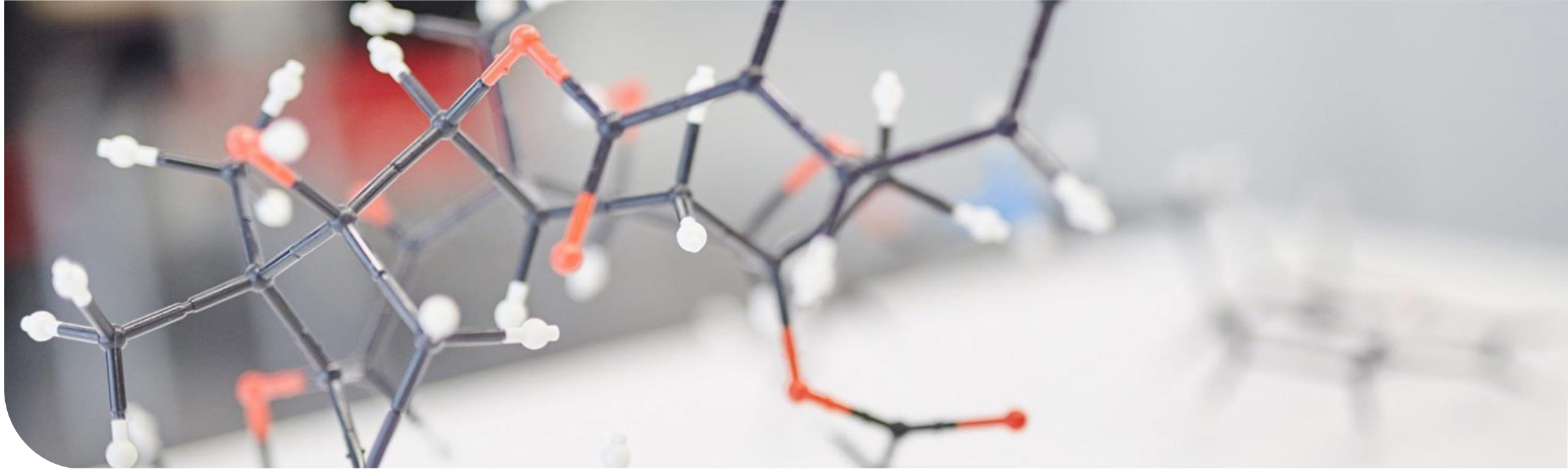

Brentuximab Vedotin 2025 Post-Congress Deck

VV-MEDMAT-123828

July 2025

Better Health, Brighter Future

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LOC, local operating company; MSL, medical science liaison.

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*IIR (investigator-initiated research) and Pfizer sponsored publications developed independently of Takeda

ASCO, American Society of Clinical Oncology; EHA, European Hematology Association; ICML, International Congress on Malignant Lymphoma

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ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; BV+AVD, brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine; BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; CHP, cyclophosphamide, doxorubicin, prednisone; EORTC, European Organisation for Research and Treatment of Cancer; escBEACOPP, escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; GHSG, German Hodgkin Study Group; N+AVD, nivolumab, doxorubicin, vinblastine, and dacarbazine

ASCO – Abstract #7077

Frontline brentuximab vedotin and CHP in patients with peripheral T-cell lymphoma with <10% CD30 expression: primary analysis results from the phase 2 SGN35-032 study

Swaminathan P. Iyer, [1] Deepa Jagadeesh,[2] Eva Domingo Domènech,[3] Fabio Benedetti,[4] Antonia Rodriguez Izquierdo,[5] Krimo Bouabdallah,[6] Umberto Vitolo,[7] Tim M. Illidge,[8] Jingmin Liu,[9] Eeman Shaikh,[9] Steven M. Horwitz[10]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Cleveland Clinic Taussig Cancer Institute and Case Comprehensive Cancer Center, Cleveland, OH, USA; [3]Institut Català d'Oncologia – Hospital Duran i Reynals, Barcelona, Spain; [4]University of Verona, Verona, Italy; [5]Hospital 12 de Octubre, Madrid, Spain; [6]Service d'hematologie clinique et therapie cellulaire, CHU Haut-Leveque, Pessac, France; [7]Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy; [8]The Christie NHS Foundation Trust, Manchester, UK; [9]Pfizer, Bothell, WA, USA; [10]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA

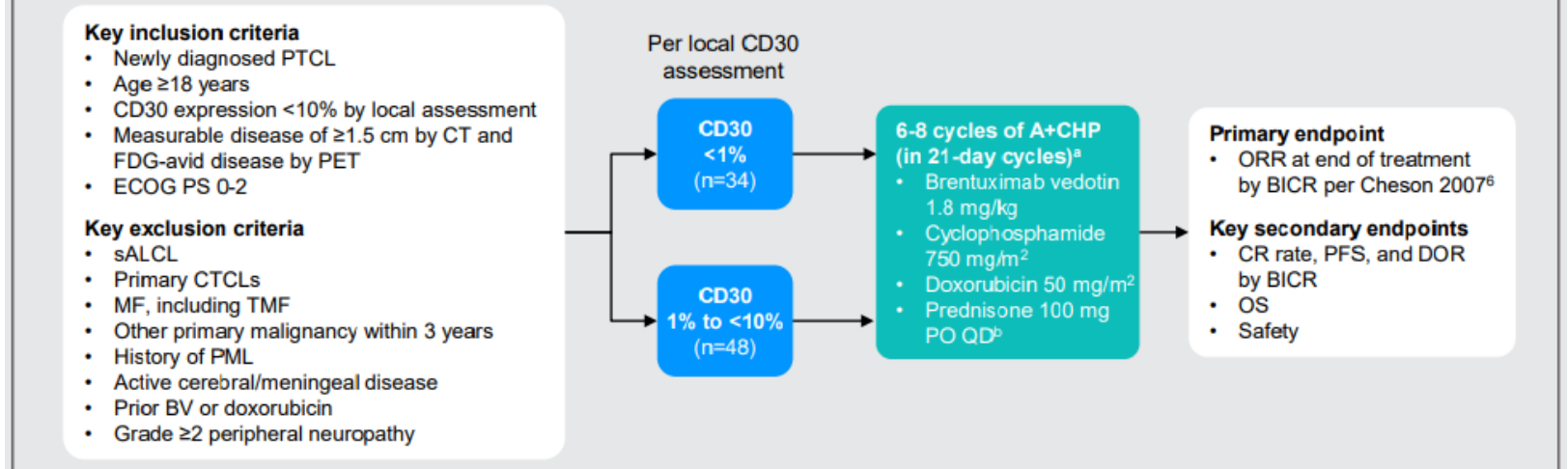
Background

- BV, an antibody-drug conjugate targeting CD30, has shown single-agent activity in several lymphomas regardless of CD30 expression[3,4]
- The BV combination therapy of A+CHP was approved as a frontline treatment for patients with sALCL or other CD30-positive PTCL subtypes based on results from the phase 3 ECHELON-2 study (NCT01777152)[1,4]
    - A+CHP had a 30% risk reduction in PFS (stratified hazard ratio [HR], 0.70; 95% CI, 0.53-0.91; P=0.0077) and an OS benefit (HR, 0.72; 95% CI, 0.53-0.99; P=0.0424)[1]
- While high CD30 expression is a diagnostic characteristic of sALCL, CD30 expression is more variable in other PTCL subtypes[1]
- The SGN35-032 study is evaluating whether frontline A+CHP may also demonstrate efficacy in patients with non-sALCL PTCL with <10% CD30 expression[5]
- We report primary analysis results of SGN35-032

Methods

- SGN35-032 (NCT04569032; EudraCT 2020-002336-74) is an open-label, dual-cohort, global, multicenter, phase 2 study (Figure 1)
- Patients with newly diagnosed non-sALCL PTCL with <10% CD30 expression (by standard immunohistochemistry by local pathology assessment) were enrolled
  - Patients were assigned to either CD30 <1% or CD30 1% to <10% cohorts
- All patients received 21-day cycles of A+CHP for up to 6 to 8 cycles
- The primary endpoint, ORR following the completion of study treatment, was assessed by blinded independent central review (BICR) per Cheson 2007[6]
- Secondary endpoints included safety and complete response (CR) rate, PFS, OS, and duration of response (DOR)
- Efficacy endpoints are reported per central CD30 assessment unless otherwise noted

Figure 1: Study design



CT, computed tomography; CTCL, cutaneous T-cell lymphoproliferative disorders and lymphomas; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; MF, mycosis fungoides; PET, positron emission tomography; PML, progressive multifocal leukoencephalopathy; PO, orally; QD, once daily; TMF, transformed mycosis fungoides.
[a]Brentuximab vedotin, cyclophosphamide, and doxorubicin were administered by intravenous infusion on day 1 of each cycle. [b]Prednisone was administered orally on days 1 to 5 of each cycle.

Results

- As of July 22, 2024, a total of 82 patients received ≥1 dose of A+CHP, including 34 in the CD30 1% to < 10% cohort and 48 in the CD30 1% to < 10% (per local assessment)
  - Per central CD30 assessment, 23 patients were included in the CD30 <1% cohort, and 31 were included in the CD30 1% to < 10% cohort
- At data cutoff, no patients were still receiving A + CHP; median follow-up was 15.7 months
- Baseline characteristics were generally balanced between the 2 cohorts (Table 1)

Table 1: Demographics and baseline disease characteristics

	CD30 <1%[a] (n=34)	CD30 1% to <10%[a] (n=48)	Total (N=82)
Age, median (range), years	63.0 (24-78)	64.0 (32-80)	63.5 (24-80)
Age group, n (%)			
<65 years	19 (56)	28 (58)	47 (57)
≥65 years	15 (44)	20 (42)	35 (43)
Race, n (%)			
Asian	2 (6)	4 (8)	6 (7)
Black or African American	2 (6)	2 (4)	4 (5)
White	26 (76)	37 (77)	63 (77)
Other/unknown/not reportable	4 (12)	5 (10)	9 (11)
ECOG PS, n (%)[b]			
0	15 (44)	21 (44)	36 (44)
1	16 (47)	22 (46)	38 (46)
2	2 (6)	5 (10)	7 (9)
Missing	1 (3)	0	1 (1)
Disease diagnosis, n (%)			
PTCL-NOS	18 (53)	19 (40)	37 (45)
Nodal TFH cell lymphoma	13 (38)	26 (54)	39 (48)
Other	3 (9)	3 (6)	6 (7)
Baseline IPI score, n (%)			
0/1	6 (18)	11 (23)	17 (21)
2/3	22 (65)	33 (69)	55 (67)
4/5	5 (15)	3 (6)	8 (10)
Missing	1 (3)	1 (2)	2 (2)

IPI, International Prognostic Index; PTCL-NOS, peripheral T-cell lymphoma, not otherwise specified; TFH, T-follicular helper.
[a]CD30 expression per local testing. [b]The last nonmissing value before or on the day of first study treatment.

Iyer SP, et al. Abstract 7077. Presented at the 2025 American Society of Clinical Oncology Annual Meeting | May 30-June 3, 2025 | Chicago, IL

Results

- Overall, the median treatment duration was 18.0 weeks (range, 3-24 weeks)
- At end of treatment, ORR was 77%, with CR rate of 63% (Table 2)
  - In the CD30 < 1% cohort, ORR was 61%, with CR rate of 52%
  - In the CD30 1% to < 10% cohort, ORR was 81%, with CR rate of 71%
- Overall median DOR was 15.9 months but NR in either cohort

Table 2: Response by BICR by CD30 status

	CD30 <1%	CD30 1% to <10%	Total
Per local CD30[a]	**n=34**	**n=48**	**N=82**
Response at EOT, n (%)[b]			
CR	19 (56)	33 (69)	52 (63)
PR	6 (18)	5 (10)	11 (13)
SD	0	3 (6)	3 (4)
PD	4 (12)	5 (10)	9 (11)
NE[c]	5 (15)	2 (4)	7 (9)
CR rate (95% CI), %[d]	56 (37.9-72.8)	69 (53.7-81.3)	63 (52.0-73.8)
ORR (95% CI), %[d]	74 (55.6-87.1)	79 (65.0-89.5)	77 (66.2-85.4)
Per central CD30[a]	**n=23**	**n=31**	**N=82[e]**
Response at EOT, n (%)[b]			
CR	12 (52)	22 (71)	52 (63)
PR	2 (9)	3 (10)	11 (13)
SD	1 (4)	1 (3)	3 (4)
PD	5 (22)	2 (6)	9 (11)
NE[c]	3 (13)	3 (10)	7 (9)
CR rate (95% CI), %[d]	52 (30.6-73.2)	71 (52.0-85.8)	63 (52.0-73.8)
ORR (95% CI), %[d]	61 (38.5-80.3)	81 (62.5-92.5)	77 (66.2-85.4)

EOT, end of treatment; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Based on response either at end of treatment or the first assessment after the last dose of study treatment. [b]CR, PR, SD, and PD per Cheson 2007 per independent assessor. CR, PR, SD, PD, and NE are mutually exclusive. [c]NE includes patient with no postbaseline response assessments. [d]Two-sided 95% exact CI, computed using the Clopper-Pearson method. [e]Per central testing, 28 patients either had CD30 ≥10% or were missing CD30 results.

