correlated with centrosomal structural aberrations confirmed by TEM.

Conclusion Our study provides evidence for a contribution of centrosome and cilia dysfunction in the etiology of cHL providing a potential target for treatment.

P-02-04 Molecular Mechanisms Involved in the Pathogenesis of Post Treatment Persistent Erythrocytosis in Patients with Hodgkin Lymphoma

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Introduction We have previously presented the characteristics and survival analyses of patients diagnosed with Hodgkin Lymphoma (HL) who developed post-treatment erythrocytosis (pt-E +). Our study aimed to investigate the molecular changes that may cause this association in these patients.

Methods This study analyzed patients diagnosed and treated for HL between 2004 and 2019. Two cohorts were evaluated: 12 patients who developed post-treatment erythrocytosis but normal hemoglobin (Hb) levels at diagnosis (pt-E^+ group) and 12 patients without erythrocytosis at any point (E^- group). For the pt-E^+ group, paired samples were assessed at diagnosis (A) and during erythrocytosis (B). Hb thresholds were defined as ≥ 16.5 g/dL for males and ≥ 16 g/dL for females (WHO, 2022). Clinical characteristics, serum erythropoietin (EPO) concentrations, and JAK2V617F mutation status were evaluated. Next-generation sequencing (NGS) targeting 33 erythrocytosis-related genes was performed using QIAGEN CLC Genomics Workbench v24.0.1, with variants included if the VAF ≥ 1 %.

Results All pt-E^+ patients were male. Median Hb was 13.7 g/dL at diagnosis (9.3–16) and 17.1 g/dL during erythrocytosis (16.8–17.9). Most (75 %) had a smoking history. All were JAK2V617F-negative with a median EPO of 14.4 mU/mL (5.2–38). In the pt-E^+ group, mutations were found in 25 genes: JAK2, EPO, HBA2, VHL, BHLHE41, EPAS1, TET2, AXSL1, EZH2, DNMT3A, SH2B3, HIF1A, HIF3A, EGLN1, EGLN2, EGLN3, KMD6A, GFI1B, GATA-1, PKLR, CALR, JAK3, MPL, CSF3R, and TP53. In controls (E−), mutations were identified in 9 genes: BHLHE41, TET2, AXSL1, EZH2, DNMT3A, HIF1A, CALR, JAK3, and MPL. Germline mutations in EGLN3, SH2B3, PKLR, JAK3, EPAS1, HIF3A, and EGLN2 were found in pt-E^+ patients; only JAK3 was seen in E^- controls. In the pt-E^+ A group, 94 somatic mutations were identified, most frequently in MPL (14.8 %), SH2B3 (10.6 %), and HIF3A (9.5 %). During erythrocytosis (B), 26 mutations were detected, with enrichment in MPL (38.4 %), BHLHE41 (19.2 %), and ASXL1 (11.5 %). In the control group (E^-), 22 somatic mutations were found, predominantly involving MPL (60 %). Eighty-three mutations were present at diagnosis but not post-treatment, notably SH2B3 (12.04 %), HIF3A (10.8 %), and EPAS1 (9.6 %). Conversely, 12 mutations appeared only post-treatment, including BHLHE41, ASXL1, MPL, CALR, DNMT3A, HIF1A, TET2, and JAK2.

Conclusion Erythrocytosis observed in the post-treatment period of HL might be linked to some mutations other than JAK2V617F.

P-02-05 Serum Soluble Immune Factor Levels in Treated Pediatric Hodgkin Lymphoma Patients

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Introduction Pediatric Hodgkin lymphoma (HL) is highly curable; however, current risk-stratification, largely based on historical tools that indirectly reflect tumor burden and offer limited biological insight into tumor–immune cell interactions, lacks precision in identifying early treatment responders. Emerging evidence underscores the role of serum detectable cytokines, chemokines, and soluble immune-factors that change dynamically during therapy. This study aims to identify serum-derived immune-factor signatures that correlate with early treatment response, as assessed by quantitative positron-emission-tomography (ERA-qPET) following OEPA induction therapy, and to stratify good versus poor responders among the newly diagnosed pediatric-HL patients.

Methods Thirteen soluble immune-factors (IL-6, IL-8, IL-10, IP-10, MCP-1, MIG, G-CSF, VEGF, CCL17, IgA, IgG, IgM, and IgE) were measured in pre-treatment samples from 61 pediatric-HL patients with varying treatment responses. Of these, 30 patients demonstrated an adequate response (ERA-qPET < 1.3), whereas 31 patients had an inadequate response (ERA-qPET ≥ 1.3) to induction-chemotherapy. Serum levels of these immune proteins were systematically analyzed using cytokine-bead-array for cytokines, turbidimetry for immunoglobulins, and ELISA for chemokine CCL17 (TARC).

Results All pediatric HL patients with median age 15.2 years were treated according to the EuroNet-PHL-C2 protocol. Soluble immune-factors were significantly elevated at diagnosis compared to healthy controls. Expression levels of these soluble factors decreased notably after induction-chemotherapy and at follow-up compared to baseline. Distinct baseline soluble factor patterns correlated with clinical response categories to OEPA-chemotherapy, effectively differentiating inadequate from adequate responders. Pre-treatment IL-6, IL-10, VEGF and Immunoglobulin-E levels were significantly higher in patients with an ERA-inadequate response.

Conclusion Elevated pre-treatment serum soluble immune-factor levels are associated with aggressive disease status and inadequate response to induc-

tion-therapy. Thus, the pre-treatment patterns, particularly IL-6, IL-10, VEGF and IgE serum levels, may help to identify pediatric-HL patients at high-risk of a slow response to induction-therapy.

P-02-06 Validation of a gene signature based on tumor microenvironment composition for risk stratification of pediatric patients with classical Hodgkin lymphoma.Update.

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DOI 10.1055/s-0045-1812969

Introduction Classical Hodgkin lymphoma (cHL) is among the most prevalent cancers affecting children and adolescents. The presence of pathognomonic Reed-Sternberg cells dispersed in a reactive microenvironment of $CD4^+$ and $CD8^+$ T cells, histiocytes, fibroblasts, plasma cells, eosinophils, and other immune cells is a peculiar feature of cHL. This distinctive cellular milieu plays a pivotal role in tumor progression and response to therapy [1, 2].
The aim of this study was to retrospectively evaluate, on tissue specimens of pediatric cHL at diagnosis, a newly tested gene transcript profile with prognostic value reflecting the composition of the tumor microenvironment.
Methods By applying NanoString-based measurements of the transcripts in the "PHL-9C" model, we sought to enhance our understanding of the disease's biology and improve the precision of risk stratification in clinical practice.
21 paraffin-embedded tissue specimens from patients with cHL at diagnosis (age 5-17 years, mean 14 years, 10/11 Male/female), processed according to AIEOP-LH-2004 protocol, were subjected to RNA extraction and profiling by nCounter platform (NanoString Technology) for digital measurement of 111 transcripts related to 9 cytotypes (CD8 + T lymphocytes, Th1 lymphocytes, Th2 lymphocytes, Treg, mast cells, myeloid suppressor cells, follicular dendritic cells, B lymphocytes, Reed Sternberg cells). 5-year event-free survival was used as the primary endpoint.
Patients were stratified into risk categories according to clinical criteria: 9 patients (42.9 %) as high-risk, 6 (28.6 %) as intermediate-risk, 6 (28.6 %) as low-risk.
Results The composition of the microenvironment was related to the 3 treatment groups by comparing the average expression of genes associated with each cytotype. Among the nine cellular components of the PHL-9C model, B cell–associated gene expression was significantly lower in high-risk patients compared to intermediate- and low-risk groups ($p = 0.04$, Kruskal–Wallis test). No significant differences were observed for the other cell types in this dataset. B cell-related gene sets were significantly enriched in low-risk patients compared to the intermediate and high-risk groups (NES = 2.0, FDR < 0.001).
Conclusion This finding reinforces the association between immune-active microenvironments and favorable outcomes in pediatric cHL. Together, these results demonstrate that the PHL-9C gene signature maintains its biological and clinical relevance in a real-world pediatric population.

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P-02-07 7 year experience in treatment of teenage and young adult (TYA) patients with escalated BEACOPDac for classical Hodgkin lymphoma (all stages) in a specialist TYA centre: An assessment of outcomes.

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DOI 10.1055/s-0045-1812970

Introduction Escalated BEACOPDac (bleomycin, etoposide, doxorubicin, vincristine, cyclophosphamide, prednisolone and dacarbazine) (eBEACOPDac) has been used as first line treatment for early unfavourable and advanced stage classical Hodgkin lymphoma in young, fit patients since studies showed an improved toxicity profile without compromise to outcomes when compared with escBEACOPP. We analysed data from our region to assess our experience of treatment with eBEACOPDac assessing toxicity, access to fertility services and efficacy of salvage therapy in relapsed/refractory disease.
Methods This is a retrospective study of TYA patients treated in the West of Scotland from 2018 to 2025. 43 patients were identified who were treated with eBEACOPDac either as first line therapy or escalated following incomplete response on interim PET with ABVD therapy. Outcomes were determined from review of electronic records [1, 2].
Results The majority of patients (36) were treated in our specialist TYA centre at the Beatson West of Scotland Cancer Centre. This includes 16–18 year-old patients who are often managed by paediatric approach in other regions. 7 patients elected for treatment with the local Haematology team in district general hospitals.
30 patients were treated with eBEACOPDac as first line therapy and 13 patients were escalated following incomplete metabolic response to 2 cycles of ABVD. Two patients required unplanned radiotherapy following completion of treatment.
One patient had refractory disease at end of treatment and a further 3 patients relapsed within one year of treatment. IVE chemotherapy is the main second line regimen used, however most patients required multiple lines of treatment in the relapsed/refractory setting following eBEACOPDac.
Our data confirms the known toxicity profile with infection and nausea reported in 42 % and 25 % of patients respectively. Given limited data on the impact on fertility following eBEACOPDac, our patients continue to be referred for fertility preservation where possible although there are often limited options for female patients.
There is one deceased patient in this cohort with suicide as cause of death.
Conclusion This data represents our experience with eBEACOPDac in a specialist TYA centre. We will further explore treatment response and impact of toxicity including hospital admissions and long term effects on fertility, cardiac function and secondary cancers. We continue to accrue information and have requested national data which will be available for our presentation.

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P-02-08 Investigating Neurofilament Light Chain as a Potential Biomarker of Chemotherapy Induced Peripheral Neuropathy in Children and Adolescents

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Introduction Chemotherapy-induced peripheral neuropathy (CIPN) is a common treatment side effect in both pediatric and adolescent young adult patients (AYAs). CIPN causes significant clinical challenges. CIPN detection in children and AYAs remains challenging, with poor sensitivity among providers, particularly in identifying less severe cases. Neurofilament light chain (NfL) is an emerging biomarker that has shown promising correlation in adult oncology studies, with the potential to serve as an early and sensitive biomarker of CIPN. This pilot study aimed to describe changes in NfL in children and AYAs with CIPN.

Methods This single-center, prospective study examined patients aged 2-25 years with leukemia or lymphoma who received a chemotherapy regimen which included a tubulin toxin. CIPN was assessed using the FACT-GOG-NTX. Outcomes were evaluated at baseline, during therapy, and 6-12 weeks after last chemotherapy. NfL values were reported as the Normalized Protein eXpression (NPX) per OLINK standard reporting on a log2 scale. Negative NfL values were excluded from percent change calculations. Values were calculated at baseline, first follow-up, and at 90 days or the closest visit to 90 days.

Results Data from participants ($n = 30$) with B-lymphoblastic leukemia ($n = 12$), Hodgkin lymphoma ($n = 14$), and mature B-cell lymphoma ($n = 4$) were analyzed. Of those, 10 participants had NfL analysis, with a median % change in baseline NfL of 57.28 %. Mean NfL levels increased from baseline timepoint (mean 2.32, median 2.16) to time point 2 (mean = 3.28, median 3.47) and remained increased at the follow-up visit closest to 90 days (mean 3.85, median 4.38). All participants had CIPN as evidenced by increased FACT-GOG-NTX scores. The majority of scores worsened longitudinally over time correlating with progressively worsening neuropathy. There was a significant correlation between NfL values and FACT-GOG-ntx scores both throughout the study ($\rho = -31$, $p = 0.004$) and between percent change from baseline value ($\rho = -.45$, $p < 0.001$), with higher NfL correlating to worse neuropathy.

Conclusion We report the first investigation of NfL in the pediatric and AYA cancer setting as a novel biomarker for CIPN detection. Changes in biomarker were detectable early in therapy and correlated with evidence of CIPN. Results from this pilot study will serve as the foundation for future studies to continue investigating NfL as an early and objective detection measure of CIPN in this unique patient population.

P-02-09 Rare occurrence of ocular metastasis of Hodgkin Lymphoma- a case report

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DOI 10.1055/s-0045-1812972

Introduction Hodgkin Lymphoma (HL) typically follows a predictable pattern of lymphatic spread. Rare extranodal manifestations include the skin, gastrointestinal tract, central nervous system, and eyes. Ocular involvement, described herein in this case study, is particularly rare.

Methods Case report

Results A 19-year-old male presented with worsening cough for one year and weight loss > 10 % body weight, anorexia, dysphagia and dysphonia. CT scan revealed a large right anterosuperior mediastinal mass causing mass effect upon the right lung apex with intense FDG avidity on PET CT scan. An IR-guided biopsy of the right paratracheal mass confirmed classical HL. Patient refused to start treatment due to distance from his home to our cancer center. About one month later, the patient presented again with new-onset blurry vision in the right eye along with fever and worsening cough. Neuroophthalmology evaluation by optical coherence tomography (OCT) was consistent with a discrete solitary sub foveal choroidal infiltrate in the right macula with overlying retinal elevation of the right eye, significant perifoveal edema, and subretinal hemorrhage. The lesion exhibited homogenous reflectivity, suggestive of neoplastic infiltration. Fundus examination demonstrated vitreous haze with scattered inflammatory cells and central scotoma. Patient was initiated on Brentuximab, Cyclophosphamide, Dacarbazine, Doxorubicin, Etoposide, Prednisone for Stage IV HL and our patient demonstrated resolution of the choroidal lesion, with persistent foveal atrophy and retinal thinning, findings that mirror post-treatment regression. Patient is in remission as of his 33 month off-therapy visit and has lingering central scotoma in the right eye.