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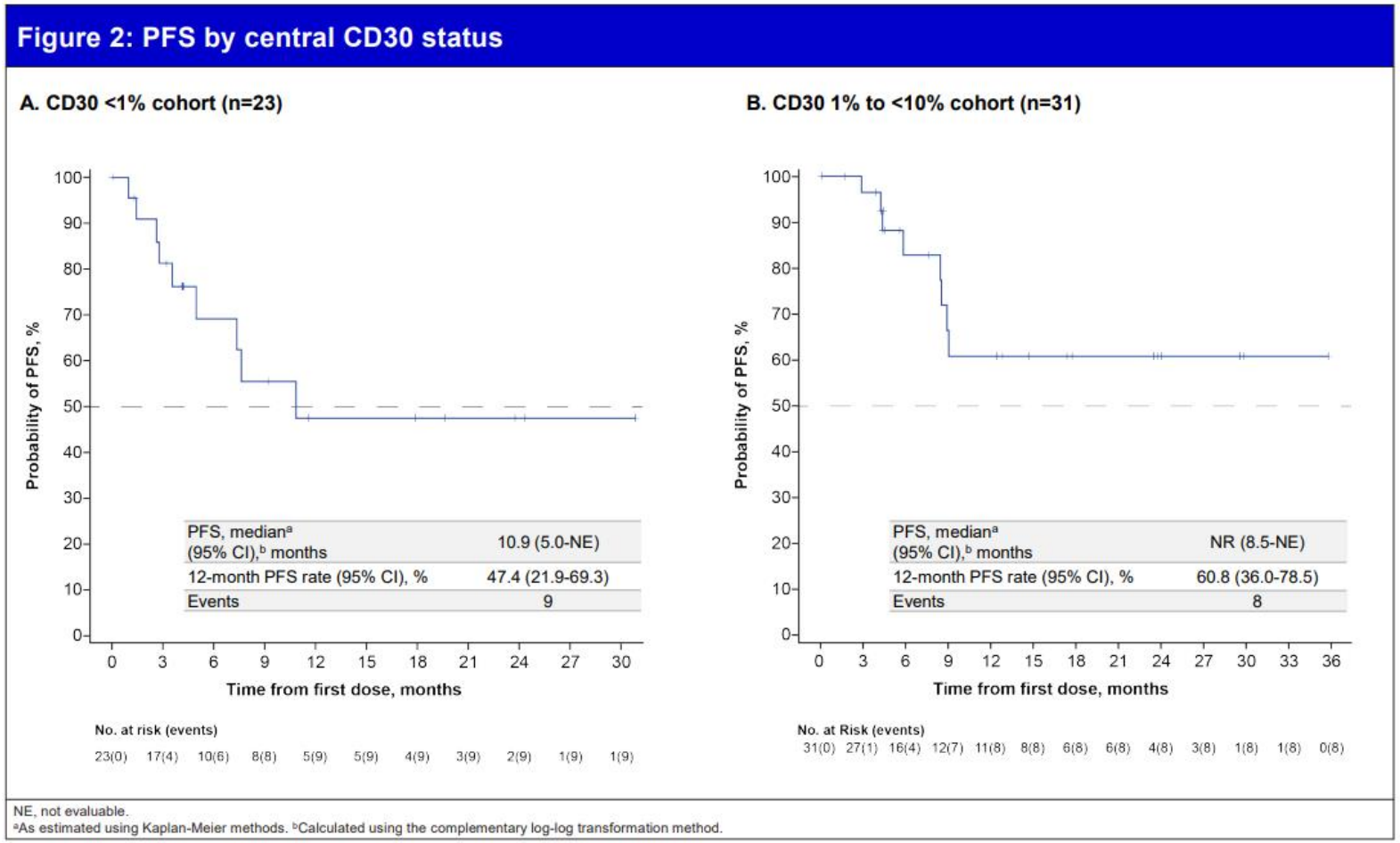
Results

- Median PFS was 10.9 months in the CD30 <1% cohort, NR in the CD30 1% to <10% cohort, and 12.7 months in the overall population (Figure 2)

Figure 2: PFS by central CD30 status



NE, not evaluable.
[a]As estimated using Kaplan-Meier methods. [b]Calculated using the complementary log-log transformation method.

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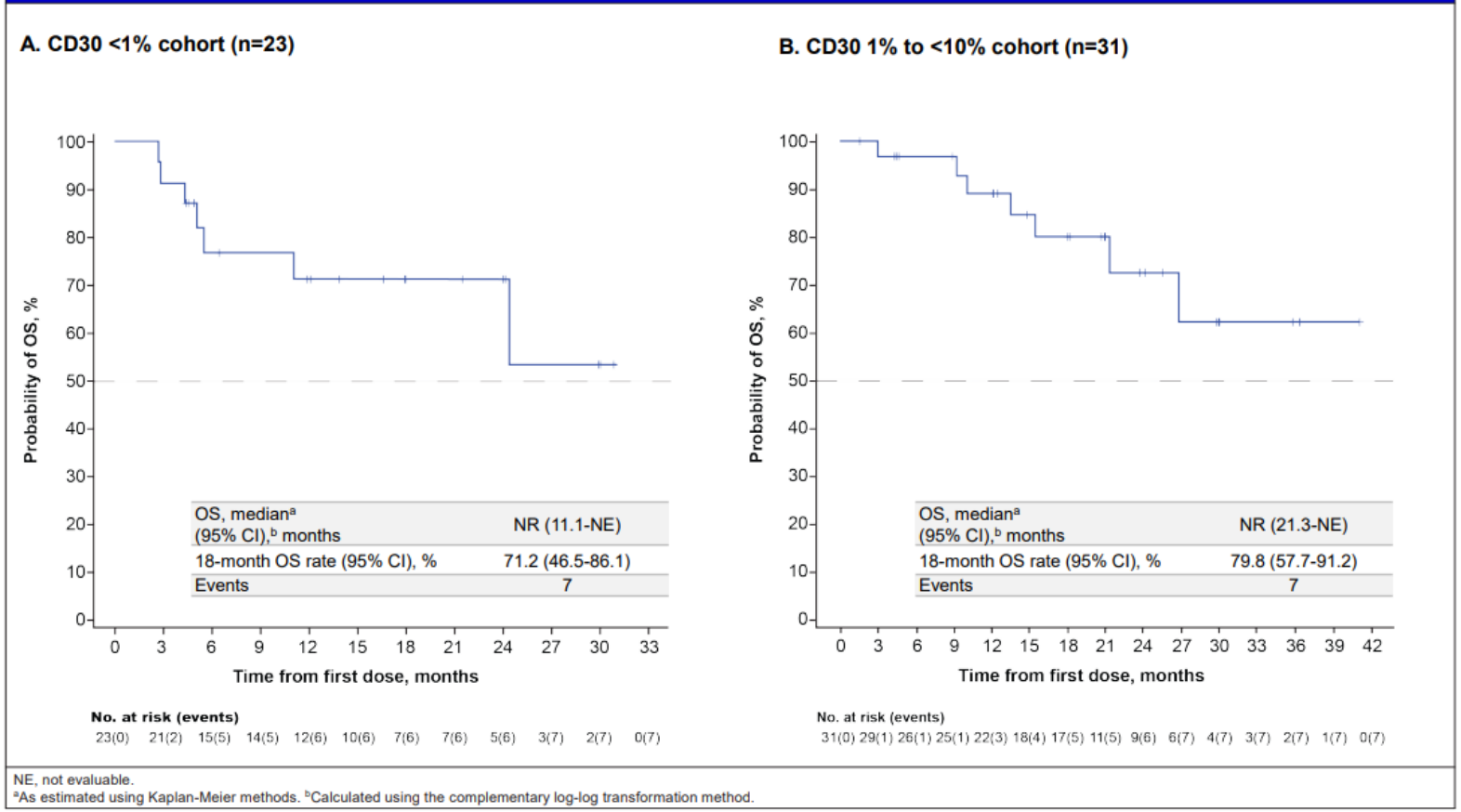
Results

- Median OS was NR in the CD30 <1% cohort, CD30 1% to <10% cohort, and overall population (Figure 3)

Figure 3: OS by central CD30 status



NE, not evaluable.
[a]As estimated using Kaplan-Meier methods. [b]Calculated using the complementary log-log transformation method.

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Safety Profile

- Most patients (95%) had a treatment-emergent adverse event (TEAE), with 59% having a grade ≥3 TEAE (Table 3)
  - The most common (≥10%) overall grade ≥3 TEAEs were neutropenia (18%), febrile neutropenia (17%), and anemia (10%)
- Treatment-related deaths were reported in 2 patients: decreased appetite and general physical health deterioration
- TRAEs led to treatment discontinuation in 3 patients (4%)
  - Decreased appetite, febrile neutropenia, and pneumonitis (1 patient each)
- After last treatment, 13 patients (38%) and 14 (29%) in the CD30 <1% and CD30 1% to <10% cohorts, respectively, received autologous stem cell transplant

Table 3: Summary of TEAEs

	CD30 <1%[a] (n=34)	CD30 1% to <10%[a] (n=48)	Total (N=82)
Any-grade TEAEs, n (%)	32 (94)	46 (96)	78 (95)
Grade ≥3 TEAEs, n (%)	22 (65)	26 (54)	48 (59)
Most common (≥10% of total patients)			
Neutropenia	4 (12)	11 (23)	15 (18)
Febrile neutropenia	6 (18)	8 (17)	14 (17)
Anemia	2 (6)	6 (13)	8 (10)
Treatment-related TEAEs[b]	25 (74)	40 (83)	65 (79)
Most common (≥20% of total patients)			
Peripheral sensory neuropathy	11 (32)	16 (33)	27 (33)
Diarrhea	7 (21)	13 (27)	20 (24)
Nausea	7 (21)	13 (27)	20 (24)
Neutropenia	4 (12)	12 (25)	16 (20)
Serious TEAE, n (%)	15 (44)	16 (31)	31 (38)
Treatment related	9 (26)	12 (25)	21 (26)
BV related	9 (26)	10 (21)	19 (23)
TEAEs leading to dose treatment discontinuation, n (%)	2 (6)	4 (8)	6 (7)[c]
Treatment related	1 (3)	2 (4)	3 (4)[d]
BV related	1 (3)	2 (4)	3 (4)

[a]CD30 expression per local testing. [b]Per investigator determination of relatedness to any study drug. [c]These included anemia, colitis, cutaneous T-cell lymphoma, decreased appetite, febrile neutropenia, and pneumonitis. [d]These included pneumonitis, decreased appetite, and febrile neutropenia.

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Author's Conclusions

- Brentuximab vedotin (BV) combined with cyclophosphamide, doxorubicin, and prednisone (A+CHP) demonstrated clinically meaningful efficacy as a frontline therapy in patients with nonsystemic anaplastic large cell lymphoma (non-sALCL) peripheral T-cell lymphoma (PTCL) regardless of CD30 expression
  - Objective response rate (ORR) at end of treatment was comparable for the CD30 <1% (61%) and CD30 1% to <10% (81%) cohorts
  - Progression-free survival (PFS) and overall survival (OS) were similar for the CD30 <1% (10.9 months and not reached [NR], respectively) and 1% to <10% (NR and NR, respectively) cohorts
- Safety was consistent with the known safety profile of A+CHP, with no new safety signals
- This study demonstrated that the efficacy and safety of A+CHP in non-sALCL PTCL with CD30 <10% were comparable to those of a similar population from ECHELON-2 with CD30 ≥10%[1,2]
- Results show that A+CHP is effective for patients with nonsALCL PTCL regardless of CD30 expression, supporting the proposed, multifaceted mechanism of action of BV in combination with CHP

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References & Acknowledgements

References

1. Horwitz S, et al. Ann Oncol. 2022;33(3):288-298. 2. Horwitz S, et al. Lancet. 2019;393(10168):229-240. 3. Jagadeesh D, et al. Oncologist. 2022;27(10):864-873. 4. Adcetris (brentuximab vedotin). Prescribing information. Seagen; 2025. 5. Iyer SP, et al. J Clin Oncol. 2024;42(16 suppl). Abstract 7069. 6. Cheson BD, et al. J Clin Oncol. 2007;25(5):579-586.