Conclusion The development of visual disturbance and the identification of a choroidal lesion emphasize the need for heightened clinical suspicion for ocular involvement, despite its extreme rarity. In a report by Yang et al. the authors highlight similar imaging characteristics, reinforcing the role of OCT in diagnosing choroidal metastases in lymphomas [1]. Fukutsu et al describe the ability of choroidal lymphoma to mimic inflammatory conditions further necessitating the need to distinguish neoplastic from inflammatory processes when evaluating subretinal lesions [2]. In our patient's case, following chemotherapy, the patient demonstrated resolution of the choroidal lesion, with persistent foveal atrophy and retinal thinning, findings that mirror post-treatment regression.

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P-02-10 Long-term Outcomes and Toxicities in Childhood, Adolescent, and Young Adult Hodgkin Lymphoma

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Introduction Advances management of Hodgkin lymphoma in children, adolescents, and young adults have resulted in survival outcomes exceeding 90 %. Risk-adapted treatment approaches, such as ABVD, OEPA CAPDAC/OPPA CAPP, and VAMP protocols, have been successfully used for Hodgkin lymphoma. Recent trials have been conducted to improve cure rates while reducing long-term toxicity with doxorubicin or irradiation [1–5].

Methods We report the treatment course of five boys at our institution. They were between 8 and 15 years of age at disease onset. Three cases were stage II and two were stage IV.

Results All patients had received ABVD or OEPA/CAPDAC treatment five years before and had been in remission, although one of these patients had brentuximab vedotin after relapse in stage II. Three patients underwent irradiation; two patients had thyroid abnormalities and received hormone replacement therapy with ABVD and irradiation.

Conclusion We focused on the outcomes and risks of long-term toxicities of the treatment in children and the novel aproach with brentuximab vedotin,

which targets CD30 or PDL-1 inhibitor. In addition, understanding prognostic markers and biology in children and AYAs may allow further therapy.

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P-02-11 RELAPSED/REFRACTORY HODGKIN LYMPHOMA IN PEDIATRIC PATIENTS. EXPERICENCE AT HOSPITAL DE PEDIATRIA DR. JUAN P. GARRAHAN – ARGENTINA.

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Introduction Approximately 10 % of patients develop relapsed or refractory (R/R) disease representing a subgroup with a guarded prognosis and significant therapeutic challenges. Refractory HL is defined as progressive/stable disease on treatment or failure to achieve complete remission (CR) following first-line chemotherapy and represents a clinical challenge, requiring second-line chemotherapy/radiotherapy/immunotherapy and eventually followed by high-dose chemotherapy with autologus hematopoietic stem cell transplantation (HSCT) or allo SCT.

Methods Descriptive, retrospective, observational study of patients under 18 years diagnosed with R/R HL treated between October 2017 / December 2024 at Hospital Dr. Juan P. Garrahan. All patients who showed evidence of progressive/stable disease on treatment or failure to achieve complete remission (CR) following first-line chemo/radiotherapy according to LH-GALOP2017protocol (ClinicalTrials.govID:NCT03500133) were included.

Results A total of 79 patients were diagnosed with HL of whom 3 developed R/R disease.

Patient 1: 11y, Female, Stage IVB High Risk. End of treatment: progressive disease (PD) Deauville 5. Second-line treatment: COPDac 2cycles, Interim-PET complete remission (CR). Autologous stem cell transplantation was performed and followed with brentuximab maintenance for 16 months. Outcome: CR (34 months).

Patient 2: 15y, Male, Stage IIA Intermediate Risk (IR). End of treatment response: PD Deauville 5. Second-line treatment: COPDac + Ifosfamide-Vinorelbine 2 cycles, Interim-PET: partial remission (PR). Third line schedule Gemcitabine + Vinorelbine 2 cycles, Interim-PET: PR. Brentuximab + Bendamustine 2 cycles, Interim-PET: CR. ASCT. PET scan after ASCT: relapsed. Brentuximab 5 cycles, Interim-PET: PR. Pembrolizumab + GVD (Gemcitabine-Vinorelbine-Doxorubicin) 6 cycles, Interim-PET: CR. Haploidentical HSCT. Outcome CR (18m).

Patient 3: 12y, Male, Stage IVB HR. End of treatment response: PD Deauville 5. Brentuximab + Bendamustine (interrupted infusion due to anaphylactic reaction). Ifosfamide + Vinorelbine 4cycles, Interim-PET PD. GVD 2 cycles, Interim-PET CR. ASCT. Outcome: relapse receiving pembrolizumab. Outcome no evidence of disease.

Conclusion R/R disease is very rare in HL. Its early detection allows for a change in treatment strategy improving the prognosis in this subgroup of patients. Furthermore, our experience highlights the continued efficacy of a conventional first-line regimen with reduced radiotherapy, supporting their use as a robust frontline therapeutic approach.

P-02-12 Real World Experience of Brentuximab Vedotin and Immune Checkpoint Inhibitor in Pediatric Refractory and Relapsed Classical Hodgkin Lymphoma: A Retrospective Study from Two Centers in Taiwan

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Introduction The Epirubicin, Bleomycin, Vinblastine, and Dacarbazine (EBVD) regimen has been the most commonly used first-line chemotherapy for pediatric classical Hodgkin lymphoma (cHL) in Taiwan. However, the event-free survival for intermediate- and high-risk groups remains suboptimal, at approximately 60–70 %. With the growing clinical experience in the use of brentuximab vedotin (BV) and immune checkpoint inhibitor (ICI) in adults, these therapies have been explored across various clinical settings—ranging from treatment of primary refractory or relapsed disease, to maintenance therapy post-auto-HSCT, and even as part of frontline treatment for patients with risk factors. Here, we aimed to report our clinical experience with novel agents in the treatment of refractory and relapsed (R/R) cHL in pediatric patients.

Methods We retrospectively analyzed seven R/R pediatric cHL patients treated with BV or ICIs at two hematology centers in Taiwan between 2015 and 2024, focusing on disease stage, risk factors, treatment timing, response, adverse events, subsequent consolidation, and outcomes.

Results This series included seven pediatric patients with multiple poor prognostic factors, such as advanced stage (42.9 %), B symptoms (85.7 %), bulky disease (71.4 %), and primary refractoriness (42.9 %). Five patients received BV ± chemotherapy during frontline or salvage therapy, and two received BV as maintenance post auto-HSCT. Among BV containing frontline and salvage regimens, responses included two complete metabolic response, three partial response, and three progressive disease. BV-based regimens enabled 50 % of patients to proceed to consolidation therapy, including radiation, auto- or allo-HSCT. All patients were alive at analysis, with two still receiving treatment. One patient with refractory disease achieved 1.5 years of remission with BV plus gemcitabine and radiation, without transplantation. BV combined with chemotherapy showed better response than BV alone. Single-agent BV was more effective as maintenance in patients with low tumor burden. No BV-specific adverse events were reported. Two patients received ICI ± chemotherapy, suggesting potential benefit despite limited numbers.

Conclusion BV-based regimens showed promising efficacy in pediatric relapsed or refractory cHL, especially when combined with chemotherapy. Half of the patients proceeded to consolidation therapy, and all remained alive at follow-up. Single-agent BV was effective as maintenance therapy. Children tolerated BV well, with no adverse events observed.

P-02-13 Nodular Lymphocyte Predominant Hodgkin Lymphoma Involving the Stomach and Bones

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Introduction NLPHL typically presents as early stage disease with localized peripheral lymphadenopathy. Primary extranodal NLPHL is exceedingly rare. Here we present the diagnostic challenges of an adolescent with NLPHL.

Methods Case report

Results A 17 year old Hispanic male presented with a two-months history of vomiting, abdominal pain and weight loss of 6 pounds, without fever or night sweats. A CT scan showed a mass in between the liver and the spleen and around the gastroesophageal (GE) junction. In the upper stomach and lower esophagus mucosal thickening was noted. In addition, splenomegaly, periaortic lymphadenopathy, cervical and supraclavicular lymphadenopathy was present. No mediastinal adenopathy was noted. The PET/CT scan showed FDG avidity in all areas of CT involvement and uncovered multiple bone involvement in the vertebri, sacrum, pelvis, proximal femurs and humerus.

An esophagogram showed an apple-core lesion involving the distal stomach and gastric fundus. An upper esophago-gastroduodenoscopy showed an exophytic mass in the stomach. Biopsies showed necrotic tissue. Bone marrow biopsy was negative.

Histopathological diagnosis was challenging. The specimen underwent 3 pathological consultations. The process took 8 weeks 1) presence of large cells with uniform CD30 expression and weak PAX5 favoring cHL but also good preservation of B cell program (positive CD79a, BOB1 and OCT2), apparent CD45 expression, and variable CD20. 2) most consistent with NLPHL variant patern D, and T cells with aberrant CD20 expression. 3) large cells that retain B cell programming expressing CD20, CD19, OCT2 and BOB1 but also strong CD30 expression, but with CD45 positivity. Cells also expressed MEF2B and negative for STAT6 both favoring NLPHL. CD20 appeared weakly expressed on T-cells population. Overall findings are consistent with NLPHL.

The patient was treated with Bv-AVEPC x5. PET2 showed incomplete metabolic response with DS of 4 in the GE junction, spleen and bones. All areas of involvement showed decrease in size. PET5 showed complete metabolic response of all sites. He then receive 6 doses of Rituximab every 3 weeks. End of therapy PET scan was negative. Radiation therapy was spared. Six months after completing treatment, the patient remained in remission [1, 2].

Conclusion This case highlights a rare case of NLPHL with extranodal involvement in the stomach and bones and the challenges of histopathological diagnosis with implications in delay in proper treatment.

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P-02-14 Brentuximab vedotin (BV) in relapsed and refractory classical Hodgkin lymphoma (cHL) in children. Thirteen years of experience of the Polish Pediatric Leukemia/Lymphoma Treatment Group

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Introduction Brentuximab vedotin (BV) provides a treatment opportunity for children with relapsed or refractory classical Hodgkin lymphoma (cHL). In Poland, BV has been used since 2012—initially as monotherapy, and from 2014 onward, in combination with chemotherapy.

Methods This study aimed to evaluate the use of BV in pediatric cHL patients who began treatment before August 30, 2024. Anonymized questionnaires were distributed to 17 pediatric oncology centers across Poland. The study assessed the disease status before BV treatment, prior treatment regimens, type of BV therapy administered, treatment response, and survival outcomes. The observation period concluded on March 31, 2025.

Results Between 2012 and 2024, BV was administered to 30 patients aged 7.4–18.2 years (median age: 16.6) with relapsed or refractory cHL. BV was used in 26 patients to treat disease progression or relapse, either as monotherapy (n = 5) or in combination with chemotherapy (n = 21). In 4 patients, BV was used as consolidation therapy following autologous stem cell transplantation (auto-SCT).

BV monotherapy was conducted between 2012 and 2015 in 5 patients who received 3–8 cycles (median: 5). Disease progression was observed in 2 patients and disease stabilization in another 2. Four patients died: 2 due to disease progression and 2 due to complications following allogeneic stem cell transplantation (allo-SCT).

Combination therapy with BV and chemotherapy was administered in 21 patients between 2016 and 2024; 17 during treatment of first relapse or progression, and 4 during second or subsequent relapses. In 16 cases, BV was combined with bendamustine, in 3 with AVD chemotherapy, and in 2 with nivolumab. One patient experienced an allergic reaction that prevented further BV administration. Two deaths occurred: one due to disease progression and one due to allo-SCT-related complications. Eight patients experienced further relapses and were subsequently treated with nivolumab, pembrolizumab, or CAR-T cell therapy. Of the 21 patients who received BV in combination with chemotherapy, 19 are currently alive, including 12 without further relapse.

Conclusion BV was initially used as monotherapy and later as part of combination regimens, particularly as salvage therapy following multiple relapses. Currently, BV combined with chemotherapy is increasingly applied as a second-line treatment option in patients with insufficient response to frontline chemotherapy.

P-02-15 Challenging Cases of Nodular Lymphocyte-Predominant Hodgkin Lymphoma with transformation.

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Introduction Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL) is a rare slow-growing subtype, accounting for 5 % of Hodkgin Lymphomas [1]. It usually has an indolent course but transformation to aggressive forms can occur with poor prognoses [2]. Immune dysregulation is linked with Hodgkin Lymphoma and is often seen in refractory disease, relapse and transformation to high-grade B-cell non-Hodgkin lymphoma.

Methods We present two cases of classical NLPHL with transformation.

Results Patient 1 5-year-old girl with chronic eczema diagnosed with NLPHL, Stage IVA after presenting with suboccipital lymphadenopathy. She was classified as intermediate risk and treated as per COG AHOD0331. PET after 2 cycles showed CMR. PET 2 years post showed nodular avidity and follicular hyperplasia and progressive transformation of germinal centres on biopsy. At age 13, she developed Nodular Sclerosing Hodgkin Lymphoma stage IIIAS with PET avid disease above and below diaphragm. She received 4 cycles of IGEV followed by mini-BEAM. PET pre and post mini-BEAM showed CMR. Significant unexpected toxicity occurred post and she entered surveillance. EBV reactivation occured 6 months later aged 14. EBV positive classical NS HL stage IVA developed 2 months later with short response to high dose steroids, Brentuximab and Rituximab. Gemcitabine and Oxaliplatin were added. Patient developed HLH, treated with steroids and etoposide. Patient and family decided not to pursue further curative treatment. She had a period of stability, improvement of disease and quality of life but passed away from refractory disease, aged 14.