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ASCO – Abstract #7044

Circulating tumor DNA assessment in patients with early-stage classical Hodgkin lymphoma treated with combination of brentuximab vedotin and nivolumab

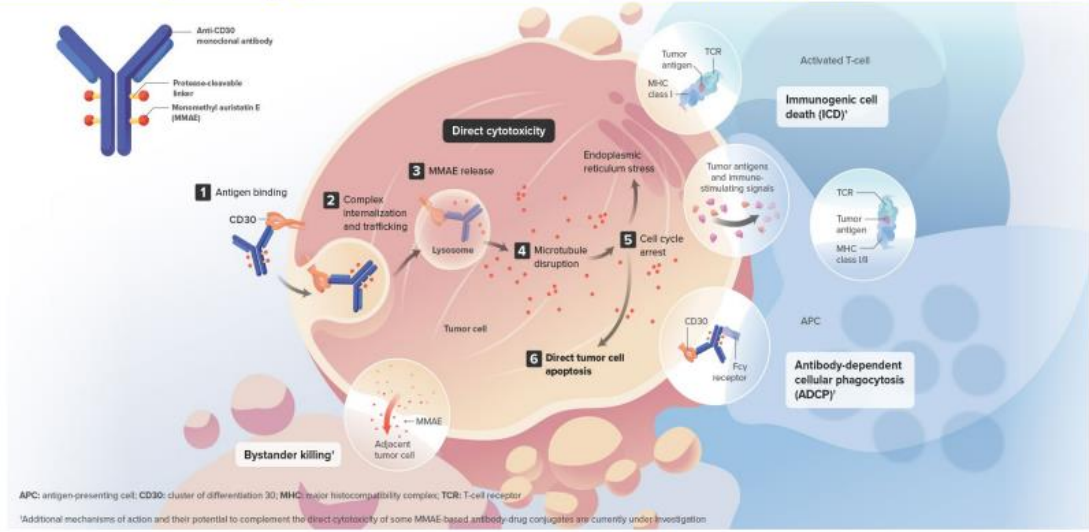
Ryan C. Lynch, [1] Nancy L. Bartlett,[2] John M. Burke,[3] Yuliya Linhares,[4] Eva Domingo Domenech,[5] Wojciech Jurczak,[6] Uwe Hahn,[7] Hun Ju Lee,[8] Radhakrishnan Ramchandren,[9] Alison Moskowitz,[10] Christopher A. Yasenchak,[11] H. Miles Prince,[12] Jin Yao,[13] Wenchuan Guo,[13] Michelle Fanale,[13] Griffith Davis,[13] Evelyn Rustia,[13] Linda Ho,[13] Hailing Lu,[13] Jeremy S. Abramson [14]

[1]Fred Hutchinson Cancer Center, University of Washington, Seattle, WA, USA; [2]Siteman Cancer Center, Washington University School of Medicine, St Louis, MO, USA; [3]Rocky Mountain Cancer Centers, US Oncology Research, Aurora, CO, USA; [4]Miami Cancer Institute, Miami, FL, USA; [5]Hospital Duran i Reynals, Institut Catala d'Oncologia, Barcelona, Spain; [6]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [7]Royal Adelaide Hospital, Adelaide, SA, Australia; [8]MD Anderson Cancer Center, Houston, TX, USA; [9]University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [10]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [11]US Oncology Research, Willamette Valley Cancer Institute and Research Center, Eugene, OR, USA; [12]Epworth Healthcare, Melbourne, VIC, Australia; [13]Pfizer, Bothell, WA, USA; [14]Massachusetts General Hospital, Boston, MA, USA

Background

- BV is an ADC approved in combination with doxorubicin, vinblastine, and dacarbazine for patients with cHL (Figure 1)[3]
- A previous study in patients with nonbulky early-stage cHL showed preserved efficacy and improved safety with BV plus doxorubicin and dacarbazine regimen after vinblastine was omitted[4]
- Results from the phase 2 SGN35-027 part C study have shown promising efficacy and tolerability with BV and nivolumab in combination with chemotherapy in patients with early-stage cHL in the first-line setting[5]
- Earlier results from the present study and in published literature suggested that ctDNA can be detected in patients with cHL, with molecular response potentially complementing imaging assessments[6,7]
- Here, we report on the use of an ultrasensitive assay for ctDNA detection in patients with early-stage cHL to explore its utility in this population

Figure 1: BV, a CD30-directed ADC consisting of 3 components: (1) an anti-CD30 monoclonal antibody (cAC10), (2) a protease-cleavable mc-vc linker, and (3) the microtubule-disrupting agent MMAE

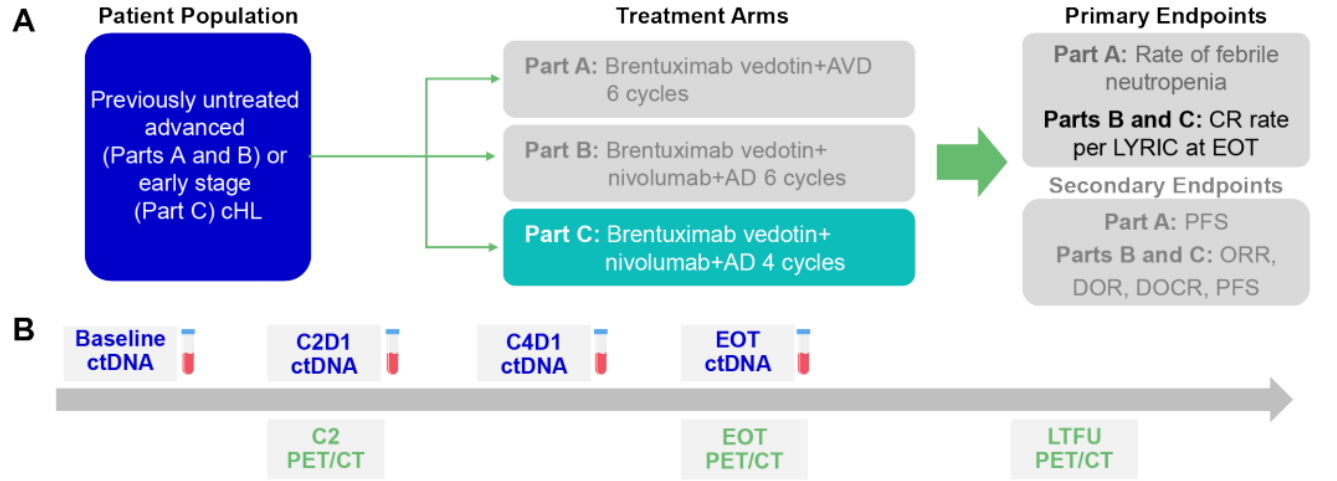


ADCP, antibody-dependent cellular phagocytosis; APC, antigen-presenting cell; CD30, cluster of differentiation 30; ICD, immunogenic cell death; mc-vc, maleimidocaproyl-valine-citrulline; MHC, major histocompatibility complex; MMAE, monomethyl auristatin E; TCR, T-cell receptor.

Methods

- SGN35-027 is an open-label, multipart, multicenter, phase 2 study (Figure 2A)
- The part C portion of the study enrolled patients with Ann Arbor stage I/II cHL without bulky disease (< 10 cm in tumor diameter on computed tomography [CT])
- Patients received 4 cycles of BV 1.2 mg/kg, nivolumab 240 mg, doxorubicin 25 mg/m^2, and dacarbazine 375 mg/m^2 (AN+AD) intravenously on days 1 and 15 of each 28-day cycle
- Responses were assessed by positron emission tomography [PET]/CT according to Lugano classification[8] with LYRIC[9] at cycle 2 day 25-28 (C2) and at EOT, 30 to 37 days after last dose of study drug (Figure 2B)
- Plasma samples were collected at baseline, cycle 2 day 1 (C2D1), C4D1, and EOT. Samples from 36 patients were submitted for ctDNA analysis using phased variant enrichment and detection sequencing (PhasED-seq, Foresight Diagnostics, Boulder, CO), an ultrasensitive minimal residual disease assay for B-cell lymphomas (Figure 2B)
- PET/CT results were compared with ctDNA dynamic changes in patients with detectable baseline ctDNA

Figure 2: SGN35-027 part C study design and ctDNA sample collection schedule



AD, doxorubicin and dacarbazine; AVD, doxorubicin, vinblastine, and dacarbazine; CR, complete response; DOCR, duration of CR; DOR, duration of response; LTFU, long-term follow-up; ORR, objective response rate; PFS, progression-free survival.

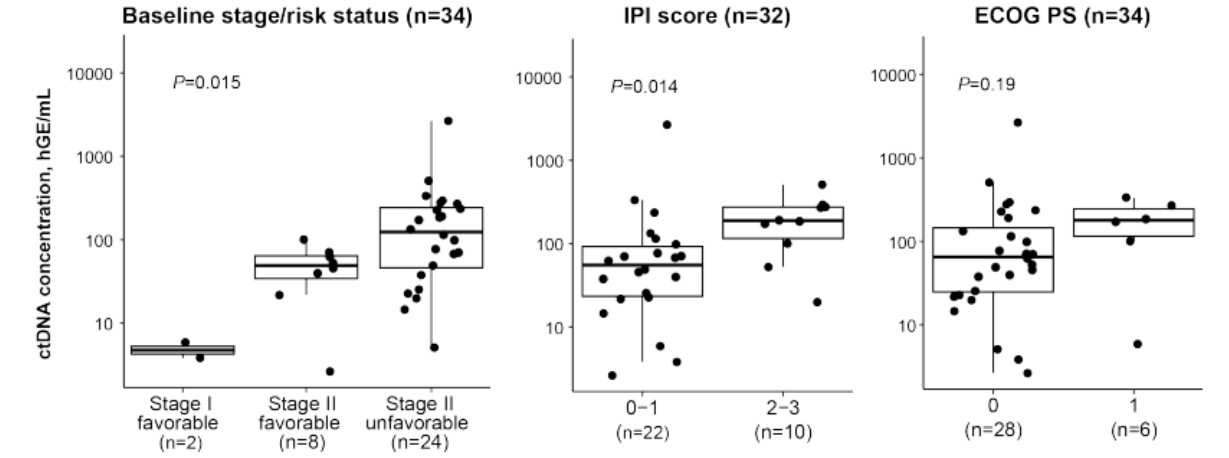
PhasEDseq is a new method to detect ctDNA through phased variants to tumor fractions on the order of ppm.[10] Quantitative levels of ctDNA were measured in hapoid genome equivalents (hGEs) per mL.

Lynch RC, et al. Abstract 7040. Presented at the 2025 American Society of Clinical Oncology Annual Meeting | May 30-June 3, 2025 | Chicago, IL

Results

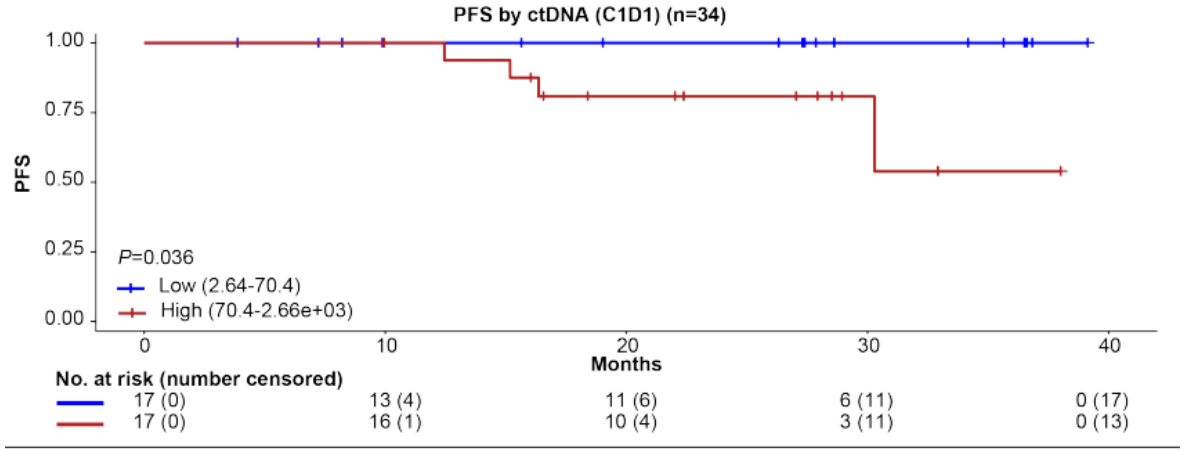
- Baseline ctDNA was detectable in 34 of 36 patients (94%)
- ctDNA concentration was higher in patients with greater disease burden, indicated by baseline stage/risk status (P=0.015) and International Prognostic Score (P=0.014) (Figure 3)
- A numerical trend was seen toward worse progression-free survival (PFS) in patients with high baseline ctDNA (Figure 4)

Figure 3: Baseline ctDNA was detected in 94% of patients with early-stage cHL and appeared to be associated with higher disease burden



ECOG PS, Eastern Cooperative Oncology Group performance status; hGE, haploid genome equivalent; IPI, International Prognostic Index.
P value from Wilcoxon rank-sum test (two groups) or Kruskal-Wallis test (more than two groups).

Figure 4: Patients with high baseline ctDNA had a numerical trend toward worse PFS



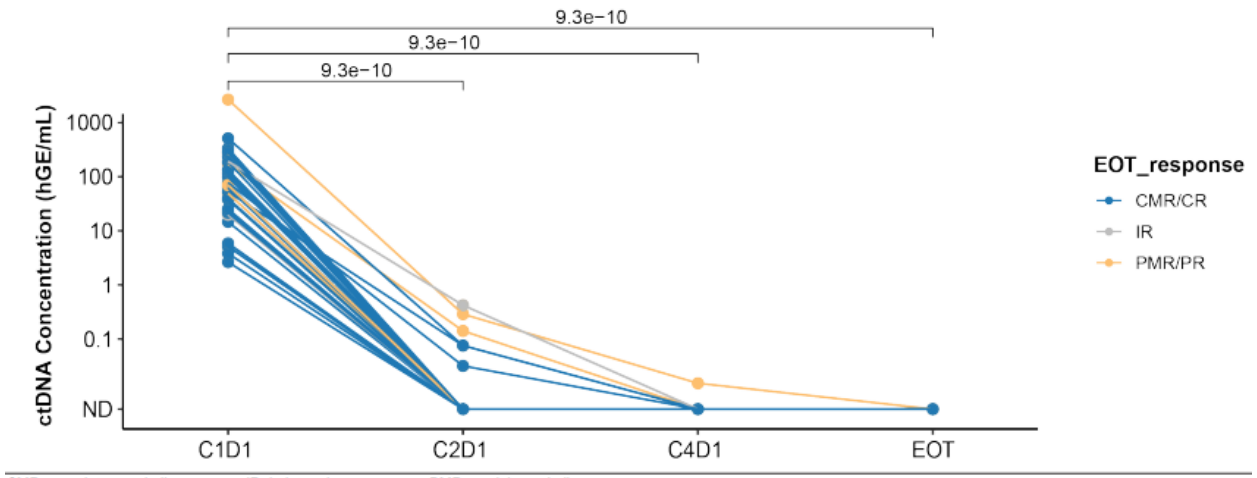
hGE, haploid genomic equivalent.
P value from log-rank test.
Patients were stratified by baseline median ctDNA. The patients with high ctDNA (≥70.4 hGE/mL) tended to have worse PFS compared with patients with low ctDNA. The group with low ctDNA did not have any PFS events.

Lynch RC, et al. Abstract 7040. Presented at the 2025 American Society of Clinical Oncology Annual Meeting | May 30-June 3, 2025 | Chicago, IL

Results

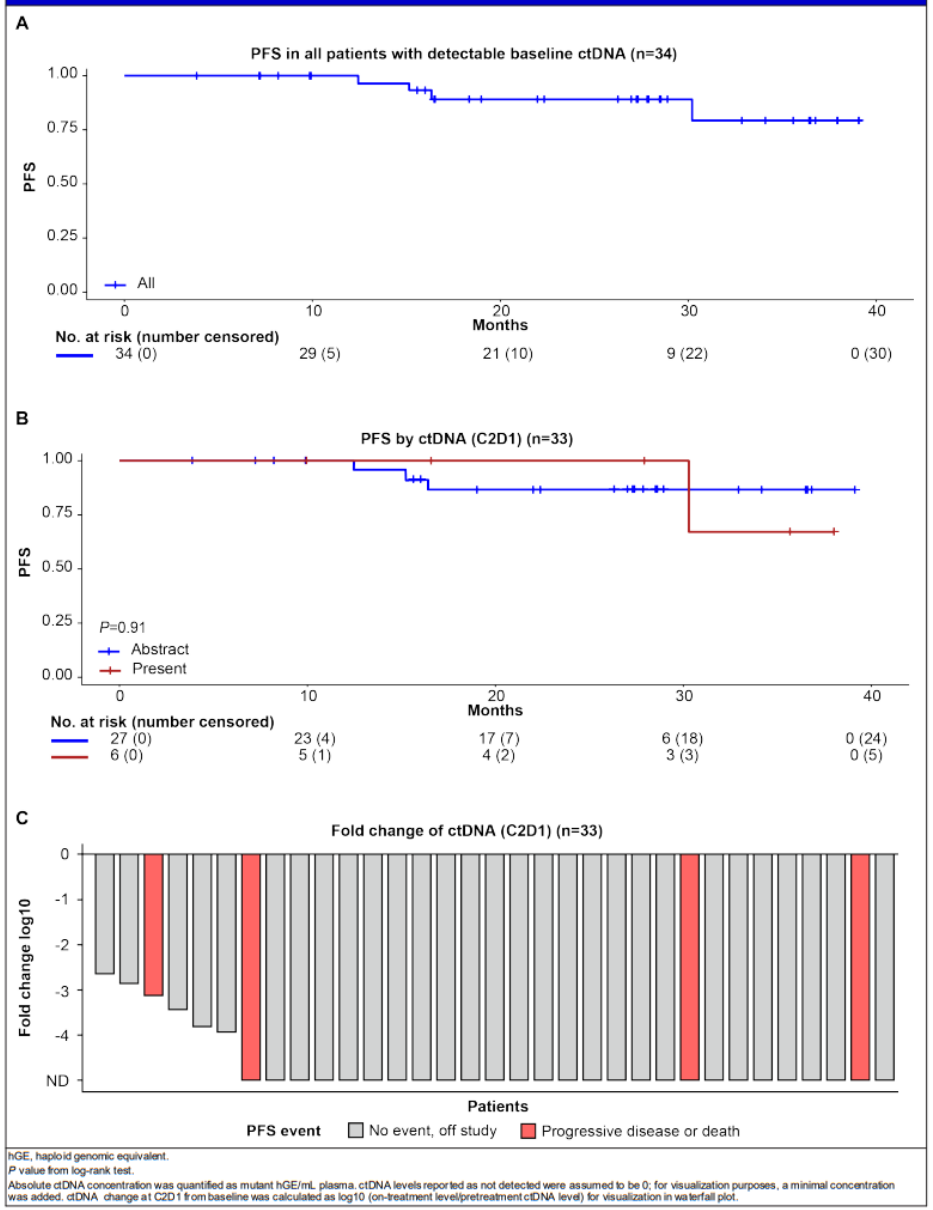
- ctDNA levels decreased in all patients after 1 cycle of treatment (Figure 5)
- There was a lack of apparent association between ctDNA clearance at C2D1 and PFS (Figure 6)

Figure 5: ctDNA concentration decline after treatment with AN+AD



CMR, complete metabolic response; IR, indeterminate response; PMR, partial metabolic response.
P value from Wilcoxon signed-rank test.
Absolute ctDNA concentration was quantified as mutant hGE/mL plasma. ctDNA levels reported as not detected were assumed to be 0; for visualization purposes, a minimal concentration was added.

Figure 6: Tumor ctDNA change from C2D1 and PFS

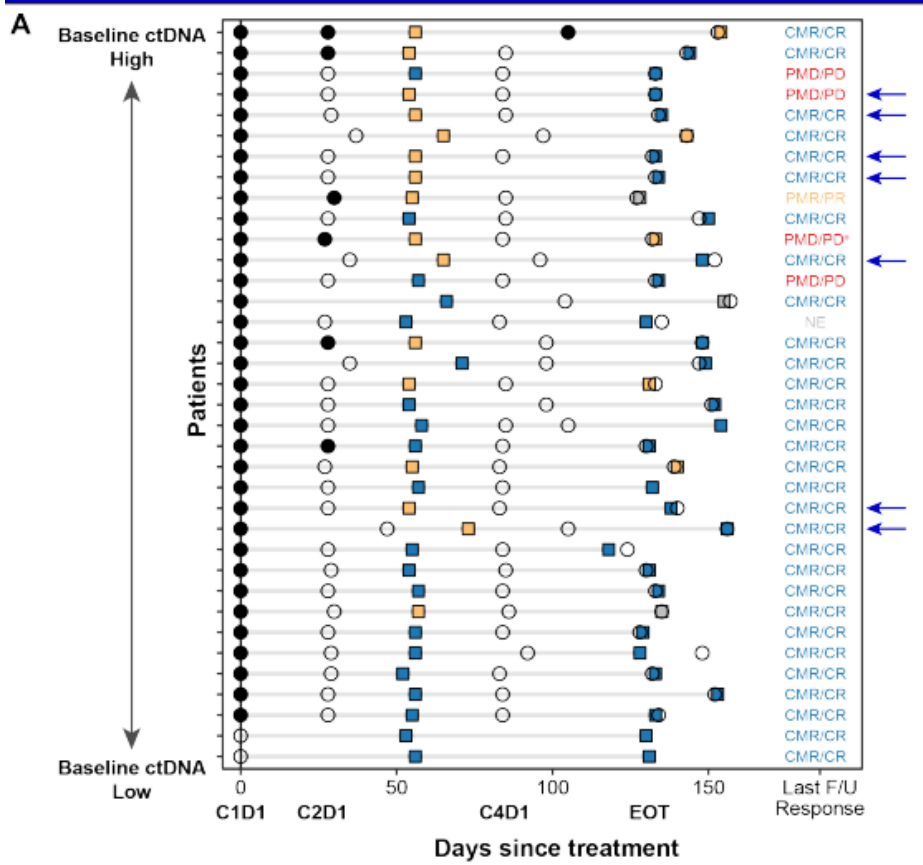


hGE, haploid genomic equivalent.
P value from log-rank test.
Absolute ctDNA concentration was quantified as mutant hGE/mL plasma. ctDNA levels reported as not detected were assumed to be 0; for visualization purposes, a minimal concentration was added. ctDNA change at C2D1 from baseline was calculated as log10 (on-treatment level/pretreatment ctDNA level) for visualization in waterfall plot.

Results

- At C2D1, ctDNA was detected in 6 of 33 patients (18%) and was undetectable in 27 of 33 patients (82%) (Figure 7A)
- At C2 interim PET/CT, 18 of 34 patients (53%) achieved complete metabolic response (CMR); of these, 17 patients had ctDNA samples evaluable, with 16 patients having undetectable ctDNA (Figure 7B)
- At C2 interim PET/CT, the remaining 16 of 34 patients (47%) achieved partial metabolic response (PMR); of these, 5 patients had detectable ctDNA, and 11 had undetectable ctDNA (Figure 7B)
  - All 11 patients with undetectable ctDNA achieved CMR at later time points
- At C4D1, only 1 patient continued to have detectable ctDNA
- At EOT, PET/CT showed that 26 of 34 patients (76%) achieved CMR, 5 achieved PMR, and 3 achieved indeterminate response (IR); none had detectable ctDNA at EOT (Figure 7B)

Figure 7: ctDNA status and PET/CT assessment over time (n=36)



B

Interim
PET/CT vs. C2D1 ctDNA

	PET+	PET-
ctDNA+	5	1
ctDNA-	11	16

EOT
PET/CT vs. EOT ctDNA

	PET+	PET-
ctDNA+	0	0
ctDNA-	8[b]	25

CR, complete response; F/U, follow-up; IR, indeterminate response; MCL, mantle cell lymphoma; NE, not evaluable; PD, progressive disease; PMD, progressive metabolic disease; PR, partial response.

Seven patients had ctDNA clearance at C2D1 but PMR at interim PET/CT and later converted to CMR on EOT PET/CT; these patients are indicated by an arrow (→) next to their last follow-up response.

[a]Patient died from MCL, not PD on cHL. [b]PET/CT at EOT showed PMR for 5 patients and IR for 3 patients. Subsequently, 4 of the 5 patients with PMR converted to CMR, and 1 patient developed a secondary primary malignancy. Of the patients with IR, 2 converted to CMR, and 1 converted to PMR.

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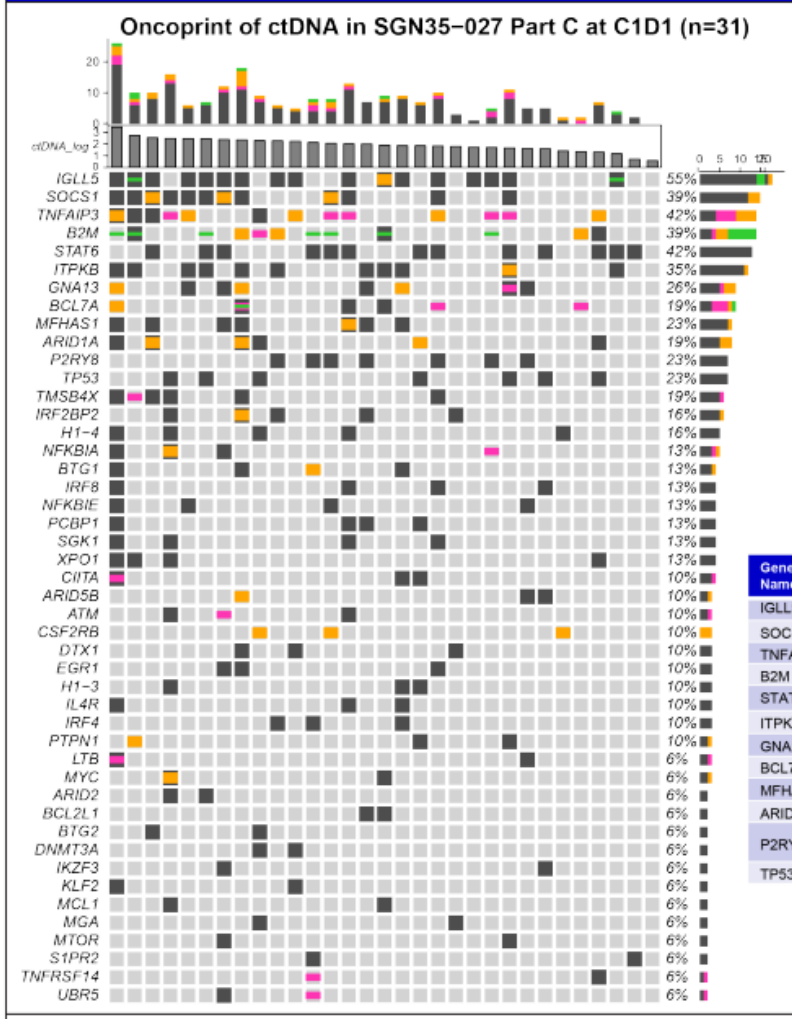
Results

- OncoPrint of ctDNA was available for 31 patients, indicating that the most frequent genetic alterations occurred in IGLL5 (55%), TNFAIP3 (42%), and STAT6 (42%) (Figure 8)

Figure 8. Genetic alterations detected by ctDNA



Most commonly identified gene alternations

(>20% in frequency)

Gene Name	Function
IGLL5	Tumor suppressor gene
SOCS1	JAK/STAT signaling
TNFAIP3	NFkB signaling pathway
B2M	Antigen presentation
STAT6	JAK/STAT signaling
ITPKB	PI3K-AKT signaling
GNA13	G-protein coupled receptor signaling
BCL7A	lymphomagenesis
MFHAS1	lymphomagenesis
ARID1A	Chromatin regulation, SWI/SNF complex
P2RY8	G-protein coupled receptor the promote the clustering of activated B cells
TP53	Tumor suppressor gene

SNV, single nucleotide variation.
Denominator of the prevalence calculation uses number of patients with ≥1 reported SNV (n=31) at baseline.