Patient 2 10 year old boy with a background of severe eczema diagnosed with Nodular lymphocyte predominant Hodgkin Lymphoma stage I. Presented with isolated left inguinal lymphadenopathy which was surgically cleared and entered close surveillance. Recurrent lymphadenopathy occured with flares of eczema but no relapse. At age 14, he was found to have T-cell Histiocyte rich B cell-Lymphoma. He received Burkitt's lymphoma protocol LMB9602 with Rituximab and he had complete metabolic response. This was consolidated using BEAM and autologous stem cell return. He tolerated this well and completed treatment in 2015. He was referred to the adult survivorship clinic at age 20 but has been lost to follow up.

Conclusion These cases highlight the uncertainty of long-term outcome of NLPHL regardless of initial stage or treatment. Research into immunological factors and molecular testing may yield improved future outcomes.

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P-02-16 Pediatric Primary Meningeal Hodgkin lymphoma: A Case Report

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Introduction Involvement of the central nervous system (CNS) and/or the meninges in Hodgkin lymphoma (HL) is extremely rare, with few cases reported in the literature to date [1]. In pediatric patients, CNS involvement occurs predominantly in the setting of metastatic disease, commonly involving extra-axial lesions of the spinal cord. Presentation as a solitary intracranial mass mimicking a meningioma is rarely described and was not reported in a recent review of pediatric clinical trial patients [2]. This report describes an 18-year-old male who presented with primary CNS HL arising in the leptomeninges with minimal systemic disease burden.

Methods The patient was an 18 y/o male with no significant past medical history who presented to the emergency room after a generalized seizure. He experienced intermittent headaches, but no focal symptoms. Upon presentation his labs were within normal limits. An MRI revealed a 4.1 x 2.7 x 2.6 cm lobulated heterogeneous T2 signal enhancing right extra-axial mass lesion with associated dural tail in the right anterolateral frontal convexity with vasogenic edema and mild subfalcine herniation. Levetiracetam was initiated and pediatric neurosurgery performed a right frontal craniotomy and resection of the mass except for a small dural tail.

Results The pathologic work up was diagnostic for classic HL that stained positive for CD30, CD15, and PAX5 (dim), while negative for CD20. A PET/CT only demonstrated occasional small hypermetabolic nodes in the neck (Deauville 4-5). He had stage IV disease and received 6 cycles of N-AVD (Nivolumab, doxorubicin, vinblastine, dacarbazine with dexrazoxane). A PET/CT after 2 cycles demonstrated a complete metabolic response. Repeat MRI imaging at the completion of therapy had a continued response with near complete resolution of flair hyperintensity.

Conclusion Primary meningeal HL is extremely rare (incidence of ~0.9 % for any CNS involvement, and no cases were identified from the 3 most recent cooperative group frontline clinical trials for high risk patients[2]. While a biopsy is challenging, sufficient tissue allowed for accurate diagnosis despite the rarity. Outcomes remain favorable for these patients with current frontline regimens and patients should be reassured that the progression-free survival remains high.

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P-02-17 Hodgkin Lymphoma in a Patient with Down Syndrome: Case Report and Literature Review

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Introduction Children with Down syndrome (DS) have a markedly increased risk of acute leukemias, but Hodgkin lymphoma (HL) is infrequent, with few cases reported in the literature. The underlying relationship between HL and DS remains unclear.

Methods We describe the case of a 7-year-old male with DS diagnosed with classical HL and review the literature. A search was conducted in PubMed using MeSH terms "Down syndrome" AND "Hodgkin disease," limited to patients aged 0–18 and articles in English or Spanish.

Results The patient presented with cervical lymphadenopathy, pallor, weight loss, fever and respiratory distress. Physical exam revealed bilateral cervical, supraclavicular and axillary lymphadenopathy, splenomegaly, and signs of pulmonary involvement. Blood tests showed leukopenia (3,410/mm³), lymphopenia (272/mm³), and anemia (Hb 7 g/dL). Imaging revealed a bulky mediastinal mass. Lymph node biopsy confirmed classical HL, nodular sclerosis subtype ($CD30^+$, $CD15^+$, PAX^+, $EBER^+$, $CD20^-$). Staging Computed Tomography(CT) showed stage IVB disease with extensive lymphadenopathy, hepatosplenomegaly and focal hepatic and splenic lesions. Treatment followed the LH GALOP 2017 protocol (ClinicalTrials.gov ID: NCT03500133): initial ABVD and ESHAP cycles. Interim PET (Positron emission tomography)-CT showed a Deauville score of 3. The patient then received 3 cycles of ABVD and 3 of ESHAP. End-of-treatment PET-CT showed Deauville score 2. Toxicities included CTCAE grade 3 hematologic/infectious complications. The patient remained in complete remission > 27 months without additional radiotherapy.

Only 7 pediatric HL cases in DS have been reported since 1971, all classical subtype, most presenting with B symptoms. Treatment-related toxicity is significant in this population, likely due to increased sensitivity to chemotherapy and underlying immunodeficiency. Some cases experienced relapse, and two were fatal. There is concern regarding long-term sequelae and secondary neoplasms, although none were reported during the limited follow-up periods.

Conclusion HL in DS children is rare and poses therapeutic challenges due to increased toxicity risk. Avoiding radiation when possible and tailoring chemotherapy intensity is essential. Longer follow-up and more reported cases are needed to understand outcomes and refine treatment strategies in this vulnerable population.

P-02-18 Complex case of Hodgkin Lymphoma with underlying Hypoplastic Left Heart Syndrome relapsed with Burkitt Leukaemia, EBV driven, likely related to thymus removal during cardiac repair.

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Introduction Hypoplastic left heart syndrome (HLHS) repair can be followed by the development of lymphoma, particularly in the context of immunosuppression after heart transplantation or in patients with HLHS who also have other conditions that weaken the immune system. There are also reported cases of Burkitt Lymphoma or leukaemia (BLL) following cases of Hodgkin lymphoma (HL), usually post radiation. Up to 40 % of HL cases are associated with the Epstein-Barr virus (EBV). This is a case of an adolescent patient presenting with HL (presented at ISCAYAHL 2022) after cardiac repair and then developing BLL, both EBV positive, with evidence found of immune dysfunction likely due to thymic removal. It raises questions about complexities of cancer treatment in this setting and immune dysregulation [1–4].

Methods Case report

Extensive literature review and expert discussions sought regarding treatment options.

Results 16 yo male presented with a short history of upper respiratory tract symptoms and cervical lymphadenopathy with a significant past history of completion of a fenestrated fontan at age 4 for HLHS, stage IIIB HL treated 2 years prior with A-AVD chemotherapy, morbid obesity (BMI 44), impaired glucose tolerance with metabolic syndrome/insulin resistance, obesity related sleep disordered breathing, plastic bronchitis, mild restrictive lung disease, acanthosis nigricans, and learning difficulties; on anticoagulant therapy as VTE prophylaxis and anti-hypertensive.