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Author's Conclusions

- The study showed that baseline circulating tumor DNA (ctDNA) was detectable in the majority of patients (34 of 36; 94%) with early-stage classical Hodgkin lymphoma (cHL) and that higher levels of ctDNA expression were associated with increased disease burden
- Treatment with brentuximab vedotin (BV), nivolumab, doxorubicin, and dacarbazine (AN+AD) reduced ctDNA levels, rendering them undetectable by end of treatment (EOT) in all patients
    - A limitation of the study was that ctDNA was not collected during long-term follow-up, and this could have limited the ability to predict relapse in long-term follow-up
- Identification of genetic alterations through ctDNA was consistent with alterations previous identified through tissue sequencing, suggesting that liquid biopsy has the potential to supplement tissue biopsy
- In 7 out of 34 patients (21%), decline in ctDNA levels was observed earlier than metabolic responses detected through imaging, suggesting the potential of ctDNA as an early indicator of treatment response
- The potential value of ctDNA as a biomarker for early detection and monitoring of treatment response in early-stage cHL should be further investigated. We plan to further explore the utility of ctDNA in the development of second-generation cluster of differentiation 30 (CD30)-directed antibody-drug conjugates (ADCs) SGN-35T and SGN-35C[1,2]

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References & Acknowledgements

References

1. Hamblett KJ, et al. Mol Cancer Ther. 2023;22(suppl 12):C132. 2. Hamblett KJ, et al. Blood. 2023;142(suppl 1):1440. 3. Adcetris (brentuximab vedotin). Prescribing information. Seagen Inc. 4. Abramson JS, et al. Blood Adv. 2023;7:1130-1136. 5. Abramson JS. Oral presentation at: 66th ASH Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA. Abstract 460. 6. Abramson JS. Oral presentation at: 65th ASH Annual Meeting & Exposition; December 9-12, 2023; San Diego, CA, and virtual. Abstract 611. 7. Lynch RC, et al. Blood. 2023;141:2576-2586. 8. Cheson BD, et al. J Clin Oncol. 2014;32:3059-3068. 9. Cheson BD, et al. Blood. 2016;128:2489-2496. 10. Kurtz MK, et al. Blood. 2019;134(suppl1):552.

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EHA – Abstract #PF1305

Safety Considerations and Related Healthcare Resource Utilization From a Study Aimed to Gather Clinicians' Insights and Perspectives On Care Provided in Front-line Hodgkin's Lymphoma in Europe

Alexa Molinari,[1] Ramón García-Sanz,[2] Julia Kopeika,[3] Alexander Fosså,[4] Irit Avivi,[5] Bastian von Tresckow,[6] Raphael Yugi,[7] Emanuele Arcà,[8] Nick Denholm,[9] Hannah Matthews,[9] Olivia Rogerson,[9] San Selveindran,[9] Athanasios Zomas[7]

[1]Takeda Pharmaceuticals America, Inc., Lexington, US; [2]University Hospital of Salamanca, Salamanca, Spain; [3]Guy's and St Thomas' Specialist Care, London, UK; [4]University of Oslo, Oslo, Norway; [5]Tel Aviv University, Tel Aviv-Jaffa, Israel; [6]West German Cancer Center and German Cancer Consortium, University Hospital Essen, University of Duisburg-Essen, Essen, Germany; [7]Takeda Pharmaceuticals International AG, Zurich, Switzerland; [8]OPEN Health, Brussels, BE; [9]OPEN Health, London, UK

Background & Objective

- Longstanding standard of care treatments for front-line Hodgkin's lymphoma (FLHL), such as chemotherapy and radiotherapy, provide high efficacy but are associated with short- and long-term treatment-related toxicity.
- New regimens are being proposed to reduce acute hematologic (HE) and non-HE (NHE) toxicities while optimizing efficacy.
- Pivotal HE (grade 4 anemia, infections, thrombocytopenia) and NHE (grade ≥3 cardiac, gastrointestinal, hepatobiliary, nervous system, renal/urinary, and respiratory, thoracic, and mediastinal disorders) toxicities during therapy are captured in the composite endpoint of treatment-related morbidity (TRMB) assessed in the HD21 trial (ClinicalTrials.gov ID: NCT02661503)[1].
- However, the implications of reduced toxicity and the potential impact on a FLHL patient's overall healthcare resource utilization (HCRU) is not clearly understood among countries where new regimens are being introduced to serve a broad range of patients with varying levels of healthcare support regionally.

Objective: To understand treatment considerations and HCRU related to TRMB elements and supportive care from the perspective of clinicians treating patients with FLHL

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Methods

- This study employed an iterative survey process modeled on Delphi method[2] principles and was designed with a practicing clinical steering committee (SC). The general study process is presented in Figure 1 below.
- Practicing hematology and/or fertility specialists with an active license in Germany, Spain, Norway, United Kingdom, or Israel were outreached for participation.
- Surveys were delivered via an email link to collect quantitative estimates, qualitative insights, and structured opinion statements to solicit expert opinion on safety/TRMB and supportive care.
- Qualitative and quantitative items on adverse events (AEs) and safety considerations, points of care for safety events, and general goals for patient treatment were analyzed.

Figure 1: INSIGHTFUL study process

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Results

- Five experts composed the SC, and 15 total hematologic (n=12 first round, n=11 second round) and fertility (n=3) experts were included in the response cohort ('respondents'), the majority practicing in an urban, public, and teaching/academically affiliated setting.
- Figure 2 presents the respondent profiles such as demographics and practice characteristics. Quantitative responses for care delivered by site were collected only from the hematology respondents.

Figure 2: INSIGHTFUL study respondent profiles

Fertility Expert Profile	Hematologist-Oncologist Profile
Proportion: 3/15	Proportion: 12/15
Urban practice (n=3, 100%)	Urban practice (n=11.5/12, 95.8%)
Public hospital (n=2, 66.7%)	Public hospital (n=10.5/12, 87.5%)
Teaching/academically affiliated (n=3, 100%)	Teaching/academically affiliated (n=12/12, 100%)
Country of Practice: UK (n=3, 100%)	Country of Practice: UK (n=2), NO (n=4 R1, n=3 R2), SP (n=3), DE (n=3)
Mean # of patients with FLHL seen annually: 15	Mean # of patients with FLHL seen annually: 34
% of patients that are male: 40%	% of patients that are male: 56.3%
	Trial participation: "often"/"sometimes" (n=8)

DE, Germany; NO, Norway; R, Round; SP, Spain; UK, United Kingdom.

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Qualitative Results

- Statements that reached consensus are provided in Table 1 below, organized by topic, then by cohort ("full" = heme-oncologists and fertility experts, "heme" = heme-oncologists only)
- The "heme" cohort reflected 12 participants versus the "full" cohort with a total of 15 respondents at Round 1. Note that, due to a dropout of one physician at Round 2, some statements were calculated with a total of 11 and 14 respondents, respectively, but still reflect the "heme" and "full" cohorts.

- Febrile neutropenia, anemia, thrombocytopenia, and infection were considered the most burdensome HE AEs while peripheral sensory neuropathy was considered the most burdensome NHE AE among heme-oncologists

Table 1: Qualitative results summary: topline statements that reached agreement

TRMB	Cohort, % agreed
The composite of TRMB is a thoughtful endpoint that I would consider when comparing chemotherapy regimen toxicity for [FLHL] treatment	Heme 91.7%
When considering patients who experience grade 3/4 AEs, [TRMB] strongly captures the majority of severe AEs facing patients initiating [FLHL] treatment	Heme 91.7%
There is need for additional treatment options for front-line treatment of HL with reduced toxicity, as measurable via TRMB	Heme 83.3%
If/when patients suffer from a TRMB event mentioned [previously], I have an understanding of the treatment and healthcare resource use they receive (including external to patient's cancer treatment) to treat the TRMB up until the TRMB resolves, treatment for their TRMB ceases, or a chronic treatment plan is formulated	Heme 100%
The conditions included in the definition of composite TRMB below would be discussed with patients when discussing regimen toxicity prior to frontline therapy initiation	Heme 82%
As a clinician, information on TRMB can be used in regular practice and in communication with patients with frontline treated HL in the following ways: • To discuss and compare different treatment options • To counsel patients on side effects including those which could lead to hospitalization and the frequency of these side effects • To advise patients on taking precautions and when to visit the emergency department • To develop an effective strategy for monitoring and responding to the occurrence of TRMBs	Full 100%
Information on TRMB should be incorporated within a holistic overview of clinical benefit to patients as an element of future HL treatment guideline considerations, as TRMB is burdensome for patients and knowledge of side effects can help guide treatment decisions	Heme 100%

Transfusions	Cohort, % agreed
Red blood cell (RBC) transfusions are an available treatment provision as part of standard of care of patients with HL treated with frontline chemotherapy within my clinical practice (similar finding for platelet transfusions)	Heme 80%
Patient characteristics of those treated for HL with frontline therapy that would be a priority for administration of RBC transfusions are advanced/older age, pre-existing cardiac disease, symptomatic anemia (i.e., shortness of breath, fatigue) and the presence of febrile neutropenia with severe anemia	Full 100%
For eligible patients with frontline-treated HL, platelet transfusions should be given if platelet count is <10,000/µL or <20,000/µL and symptomatic or with underlying bleeding disorders	Full 92%
Patient characteristics of those treated for HL with frontline therapy that would be a priority for administration of platelet transfusions are underlying bleeding disorders, history of severe bleeding, treatment with anticoagulants, and febrile neutropenia or presence of infection	Full 93%

Fertility	Cohort, % agreed
All female patients of reproductive age who want to be referred to a gynecologist to discuss fertility preservation methods are referred prior to starting gonadotoxic frontline chemotherapy	Full 86%
Female patients are more willing to delay first-line chemotherapy in the interest of pursuing fertility preservation if regimens they are designated to initiate are increasingly gonadotoxic	Full 92%
Females' long-term (3–5-year post treatment initiation) fertility goals are a factor in deciding frontline chemotherapy administered in younger patients (<40 years)	Full 92%

Oversight	Cohort, % agreed
I am aware and discuss my patients' fertility goals before initiating frontline treatment for HL	Heme 100%
I have oversight of the specific fertility preservation or assisted reproductive therapy my patients receive prior to or post their frontline treatment for HL	Heme 83.3%
I have oversight of how long patients are treated with assisted reproductive therapies (ART) whilst it is incorporated within their frontline treatment for HL	Heme 90.9%
Oncologists treating patients with HL are aware of supportive treatment that occurs outside of their department/immediate care for these patients	Heme 82%

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Quantitative Results

- Participants were asked to respond to the following prompt on HCRU per site of care on the per-patient basis, with the exception of at-home care which was engaged as the number of patients: “For each requested estimate, responses should be numeric free-text based on your practical experience (note: you are not obliged to review patient clinical notes to final actual quantitative values, please provide your best estimations only). You may respond with 0.”
- Totals were calculated by care site type per each TRMB element and reported in highlighted bands below, in Table 2; peripheral sensory neuropathy and peripheral motor neuropathy were included in the overall reporting to provide context on complexity of nervous system management vs neuropathy-specific management

Table 2. Per-patient treatment summaries by TRMB element

Care Delivery		Hematologic TRMB			Non-hematologic TRMB							
		Anemia	Thrombo-cytopenia	Infections	Cardiac disorder	Gastro-intestinal disorders	Hepatobiliary disorders	Nervous system disorders	*PSN*	*PMN*	Renal and urinary disorders	Respiratory, thoracic & mediastinal disorders
Site delivered care	IP+OP care	31.8	26.8	9.4	7.9	8.2	5.0	0.0	*3.9*	*2.8*	6.2	10.6
IP admissions	Total adm	5.3	5.1	1.6	1.1	0.6	0.6	0.0	*0.0*	*0.2*	1.2	1.9
	%	17%	19%	16%	15%	7%	12%	0%	*0%*	*6%*	19%	18%
Floor IP admission	Admissions	5.3	4.4	1.3	0.7	0.6	0.6	0.0	*0.0*	*0.2*	1.0	1.7
	%	17%	17%	14%	9%	7%	12%	0%	*0%*	*6%*	16%	16%
ICU IP admission	Admissions	0.0	0.7	0.2	0.4	0.0	0.0	0.0	*0.0*	*0.0*	0.2	0.2
	%	0%	2%	2%	5%	0%	0%	0%	*0%*	*0%*	3%	2%
OP admissions	Total adm	12.9	10.8	3.7	3.2	3.8	2.2	0.0	*1.8*	*1.1*	2.4	4.2
	%	41%	40%	39%	41%	46%	44%	0%	*47%*	*41%*	39%	40%
Ambulatory admission	Admissions	1.6	5.2	2.2	1.0	1.0	0.4	0.0	*0.3*	*0.3*	0.8	1.7
	%	5%	20%	24%	13%	12%	8%	0%	*7%*	*12%*	13%	16%
Specialist appointment	Visits	5.9	4.7	1.0	1.5	1.9	1.4	0.0	*1.2*	*0.8*	1.0	2.1
	%	19%	18%	11%	19%	23%	28%	0%	*30%*	*29%*	16%	20%
Generalist appointment	Visits	5.4	0.9	0.4	0.7	0.9	0.4	0.0	*0.4*	*0.0*	0.6	0.4
	%	17%	3%	5%	9%	11%	8%	0%	*9%*	*0%*	10%	4%
Home visits	Referrals	0.7	0.0	0.6	0.3	0.1	0.0	0.0	*0.3*	*0.3*	0.2	0.2
	%	2%	0%	6%	4%	1%	0%	0%	*7%*	*12%*	3%	2%

Adm, admission(s); ICU, intensive care unit; IP, inpatient; OP, outpatient; PSN, peripheral sensory neuropathy; PMN, peripheral motor neuropathy
*No overall event management was reported in the INSIGHTFUL study for Nervous System Disorders overall (see table 2), so these were adjusted to £0 while the sections for PSN and PMN were included as separate entities

- To contextualize INSIGHTFUL quantitative results, these rates of care provided by site were applied to the HD21 trial and costed according to the event at hand and the setting of care a patient would be theoretically treated at based on the respondents’ reflections. For example, the rate of anemia being treated in the inpatient setting was applied to the number of patients in HD21 who experienced anemia and then conservatively costed based on the length of stay in the HD21 trial per NHS rates[1] in pound sterling. Similarly, ambulatory care/specialist/generalist visits were costed as a single visit or day-case while home-care was readjusted to a per-patient rate and costed for an average length of stay per the HD21 trial.

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Results

- Greatest theoretical savings of treating with BrECADD versus eBEACOPP were observed for thrombocytopenia (£57,113 vs £96,363, a difference of £39,250 in favor of BrECADD), hepatobilary disorders (£17,965 vs £15,537, a difference of £2428 in favor of eBEACOPP), and respiratory, thoracic & mediastinal disorders (£11,714 vs £16,399, a difference of £4,685 in favor of BrECADD) as a consequence of the number and severity of admissions to adequately treat patients with these types of adverse events.

Table 3: HD21 Trial example of applied costs by site of care: BrECADD vs eBEACOPP

	Heme-related TRMB			Non-heme related TRMB							
Care Delivery	Anemia	Thrombo-cytopenia	Infections	Cardiac disorder	Gastro-intestinal disorders	Hepato-biliary disorders	Nervous system disorders*	*PSN*	*PMN*	Renal & urinary disorders	Respiratory, thoracic & mediastinal disorders
Total PP excluding home-care: BrECADD	£783	£57,113	£5,995	£6,039	£16,813	£17,965	£0	£1,451	£416	£5,518	£11,714
Total PP excluding home-care: eBEACOPP	£783	£96,363	£4,612	£3,355	£9,276	£15,537	£0	£2,467	£139	£7,883	£16,399
IP admissions (critical and non-critical)											
PP cost: BrECADD	£435	£14,785	£2,177	£3,587	£9,958	£13,441	£0	£0	£0	£2,431	£8,642
PP cost: eBEACOPP	£435	£24,945	£1,674	£1,993	£5,494	£11,624	£0	£0	£0	£3,473	£12,099
Floor IP admissions (non-critical)											
PP cost: BrECADD	£435	£27,477	£3,424	£3,587	£9,958	£13,441	£0	£0	£0	£3,077	£8,642
PP cost: eBEACOPP	£435	£46,360	£2,634	£1,993	£5,494	£11,624	£0	£0	£0	£4,395	£12,099
ICU IP admissions (critical)											
PP cost: BrECADD	£0	£2,092	£929	£0	£0	£0	£0	£0	£0	£1,786	£0
PP cost: eBEACOPP	£0	£3,530	£715	£0	£0	£0	£0	£0	£0	£2,552	£0
OP admissions (ambulatory, specialist, & generalist)											
PP cost: BrECADD	£350	£9,181	£547	£818	£2,285	£1,508	£0	£484	£139	£218	£1,024
PP cost: eBEACOPP	£350	£15,491	£421	£454	£1,261	£1,304	£0	£822	£69	£312	£1,433
Ambulatory admission											
PP cost: BrECADD	£45	£13,200	£822	£698	£1,978	£876	£0	£181	£77	£267	£1,121
PP cost: eBEACOPP	£45	£22,271	£632	£388	£1,091	£758	£0	£308	£26	£382	£1,570
Specialist appointment											
PP cost: BrECADD	£171	£12,401	£660	£1,385	£3,357	£2,890	£0	£1,061	£339	£215	£1,692
PP cost: eBEACOPP	£171	£20,923	£508	£770	£1,852	£2,500	£0	£1,804	£113	£306	£2,368
Generalist appointment											
PP cost: BrECADD	£132	£1,943	£160	£370	£1,520	£758	£0	£209	£0	£173	£259
PP cost: eBEACOPP	£132	£3,279	£123	£205	£839	£655	£0	£355	£0	£248	£362
Home visit											
PP cost: BrECADD	£1	£0	£10	£29	£0	£0	£0	£92	£3	£3	£379
PP cost: eBEACOPP	£33	£0	£225	£481	£0	£0	£0	£4,684	£33	£121	£530

BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone; eBEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; PP, per patient; PSN, Peripheral sensory neuropathy; PMN, Peripheral motor neuropathy

*No overall event management was reported in the INSIGHTFUL study for nervous system disorders overall (see table 2). Nervous system disorders were adjusted to £0 while sections for PSN and PMN were included as separate entities and accounted for according to care reported in the INSIGHTFUL study.

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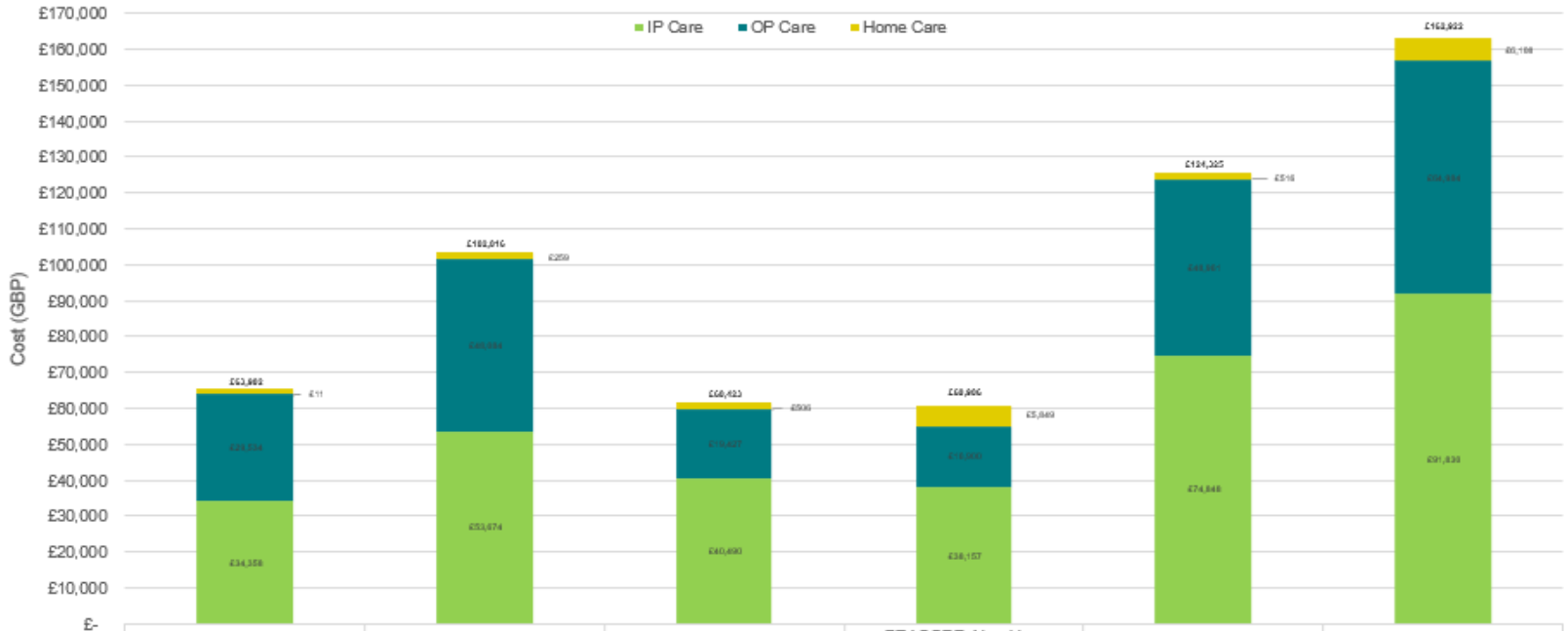
Results

- The summary findings of Table 3 are presented in Figure 3 below, but instead organized collectively by heme-related TRMB elements, non-heme related TRMB elements, and all-TRMB elements.
- An illustrative total savings of £38,597 was observed in favor of BrECADD when accounting for all TRMB.

Figure 3: Illustrative per-patient costs by site of care and TRMB classification



	BrECADD: Heme TRMB	eBEACOPP: Heme TRMB	BrECADD: Non-Heme TRMB	eBEACOPP: Non-Heme TRMB	BrECADD: All TRMB	eBEACOPP: All TRMB
All Care	£63,902	£102,016	£60,423	£60,906	£124,325	£162,922
Home Care	£11	£259	£506	£5,849	£516	£6,108
OP Care	£29,534	£48,084	£19,427	£16,900	£48,961	£64,984
IP Care	£34,358	£53,674	£40,490	£38,157	£74,848	£91,830

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Limitations

- The INSIGHTFUL study presented a unique view on safety and supportive care elements related to FLHL treatment, but with caveats of a small sample size (due to recruitment challenges and a restricted scope of participating countries) and targeted objectives for exploration
- The objective to better understand safety and TRMB versus exploring broader disease and regimen implications (e.g. dosing considerations, relapse risk, etc) introduces additional questions on remaining core elements of the FLHL experience to be investigated in a larger forum
- The costing exercise was performed under a number of assumptions. Of note, event rates utilized could have differed appreciably if this example was otherwise conducted with rates from real-world data sources.

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Author’s Conclusions

- Participating hematologists reflect favorably on TRMB as a clinical endpoint and would support its inclusion in guidelines as it delivers a broad reflection on HL regimen safety profiles. Secondary life-goals (e.g fertility/family planning) are considered prior to front-line therapy initiation.
- The example HD21 trial application demonstrates how impactful AE-sparing regimens such as BrECADD could be for reducing healthcare spending, especially in the presence of high efficacy
- TRMB would be a valuable addition to the community’s assessment of chemotherapy options in FLHL in terms of decision making and healthcare spending consequences

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References, Acknowledgements, & Disclosures

References

1. Borchmann P, Stein H, Goergen H, et al. Assessing the efficacy and tolerability of PET-guided BrECADD versus eBEACOPP in advanced-stage, classical Hodgkin lymphoma (HD21): a randomised, multicentre, parallel, open-label, phase 3 trial. Lancet. 2024;402(10324):2552–66.
2. RAND Corporation. RAND methodological guidance for conducting and critically appraising Delphi panels. RAND Report. Published 2021. Accessed 21 May 2025. Available at: https://www.rand.org/pubs/tools/TLA3082-1.html.
3. NHS England. National Cost Collection for the NHS. Published 2023. Accessed May 22, 2025. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/

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Disclosures

AM, RY, and AZ: employment with and hold stock in Takeda Pharmaceuticals. RGS: employment with University Hospital of Salamanca. JK: employment with Guy's and St Thomas' Specialist Care. AF: employment with University of Oslo. IA: employment with Tel Aviv University. BvT: employment with West German Cancer Center and German Cancer Consortium (University Hospital Essen). EA, ND, HM, OR, and SS: employment with OPEN Health.

EHA – Abstract #PF1302

A matching-adjusted indirect treatment comparison of BrECADD vs PET-Guided ABVD and eBEACOPP in advanced Hodgkin lymphoma

Alexa Molinari,[1] Thomas Melchardt,[2] Fjoralba Kristo,[3] Zhiyi Lan,[4] Zijiao Yuan,[4] Athanasios Zomas,[5] Vanessa Stache,[5] Abbey Poirier,[4] Victoria Federico Paly[1]

[1]Takeda Pharmaceuticals America, Inc., Lexington, MA, USA; [2]Paracelsus Medical University, Salzburg, Austria; [3]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [4]Cytel Inc., Cambridge, MA, USA; [5]Takeda Pharmaceuticals International AG, Zurich, Switzerland

Question

What is the comparative effectiveness of BrECADD versus PET-guided ABVD, BEACOPP, and eBEACOPP among patients aged 18–60 years, patients >60 years, and the overall adult patient population with aHL?

Study design

A feasibility assessment and matching-adjusted indirect comparison were conducted to evaluate the comparative effectiveness of different therapies for adults with aHL.