Acute Burkitt leukaemia was diagnosed on peripheral blood flow with MYC-IGH fusion detected. Extensive lymphadenopathy and hepatosplenomegaly on scans. Given his previous morbidities and chemotherapy, he proceeded successfully with modified treatment. This included R-COP and dose adjusted EPOCH-R with intercalated methotrexate. He tolerated the treatment and is over 6 months from completion with complete remission. Immunology were extensively involved as well as other subspecialists including palliative care. He remains on Rituximab, needing a desensitisation program due to reaction, and on subcutaneous immunoglobulin.

Conclusion This complex case illustrates many aspects of treating lymphoma. Immune dysregulation can lead to lymphoma amongst other cancers. Treatment can be modified on a per patient basis to enable curative treatment and management of underlying organ dysfunction. Regular immune replacement may need to be considered to prevent development of further issues.

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P-02-19 Role of nivolumab support after autologous stem-cell transplantation in relapsed and refractory Hodgkin lymphoma

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Introduction PURPOSE: to evaluate the efficacy of nivolumab maintenance after autologous stem cell transplantation (autoHSCT) in relapsed or refractory (r/r) classical Hodgkin lymphoma (cHL).The choice for r/r cHL is autoHSCT preceded by chemotherapy. The choice of salvage therapy depends on the treating physician and hospital.

Methods Since 2018, the National Medical Research Center for Hematology of the Russian Ministry of Health has a clinical trial (NCT05660993): Nivo-BeGEV (Nivolumab, Bendamustine, Gemcitabine, Vinorelbine) in patients with r/r cHL. Patients received 2-6 courses of Nivo-BeGEV after confirmation of relapse. Candidates for auto-HSCT received conditioning with BeEAM and auto-HSCT after achieving remission.

Since 2022, the algorithm has been changed: the physician could choose maintenance nivolumab after autoHSCT. The patients could be given maintenance therapy with nivolumab at a dose of 3 mg/kg or 40 mg every two weeks for a year at the discretion of the physician. After the auto-HSCT, patients underwent control PET-CT every 3 months during the first year, every 6 months during the second year, and yearly thereafter. If relapse was suspected after auto-HSCT, PET-CT and biopsy were performed to confirm it and exclude pseudo-progression.

Results Between 2018 and 2024, 115 patients were included in the study: women – 63/115 (50.5 %) and men – 52/115 (49.5 %). The groups of patients were comparable. At the time of data cutoff, all patients are alive. The 1-year event-free survival after auto-HSCT with maintenance nivolumab was 94 % [95 % CI 0,88–1] and without maintenance nivolumab 89 % [95 % CI 0,81–0,98] (p = 0,2342).

Conclusion Study shows that auto-HSCT demonstrates good results in terms of event-free survival. We do not see significant differences within the 20 % confidence interval. This may be due to the inclusion of checkpoint inhibitors in salvage therapy.

S-09 | Adolescents and Young Adults

Chairs: Alex Herrera (Duarte, USA),
Kara Kelly (Buffalo, USA)

S-09-02 Applying Recent Adolescent and Young Adult Clinical Trial Results to Standard of Care Treatment for Adolescents with Hodgkin Lymphoma

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Hodgkin lymphoma (HL) is a highly curable malignancy predominantly affecting adolescents and young adults (AYAs). Treatment options for AYAs with Hodgkin lymphoma (HL) are plentiful, though standard of care therapy varies both across institutions, and also between pediatric and medical oncology providers. As such, therapy for patients of the same age may be significantly different depending on the location to which patients present. Furthermore, risks for acute toxicities and late effects of therapy are significantly different across therapeutic regimens. Given the high cure rates of HL in this patient population, consideration should be given to the impact of these toxicities on individual patients. This session will review the results of recent AYA trials and utilize a case based approach to discuss standard of care therapy for adolescent patients with HL.

S-09-03 A Response-Based ABVD Regimen with or without Radiotherapy for Pediatric Low and Intermediate Risk Hodgkin Lymphoma in Central America and Dominican Republic. A report from AHOPCA

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Introduction 2012 AHOPCA designed a treatment regimen for low-risk (LR) (stage IA, IIA without bulky disease, less than 4 nodal regions) and intermediate-risk (IR) (stage IA or IIA bulky disease, IB, IIA with more than 4 nodal regions, or stage IIIA) Hodgkin lymphoma (HL). The purpose of the protocol was to provide proven effective therapy to improve survival of children with HL in Central America while decreasing the amount of radiation therapy required based on response to chemotherapy.

Methods LR patients received 4 cycles of ABVD (doxorubicin 25mg/m2, bleomycin 10 units/m2, vinblastine 6mg/m2, and dacarbazine 375mg/m2 on days 1 and 14 of every 28-day cycle). Involved field radiotherapy (IFRT) 20 Gy was given only to patients that did not achieve an early adequate response (EAR) after the second cycle of ABVD. IR patients received 6 cycles of ABVD and IFRT at the end of all chemotherapy, according to response status after the second cycle of ABVD (EAR = no RT and not EAR 20Gys).

Results From 8/2012 to 12/2023, 127 eligible patients were evaluable (101 IR and 26 LR). There was a male predominance of 78 % and a median age of 8 years (2-18 years). Eighty-seven percent of LR patients had an EAR and did not require IFRT. Seventy-three percent of IR patients had EAR and did not require IFRT. Of the LR patients with a median follow-up of 5 years 2 (7 %) relapsed and 1 (3.8 %) died. In the LR group the 3-years EFS was 91 % ± 5.9 SE and the OS 97 % ± 3.7SE %. In the IR group 6 (6 %) relapsed, 2 (2 %) abandoned therapy and 3 (3 %) died. In the IR group the 3-year EFS was 91 % ± 3.0 SE % and OS 96 % ± 1.9SE %. Abandonment of therapy was considered an event. There were no grade 4/5 toxicities.

Conclusion This regimen was well tolerated with excellent results for our setting and better than our previously reported results (EFS of 63.3 %), with less toxicity. Abandonment among the intermediate risk group is still a problem and earlier and more aggressive support interventions are needed.

S-09-04 Experience of the Polish Pediatric Leukemia/Lymphoma Study Group with consecutive EuroNet-PHL treatment protocols for classical Hodgkin lymphoma (cHL) in Poland: A real-life summary

Authors Klekawka T[1], Rutynowska-Pronicka O[2], Brozyna A[2], Radwnska M[3], Chaber R[3], Karolczyk G[4], Urbanek-Dadela A[4], Styczynski J[5], Koltan A[5], Kalwak K[6], Kwasnicka J[6], Drabko K[7], Mitura-Lesiuk M[7], Krawczuk-Rybak M[8], Muszynska-Roslan K[8], Badowska W[9], Brzeski T[9], Szczepanski T[10], Ruranska I[10], Laguna P[11], Cieslak M[11], Strek-Cholewinska A[12], Mizia-Malarz A[12], Irga N[13], Stachowicz-Stencel T[13], Mlynarski W[14], Stolarska M[14], Urasinski T[15], Wziatek A[16], Zielezinska K[15], Derwich K[16], Balwierz W[1, 17]
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Introduction Currently available therapies for cHL in children achieve cure rates exceeding 90 %. In the first European treatment program for children and adolescents with cHL, gradually introduced across Europe since January 2007 and implemented in Poland since 2009, a treatment strategy was adopted that aimed to maximize cure rates while minimizing the risk of long-term complications, primarily by reducing indications for radiotherapy (RT). Modifications introduced in subsequent protocols further aimed to limit the use of RT. To evaluate treatment outcomes in children with cHL in Poland treated according to the EuroNet-PHL-C1 protocol, the EuroNet-PHL Interimphase 2013 protocol, and post-C2 recommendations.