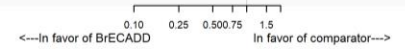
Table 1: Studies considered in the feasibility assessment

Study	Intervention	Comparator	Age range (years)	Stage
HD21	BrECADD	eBEACOPP	18–60	IIB, III, IV
HD21 nonrandomized	BrECADD	N/A	61–75	IIB, III, IV
SWOG S0816	PET-guided ABVD	N/A	18–60	III, IV
RATHL	PET-guided ABVD	N/A	18–79 (9.5% >60y)	IIB, III, IV
HD9 (ages 66–75)	BEACOPP	ABVD	66–75	III, IV
Mondello 2020	ABVD	eBEACOPP	19–75 (3.3% >60y)	III, IV

Results

Figure 1: Fully-adjusted Cox regression results for progression-free survival and overall survival

Comparison	Age	Stage	Index arm	Comparator arm	HR (95% CI)	p value
Progression-free survival						
BrECADD vs PET-guided ABVD	18-60	III,IV	HD21 randomized (stage III & IV)	SWOG S0816 ITT	0.24 (0.16, 0.35)	<0.001
BrECADD vs PET-guided ABVD	18-60	IIB,III,IV	HD21 randomized ITT	RATHL (age ≤ 60)	0.24 (0.16, 0.37)	<0.001
BrECADD vs PET-guided ABVD*	61-75	IIB,III,IV	HD21 nonrandomized ITT	RATHL (age > 60)	0.45 (0.21, 0.97)	0.036
BrECADD vs PET-guided ABVD	18-75	IIB,III,IV	HD21 pooled ITT	RATHL ITT	0.24 (0.16, 0.36)	<0.001
BrECADD vs PET-guided ABVD	18-75	III,IV	HD21 pooled (stage III & IV)	RATHL (stage III & IV)	0.24 (0.16, 0.35)	<0.001
BrECADD vs eBEACOPP	18-75	III,IV	HD21 pooled (stage III & IV)	Mondello 2020 ITT	0.58 (0.29, 1.19)	0.194
BrECADD vs BEACOPP	66-75	III,IV	HD21 nonrandomized (stage III & IV, age >65)	HD9 ITT (age 66-75)	0.63 (0.28, 1.44)	0.260
Overall survival						
BrECADD vs PET-guided ABVD	18-60	III,IV	HD21 randomized (stage III & IV)	SWOG S0816 ITT	0.30 (0.14, 0.63)	0.004
BrECADD vs PET-guided ABVD	18-60	IIB,III,IV	HD21 randomized ITT	RATHL (age≤60)	0.32 (0.14, 0.70)	<0.001
BrECADD vs PET-guided ABVD*	61-75	IIB,III,IV	HD21 nonrandomized ITT	RATHL (age>60)	0.77 (0.32, 1.82)	0.544
BrECADD vs PET-guided ABVD	18-75	IIB,III,IV	HD21 pooled ITT	RATHL ITT	0.47 (0.25, 0.89)	0.010
BrECADD vs PET-guided ABVD	18-75	III,IV	HD21 pooled (stage III & IV)	RATHL (stage III&IV)	0.45 (0.24, 0.84)	0.011
BrECADD vs BEACOPP	66-75	III,IV	HD21 nonrandomized (stage III & IV, age >65)	HD9 ITT (age 66-75)	0.29 (0.09, 0.92)	0.014



*Naïve (unweighted) results presented as patient characteristics were not available for the RATHL age 61–75 subgroup.

Key take aways

This study supports the use of BrECADD over PET-guided ABVD and BEACOPP-based treatment in both younger and older adult patients with aHL. Results should be interpreted with caution due to methodological and comparator trial-related limitations.

Background & Objectives

- In advanced Hodgkin lymphoma (aHL), brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone (BrECADD) is a preferred front-line regimen in the United States
- Positron emission tomography (PET)-guided doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) and escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (eBEACOPP) are also widely used regimens
- In the HD21 randomized, open-label, phase 3 trial comparing the efficacy and safety of BrECADD and eBEACOPP, BrECADD was associated with improved progression-free survival (PFS) and lower treatment-related morbidity compared to eBEACOPP among patients aged 18–60 years with Stage IIb, III, or IV HL[1-3]
- In the single-arm nonrandomized extension cohort of the HD21 trial, patients aged 61–75 years were treated with BrECADD exclusively, as eBEACOPP has been shown to be associated with a severe toxicity profile in patients older than 60 years and therefore is not recommended as first-line therapy in this patient population
- No head-to-head randomized trials have been conducted comparing BrECADD to ABVD-based regimens in adult patients with aHL or to eBEACOPP in older adults to date

Objectives: In the absence of head-to-head trials, the objective of this study was to evaluate the comparative effectiveness of BrECADD versus PET-guided ABVD, BEACOPP, and eBEACOPP among patients aged 18–60 years, >60 years, and the overall adult patient population with aHL

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Methods

Data sources

- Individual patient-level data (IPD) from the HD21 clinical trial[1-3] for BrECADD, and published evidence reporting on risk-adapted therapy for aHL (RATHL)[4,5] and SWOG S0816[6] clinical trials for PET-guided ABVD, HD9 trial[7] for BEACOPP, and Mondello 2020[8] observational study for eBEACOPP were used in this analysis (Table 1)
  - For the PET-guided ABVD trials, the overall study population was used, with no differentiation based on the post-PET randomization of patients
  - The main study cohort from HD9 (patients aged 15–65 years) was not assessed as HD21 already includes a direct comparison of BrECADD versus eBEACOPP for this age group. The cohort of patients aged 66–75 in HD9 was included to allow for comparison to BEACOPP in the older adult population

Feasibility assessment

- In RATHL and Mondello 2020, only 9.5% and 3.3% of the patient populations were comprised of patients >60 years, respectively
- SWOG S0816 only included patients from the United States, whereas HD21 and all other comparators only included patients from outside of the United States
- SWOG S0816 and HD9 did not report information on Eastern Cooperative Oncology Group performance status (ECOG PS). Extranodal site was not reported in S0816, RATHL, or Mondello 2020
- PFS and overall survival (OS) outcomes were available for SWOG S0816, RATHL, and Mondello 2020. Although HD21 and RATHL included patients with Stage IIB HL, Stage III/IV subgroup results were available for PFS and OS
- In HD9, OS was available, and freedom from treatment failure (FFTF) was used as a survival endpoint, rather than PFS. Therefore, modified PFS (mPFS) was generated using IPD from HD21 to match the definition of FFTF in HD9, defined as the time from registration to occurrence of death from any cause, progressive disease, no complete remission at the end of protocol treatment, relapse, or non-study treatment

Methods

Statistical analyses

- Based on the feasibility assessment, there were no potential anchors for the comparison of HD21 and the comparator studies (Table 1); therefore, an unanchored matching-adjusted indirect comparison (MAIC) was conducted to compare BrECADD versus PET-guided ABVD, BEACOPP, and eBEACOPP using IPD from HD21 and aggregate data from the comparator trials. Analyses were conducted for subgroups based on age group and Stage to best align the trial populations prior to matching
- Treatment effect modifiers (TEMs) and prognostic variables (PVs) for matching were identified based on literature review, results of Cox regression analyses of the HD21 trial IPD, and clinician input from external key opinion leaders. Age, sex, International Prognostic Score (IPS), ECOG PS, Stage, and B symptoms (fever, weight loss, night sweats) at baseline were identified as potential TEMs/PVs and were used as matching factors in the base case analyses based on data availability
- Weighted Cox regression was employed to generate hazard ratios (HR) with 95% confidence intervals (CI) for PFS and OS. Scenario and sensitivity analyses were conducted to explore the inclusion/exclusion of covariates in the model and various censoring cut-off timepoints
- In situations where the proportional hazard assumption was violated (Schoenfeld residual P value <0.05), analysis of restricted mean survival time (RMST) was conducted

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Results

- In all analyses performed, MAIC reweighting resulted in effective sample sizes between 48–98% of the original sample size in the HD21 population (Table 2)
- Results of the fully-adjusted base case models are presented in Figure 1. Results of additional scenarios, with adjustments for study variation and follow-up time, will be reported in future publications

Table 2: Matching variables and effective sample sizes

BrECADD, HD21 subgroup	Comparator		Matching variables	HD21 effective sample size	
	Intervention (study)	Subgroup (n)		Before matching	After matching
Age 18–60, stage III & IV	PET-guided ABVD (SWOG S0816)	ITT (n=336)	Age, sex, IPS, stage, B symptoms	631	620 (98%)
Age 18–60, stage IIB, III & IV	PET-guided ABVD (RATHL)	Age ≤60 (n=1,103)	Sex, IPS, ECOG PS, stage, B symptoms	748	441 (59%)
Age 61–75, stage IIB, III & IV	PET-guided ABVD (RATHL)	Age >60 (n=98)	Sex, IPS, ECOG PS, stage, B symptoms	85	*
Age 18–75, stage IIB, III & IV, HD21 pooled ITT	PET-guided ABVD (RATHL)	ITT (n=1,201)	Age, sex, IPS, ECOG PS, stage, B symptoms	833	439 (53%)
Age 18–75, stage III & IV, HD21 pooled	PET-guided ABVD (RATHL)	Stage III & IV (n=702)	Age, sex, IPS, ECOG PS, B symptoms	713	632 (89%)
Age >65, stage III & IV	BEACOPP (HD9)	Age 66-75 (n=42)	Age, sex, IPS, stage, B symptoms	47	26 (55%)
Age 18–75, stage III & IV, HD21 pooled	eBEACOPP (Mondello 2020)	ITT (n=121)	Age, sex, IPS, ECOG PS, stage, B symptoms	713	340 (48%)

*Only naïve (unweighted) comparisons possible as patient characteristics were not available for the RATHL age >60 years subgroup.

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Results

- Among patients aged 18–60 years, BrECADD (HD21 randomized, Stage III and IV subgroup) was associated with significantly improved PFS and OS compared to PET-guided ABVD in SWOG S0816 (PFS HR: 0.24 [95% CI: 0.16–0.35], P<0.001; OS HR: 0.30 [0.14–0.63], P=0.004)
- PET-guided ABVD RATHL comparison results for patients aged 18–60 years and 61–75 years were generally consistent with those for the overall adult population of SWOG S0816, with the exception of OS for the age 61–75 subgroup, which did not reach statistical significance
- Patient characteristics were not available for the 61–75-year age group in RATHL for matching; therefore, only naïve (unweighted) comparisons are presented for PFS and OS
- In patients aged 18–75 years, BrECADD (HD21 pooled, Stage III and IV subgroup) also demonstrated significantly improved PFS and OS compared to PET-guided ABVD in RATHL (PFS HR: 0.24 [95% CI: 0.16–0.35], P<0.001); OS HR: 0.47 [0.25–0.89], P=0.01)
- For OS, among patients aged 66–75, BrECADD (HD21 nonrandomized, Stage III and IV, age >65 subgroup) was associated with a 71% reduced risk of death when compared to BEACOPP in the HD9 trial (OS HR: 0.29 [0.09–0.92], P=0.014). A trend favoring BrECADD for PFS was observed, but results were not statistically significant
- In adults aged 18–75 years, there was a trend for improvement in PFS in favor of BrECADD (HD21 pooled, Stage III and IV subgroup) compared to real-world use of eBEACOPP (Mondello 2020).
- RMST analyses conducted to account for any violation to the proportional hazard assumptions were consistent with the Cox regressions, favoring BrECADD over comparators
- The sensitivity and scenario analyses results to explore the inclusion/exclusion of covariates in the model and various censoring cut-off timepoints were consistent with the base case results

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Limitations

Methodological limitations

- There are substantial differences in locations, populations, and follow-up timepoints between studies and cohorts compared that could not be fully addressed by the methods applied
- Not all variables identified as TEMs or PVs were available for matching in all included studies. In the presence of residual confounding, unanchored comparisons are more susceptible to bias and systematic error from improper model specification

Comparator trial-related limitations

- IPD from the HD21 nonrandomized single-arm cohort of patients were used to generate mPFS to match FFTF in the HD9 study. Assumptions were required for some patients where complete remission was not achieved or assessed
- The HD21 nonrandomized cohort (the elderly cohort, 60+) had a relatively short median follow-up time of 27.1 months and a small sample size, which limited the power of any analysis involving these data and prompts the need for further analysis
- In RATHL, although outcome data were available for Stage III or IV patients, the aggregate patient characteristics of the overall population, which included Stage IIa patients (41.5%), were used as a proxy for Stage III or IV patients

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Author’s Conclusions

- Among adult patients with aHL, BrECADD was robustly associated with significantly improved PFS and OS compared to PET-guided ABVD per RATHL and SWOG S0816 protocols
- OS results were also significantly in favor of BrECADD versus BEACOPP in older adults. A similar trend in PFS was observed in eBEACOPP comparisons in all adults over the age of 18
- These results further support the use of BrECADD over PET-guided ABVD and BEACOPP-based treatment in both younger and older adult patients with aHL

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References, Acknowledgements, & Disclosures

References

1. Borchmann P, Moccia A, Greil R, et al. Treatment related morbidity in patients with classical Hodgkin lymphoma: results of the ongoing, randomized phase III HD21 trial by the German Hodgkin Study Group. *Blood*. 2022;140(Supplement 1):771–3
2. Borchmann P, Moccia AA, Greil R, et al. Tolerability and efficacy of BrECADD versus BEACOPP in advanced stage classical Hodgkin lymphoma: GHSG HD21, a randomized study. *J Clin Oncol*. 2024;42(17_suppl):LBA7000–LBA
3. Borchmann P, Ferdinandus J, Schneider G, et al. Assessing the efficacy and tolerability of PET-guided BrECADD versus eBEACOPP in advanced-stage, classical Hodgkin lymphoma (HD21): a randomised, multicentre, parallel, open-label, phase 3 trial. *Lancet*. 2024;404(10450):341–52
4. Luminari S, Fossa A, Trotman J, et al. Long-term follow-up of the response-adjusted therapy for advanced Hodgkin lymphoma trial. *J Clin Oncol*. 2023:Jco2301177
5. Luminari S, Fossa A, Trotman J, et al. Long follow-up of the response-adjusted therapy for advanced Hodgkin lymphoma (RATHL) trial (CRUK/07/033) confirms the safety of both de-escalation and intensification of chemotherapy. *Blood*. 2022;140(1):766-767
6. Stephens DM, Li H, Schöder H, et al. Five-year follow-up of SWOG S0816: limitations and values of a PET-adapted approach with stage III/IV Hodgkin lymphoma. *Blood.* 2019;134(15):1238–46
7. Ballova V, Rüffer JU, Haverkamp H, et al. A prospectively randomized trial carried out by the German Hodgkin Study Group (GHSG) for elderly patients with advanced Hodgkin's disease comparing BEACOPP baseline and COPP-ABVD (study HD9elderly). *Ann Oncol*. 2005;16(1):124–31
8. Mondello P, Musolino C, Dogliotti I, et al. ABVD vs BEACOPP escalated in advanced-stage Hodgkin's lymphoma: results from a multicenter European study. *Am J Hematol*. 2020;95(9):1030–7

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Disclosures

AM, FK, AZ, VS, VP: employment with and own stock in Takeda Pharmaceuticals. TM: employment with Paracelsus Medical University. ZL, AP: employment with Cytel, Inc at the time of analysis.