Methods Between June 2009 and August 30, 2024, a total of 848 patients with cHL were reported. Of these, 788 patients were evaluated: 416 boys and 372 girls aged 1.8 to 21.9 years (median: 14.7 years). The predominant histological

subtype was nodular sclerosis (NS, n = 606; 76.9 %), followed by mixed cellularity (MC, n = 91; 11.5 %). Central pathology review was performed in 373 cases, while 415 were assessed locally. Based on treatment stratification, 156 patients (19.8 %) were assigned to therapeutic level TL-1, 297 (37.7 %) to TL-2, and 335 (42.5 %) to TL-3.

Results Based on early treatment response assessment, radiotherapy (due to inadequate response) was administered to 295 patients (37.4 %), while it was omitted in 493 patients (62.6 %) who demonstrated adequate response. Events (progression, relapse, or secondary malignancies) occurred in 90 patients (11.4 %). For the entire cohort, the 5-year overall survival (OS) and event-free survival (EFS) rates were 99.7 % and 87.9 %, respectively. In the subgroup treated with both chemotherapy and radiotherapy, the 5-year EFS was 90.9 %, while in the chemotherapy-only group, it was 86.6 %. No statistically significant difference in EFS was observed based on the use of radiotherapy.

Conclusion The treatment outcomes achieved in accordance with EuroNet-PHL protocols suggest that in a selected group of patients with adequate early treatment response, radiotherapy can be safely omitted without significantly compromising treatment efficacy.

S-09-05 Scientific update from the Global NLPHL One Working Group (GLOW)

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Introduction There is no standard of care for patients diagnosed with nodular lymphocyte predominant Hodgkin lymphoma (NLPHL). No frontline clinical trials have included NLPHL patients since the 2010's, thus hindering NLPHL research progress. The Global NLPHL One Working Group (GLOW), an international research network initiated in 2020, collaboratively optimizes diagnosis, care, and outcomes for, and with, patients of all ages diagnosed with NLPHL.

Methods Since 2020, GLOW established working groups and strategic projects to describe and address critical gaps in progressing NLPHL research worldwide. Four research committees, overseen by an executive committee, were tasked with initiating collaborative NLPHL research, with an additional committee tasked with disseminating research findings. Initial projects included building an international retrospective database, describing global practice patterns, and collecting baseline patient-reported outcomes. Recent projects explored healthcare professional, patient, and care partner research and care needs [1–4].

Results In 5 years, GLOW has grown to include over 200 researchers and patient advocates from 34 countries, published 5 papers, and built the largest cohort of clinical NLPHL data to date. Its research roadmap (Palese et al. 2025), informed by NLPHL experts, patients, and care partners, outlines a strategic framework and initial objectives for NLPHL research. The GLOW practice patterns paper describes worldwide variation in NLPHL care between clinicians treating pediatric versus adult populations (Lo et al. 2022). In 2024, after expanding its early stage retrospective cohort (Binkley et al. 2020), GLOW published results from over 2000 patients across all ages and stages and created the risk-predictive Lymphocyte-Predominant International Prognostic Score (LP-IPS) (Binkley et al. 2024). These data show that progression-free survival curves continue to fall over time regardless of initial therapy intensity. Thus, care decisions over time must be strategic given that most patients (> 70 %) equire further treatment during their lifetime. GLOW continues to recruit patients on its NLPHLPRO study and is testing a decision aid for patients diagnosed with stage IA NLPHL.

Conclusion GLOW's strategic framework and initial priorities are working to deepen global, collaborative NLPHL research. GLOW is applying this knowledge in its planned prospective trial to establish a standard of care and optimize treatment for patients of all ages diagnosed with NLPHL.

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S-10 | Relapse Treatments & Challenging Cases

Chairs: Christopher Forlenza (New York, USA), Mathieu Simonin (Paris, France)

S-10-01 Therapeutic Success and Strategic Uncertainty: The Evolving Role of Salvage Therapy in Hodgkin Lymphoma in the United States

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Recent therapeutic advances for relapsed or refractory (R/R) Hodgkin lymphoma (HL) has been most notable for the emergence of novel immunotherapeutic agents, chiefly brentuximab vedotin and checkpoint inhibitors, which reshaped salvage therapy in the United States and throughout the world . Clinical trials have evaluated these agents across various strategies, examining mono- and combination regimens in both the pre- and post-transplant settings (Cole et al., 2018, Moskowitz et al., 2021, Advani et al., 2021, Armand et al., 2019, Armand et al., 2023, Herrera et al., 2023, Moskowitz et al., 2015, Harker-Murray et al., 2023). These efforts have led to well-tolerated modern salvage regimens administered in the ambulatory setting, with excellent response rates, declining utilization of radiation therapy, and improved long-term progression-free survival in comparison to historical outcomes. As a result, while high-dose chemotherapy and autologous stem cell transplant remain the standard of care for the majority of patients with R/R HL, there is a growing interest in transplant-free approaches to salvage meant to minimize late effects from therapy (Daw et al., 2025).

However, the increased utilization and success of immunotherapy-based regimens in the frontline setting have introduced a new era of uncertainty for patients with R/R HL (Herrera et al., 2024). Although fewer patients now progress after frontline therapy, the treatment approach to patients requiring salvage therapy remains an area of ongoing debate. The mechanisms of resistance and the possibility of re-challenging patients with immunotherapy agents,

optimal sequencing of salvage regimens, the role for radiation in an increasing radiation-naïve population, and the need for transplant in this evolving context remain largely undefined. We will aim to explore these critical knowledge gaps facing oncologists today, including the need for biomarker-driven risk stratification and clinical trials designed for patients with prior exposure to immunotherapy. Addressing these challenges will be essential to sustain current levels of success in salvage therapy while continuing to minimize long-term treatment related toxicity [1–10].

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S-10-03 Safety and Efficacy in Pediatric Patients with Relapsed/Refractory Classic Hodgkin Lymphoma enrolled on an Intergroup Randomized Phase II Study of the Combinations of Ipilimumab, Nivolumab and Brentuximab Vedotin (E4412)

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Introduction The Phase 1/2 ECOG-ACRIN sponsored intergroup trial E4412 (NCT01896999) investigated brentuximab vedotin (BV) combined with the checkpoint inhibitors nivolumab (N) and ipilimumab (I) in patients with relapsed or refractory classic Hodgkin lymphoma (R/R HL). Here we present the safety and efficacy results for the cohort of pediatric patients aged 12-17 years.

Methods Patients were randomly assigned to treatment with the doublet of BV/N or triplet of BV/N/I, with the following dosing: BV 1.8 mg/kg every 21 days for up to 16 cycles; Nivolumab 3 mg/mg every 21 days for up to 34 cycles; Ipilimumab 1 mg/kg every 9 weeks for up to 9 doses. Response evaluation by PET/CT was performed after 4 cycles. Transplant-eligible patients with CR could discontinue protocol therapy to receive a consolidative autologous stem cell transplant (ASCT).

Results Sixteen pediatric patients with a median age of 16 (range 12-17) were randomized. 75 % of patients had received only 1 prior line of treatment with none having previously received BV and only 1 patient with prior ASCT. All patients were treated (8 in each arm) and included in the pediatric safety analysis cohort receiving at least one cycle of therapy. There were four reported grade (gr) 3 or greater treatment-related toxicities: lymphopenia (gr 3) and neutropenia (gr 3) on the BV/N arm; and neutropenia (gr 4) and rash (gr 3) on the BV/N/I arm. Rash of any grade was more common in patients treated with BV/N/I arm (n = 6) compared to BV/N (n = 1). Peripheral sensory neuropathy was reported in 2 patients (BV/N, gr 2, n = 2) There were no grade 5 toxicities. Fourteen patients (7 in each arm) were evaluable for response. The CR rate on both the BV/N and BV/N/I arms was 100 %. The median progression-free survival (PFS) follow up was 31.5 months (15.4 – 48.6). The 24-month PFS was 42.9 % for BV/N (95 % CI: 9.8-73.4) and 100 % for BV/N/I (p = 0.02). Six patients (2 BV/N; 4 BV/N/I) discontinued protocol therapy to receive a consolidative ASCT. The 24-month PFS for patients consolidated with an ASCT was 100 %.

Eight patients (3 BV/N and 5 BV/N/I) treated without an ASCT had a 12-month PFS of 20 % (95 % CI: 0.8 – 58.2) and 100 % for the BV/N and BV/N/I patients, respectively (p = 0.05).

Conclusion Pediatric patients receiving both BV/N and BV/N/I had 100 % CR rate with limited toxicity. Although, this is a small cohort, there have been no progression events observed in patients treated with BV/N/I, including patients treated without a consolidative ASCT.

S-10-04 Relapsed Hodgkin Lymphoma: Not suited to “one size fits all” approach

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DOI 10.1055/s-0045-1812989

Introduction The “standard-of-care” for Relapsed/Refractory Hodgkin lymphoma (R/R HL) remains elusive. Chemotherapy combined with brentuximab or immune-checkpoint inhibitors is widely practiced in adequately resourced settings. However, in resource-limited settings, salvage regimen continue to comprise of chemotherapy alone with optimal salvage chemotherapy continuing to be unclear. Limited access to ASCT/immunotherapy further makes management at relapse challenging in LMIC. InPOG-HL-17-02, a prospective/collaborative study evaluated outcomes using a risk-stratified, response-adapted approach.

Methods Patients were risk-stratified based on time since frontline-therapy, Stage, B- symptoms and previous radiation. Gemcitabine-Vinorelbine (GV) was planned as salvage chemotherapy. Patients with low-risk relapse were to receive GV and radiation subject to complete metabolic response (CMR) after two cycles. Those with suboptimal response received ICE chemotherapy followed by ASCT. Patients with high-risk relapse were to proceed to ASCT after CMR.

Results Seventy patients were enrolled from 9 centers over 58 months (December 2018-September 2023). The median age of this cohort was 12.5 years, with M:F ratio of 6:1. Recruitment/compliance were significantly compromised due to the COVID-19 pandemic. 37.1 % and 62.9 % patients were classified as low and high-risk relapse respectively. Sixty-two patients had received ABVD and 11 patients had previously received radiation as frontline therapy. 80 % received GV as first salvage therapy. 20 % received alternative protocols/additional drugs. Only 27 had CMR at response evaluation. Twelve were switched to ICE chemotherapy with 2 achieving CMR. 51 patients were eligible to receive ASCT but only 14 underwent the procedure. Eighteen and 10 patients received consolidative radiation and immunotherapy respectively. All 7 patients who received immunotherapy as part of first salvage treatment continue to be alive in remission. At a median of 35 months from relapse the OS and EFS are 74.3 % and 67.1 %.

Conclusion R/R HL is eminently salvageable even in LMIC. GV achieved CMR only in 37.5 %. Switching to ICE regimen did not yield additional benefit. Novel strategies for these patients may be more prudent. Only a third of those eligible for ASCT could undergo the procedure. Access to immunotherapy and ASCT offered significant survival advantage [1–4].

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S-10-05 Hodgkin lymphoma associated hemophagocytic lymphohistiocytosis

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Introduction Hemophagocytic lymphohistiocytosis (HLH) secondary to malignancy is a lifethreatening disorder characterized by high inflammatory cytokine production induced by excessive immune activation.

Methods 15 years old boy was diagnosed with classical Hodgkin lymphoma, nodular sclerosis, stage IVB. He started treatment according to EuroNet-PHL-C2 protocol. Early response assessment after two OEPA cycles showed mixed response with decresed volume and FDG accumulation in lymph node regions and progression in bone/bone marrow lesions with recurrence of B symptoms. Progression was confirmed histologically by trephine biopsy in iliac crest region. First cycle of salvage chemotherapy IGEV was complicated with HLH, which was succesfully treated with corticosteroids. After the second IGEV cycle a more severe episode of HLH developed and treatment with corticosteroids and i.v. etoposide was introduced with clinical improvement after second dose of etoposide. Response assessment by PET/CT showed progressive disease, therefore Brentuximab vedotin and bendamustine were given together with continuing treatment of HLH (corticosteroids, etoposide). Due to prolonged bone marrow aplasia autologous stem cells were transfused and immediately hepatosplenomegaly together with laboratory findings of HLH worsened, PCR exams showed repeatedly no presence of EBV, genetic testing detected no pathogenic variant or a likely pathogenic variant related to congenital predispositions to oncological diseases or imunological disorders, CGH array confirmed normal male profile and no significant aberration (microdeletion or microduplication) was detected. Subsequently, further progression of Hodgkin lymphoma was documented, patient became critically ill. Treatment was changed to a regimen with brentuximab and nivolumab (BV + Nivo). The first cycle of BV + Nivo led to swift improvement of the patient’s health condition and alleviation of HLH symptoms with possibility to discontinue corticosteroids. Response assessment after the 4th cycle of BV + Nivo showed first complete remission. Afterwards BEAM megachemotherapy with autologous stem cell transplantation and maintanance treatment with a total eight doses of nivolumab was given, patient remained in complete remission.

Results Further immunologic testing confirmed a disruptive variant of RELA without clinical symptoms of this disorder in the medical history.

Conclusion Primary targeting of HLH followed by HL treatment once the HLH condition was stabilized was an effective approach in our patient.

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