EHA – Abstract #865

Treatment efficacy for advanced-stage classic Hodgkin lymphoma: a systematic review and meta-analysis of randomised controlled trials

Da-Hui Li[1], Wen-Hao Zhang[1], Yi Ding[2], Jian-Li Wang[3], Rong Tao[1]

[1]Research Center for Lymphoma, Fudan University, Shanghai, China, [2]Tongji Hospital of Tongji University, Shanghai, China,[3]Takeda Medical Affairs, Takeda (China) International Trading Co., Ltd, Shanghai, China

Question

What is the treatment efficacy for newly diagnosed advanced-stage classic Hodgkin lymphoma who received BV-based PET-guided regimens, Non-BV PET-guided regimens, and Non-PET guided chemotherapy combinations?

Results

This meta-analysis included 14 RCTs[1-16] (Table 1) with a total of 6,483 patients (range of median age: 28-49 years). The ECHELON-1 study provided 3 reports [1, 15, 16]. Ten studies[1, 2, 5-9, 12-16] were finally included in this analysis, which simultaneously reported survival rates and 95% confidence intervals (CIs), while the remaining 4 studies[3, 4, 10, 11] only provided point estimates for survival outcomes. One study[5] included 742 patients received BV based PET-guided regimens, 3 studies[5, 6, 14] included 1,402 patients received non-BV PET-guided regimens, and 13 studies[1-4, 6-16] included 4,339 patients received Non-PET guided chemotherapy combinations.

Figure 2 Forest diagrams for 3-year OS

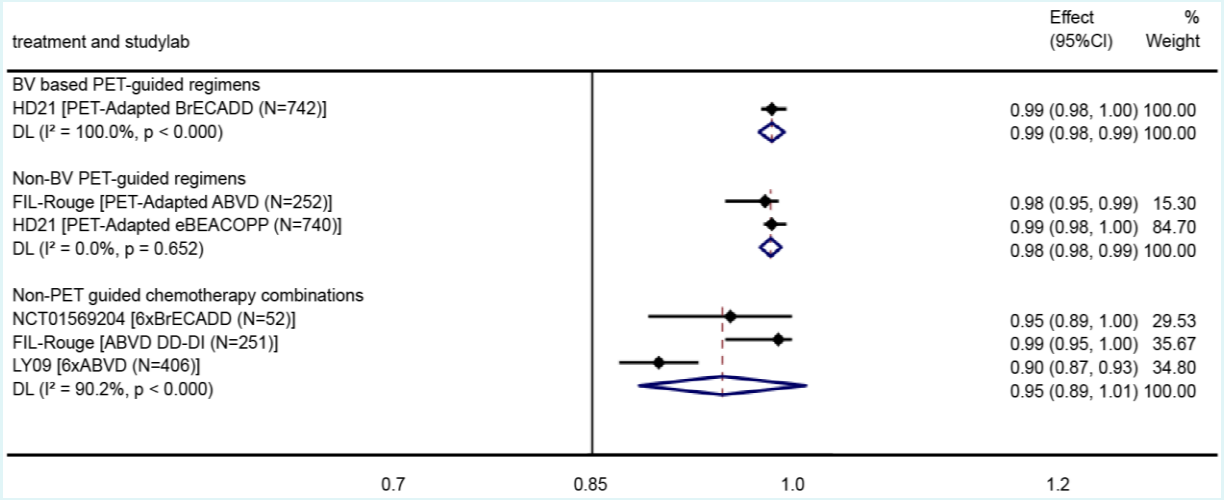
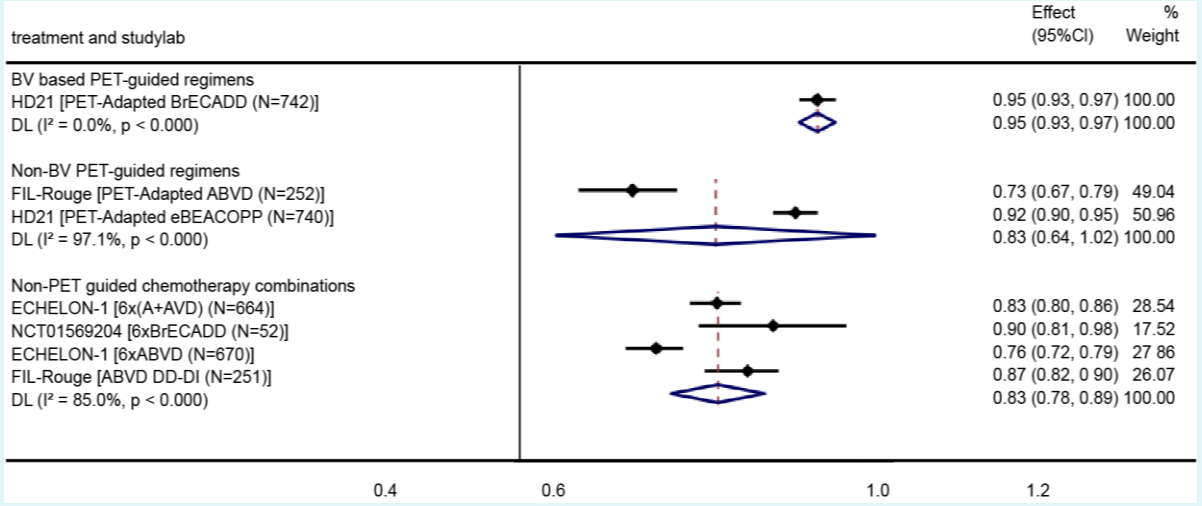


Figure 3 Forest diagrams for 3-year PFS



Notes: PET-Adapted BrECADD, PET driven BrECADD *2 cycles→BrECADD *2 cycles negative or BrECADD *4 cycles postive; PET-Adapted eBEACOPP, PET driven eBEACOPP *2 cycles→eBEACOPP *2 cycles negative or eBEACOPP *4 cycles postive; PET-Adapted eBEACOPP/ABVD, PET driven eBEACOPP *2 cycles →ABVD *2 cycles negative or eBEACOPP *2 cycles positive.

When using the DL (DerSimonian-Laird) method for a pooled analysis of survival rates, if the upper limit of the 95% CI exceeded 100%, the result was textually described as 100% in order to be consistent with the actual situation.

- The pooled **3-year OS** rates were **99%** (95% CI, 98%-99%), **98%** (95% CI, 98%-99%), and **95%** (95% CI, 89%-100%) for BV based PET-guided regimens, non-BV PET-guided regimens and non-PET guided chemotherapy combinations, respectively (Figure 2).
- The pooled **3-year PFS** rates were **95%** (95% CI, 93%-97%), **83%** (95% CI, 64%-100%), and **83%** (95% CI, 78%-89%) across the three treatment modalities, respectively (Figure 3).

Background & Objective

- The goal of treatment in classical Hodgkin Lymphoma (cHL) is to achieve cure with less toxicity.
- Traditional chemotherapy regimens for frontline advanced-stage cHL like ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) have been widely used but are associated with toxicities and a 30% relapse/progression rate.
- Several clinical trials confirmed the high efficacy of the incorporation of brentuximab vedotin (BV) to chemotherapy regimens with positron emission tomography (PET)-guided approaches to adapt the intensity and length of therapy.

Objective: This study aims to evaluate the efficacy of various therapeutic interventions in advanced-stage cHL through a meta-analysis of published randomised controlled trials (RCTs).

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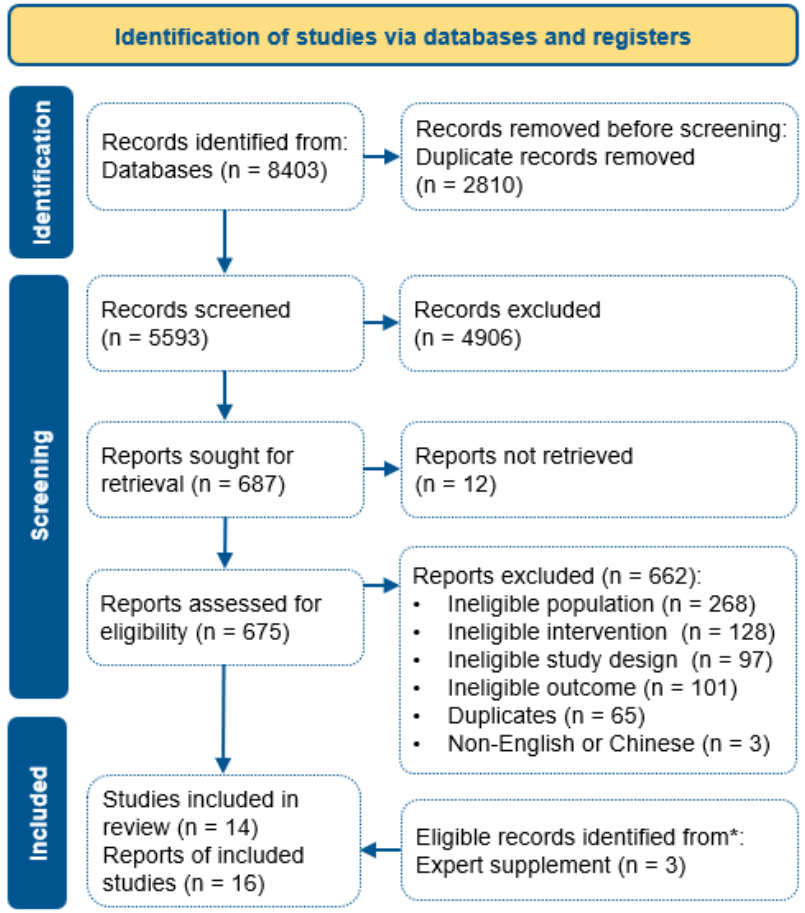
Methods

- A systematic search of databases (PubMed, EMBASE, the Cochrane Library, Web of Science, CBM, CNKI, Wanfang and VIP) was conducted to identify RCTs involving adult patients with newly diagnosed advanced stage cHL, with experts providing gray literature as a supplement. A PRISMA flow diagram was presented after study screening (Figure 1).
  - **Population**: adult patients with newly diagnosed advanced stage cHL
  - **Interventions**: categorized into three non-overlapping groups based on common clinical practice:
    1. BV based PET-guided regimens.
    2. Non-BV PET-guided regimens.
    3. Non-PET guided chemotherapy combinations (included BV-based chemotherapy and non-BV based chemotherapy).

    Notes: BV-based regimens only included BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) and BV-AVD (brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine); Chemotherapy regimens only included ABVD and eBEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone in escalated doses) *4-6 cycles regimen.
  - **Outcomes**: 3- and 5-year cumulative overall survival (OS) and progression-free survival (PFS) rates. If data is missing in a group, we used the closest data result to the target time point. For instance, data from the 4- or 6- year can be used to replace the missing data from the 5-year.
- We extracted cumulative incidence for PFS and OS rates with 95% confidence interval (CI) for each study. The Cochrane risk-of-bias tool (RoB) for RCTs were employed. Meta-analysis were performed using Stata (version 16.0) with the DerSimonian-Laird (DL) random-effects model.

Figure 1: PRISMA flow diagram



* Identification of studies via other methods.

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Baseline Characteristics

Table 1: Baseline characteristics of the included studies

trial name	Sample size	Intervention	Outcome
H34[13]	80	8×ABVD (N=80)	cd
HD2000[9]	99	6×ABVD (N=99)	cd
Avilés 1999[3]	56	6×EBVD (N=56)	cd
HD15[8]	711	6×eBEACOPP (N=711)	cd
AHL2011[6]	823	6×eBEACOPP (N=413) PET-Adapted eBEACOPP/ABVD (N=410)	cd
Bakemeier 1984[4]	147	6×BCVPP (N=147)	c
ECHELON-1[1,15,16]	1334	6×(A+AVD) (N=664) 6×ABVD (N=670)	bcd
HD21[5]	1482	PET-Adapted BrECADD (N=742) PET-Adapted eBEACOPP (N=740)	abcd
NCT01569204[7]	52	6×BrECADD (N=52)	ab
Avilés 2003[2]	134	6×EBVD (N=134)	c
LY09[12]	406	6×ABVD (N=406)	a
E2496[10]	395	6 to 8×ABVD (N=395)	c
ISRCTN 64141244[11]	261	6 to 8×ABVD (N=261)	cd
FIL-Rouge[14]	503	ABVD DD-DI (N=251) PET-Adapted ABVD (N=252)	ab

Notes: a, 3-year OS;b, 3-year PFS;c, 5-year OS;d, 5-year PFS.
PET-Adapted BrECADD, PET driven BrECADD *2 cycles→BrECADD *2 cycles negative or BrECADD *4 cycles positive; PET-Adapted eBEACOPP, PET driven eBEACOPP *2 cycles→eBEACOPP *2 cycles negative or eBEACOPP *4 cycles positive; PET-Adapted eBEACOPP/ABVD, PET driven eBEACOPP *2 cycles →ABVD *2 cycles negative or eBEACOPP *2 cycles positive.

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Results

- For long-term outcomes, **the 5-year pooled OS** rates were **99**% (95% CI, 98%-100%), **98**% (95% CI, 96%-99%), and **93**% (95% CI, 90%-95%) across the three treatment modalities, respectively (Figure 4).
- Corresponding the **5-year pooled PFS** rates were **94**% (95% CI, 93%-96%), **89**% (95% CI, 83%-94%), and **81**% (95% CI, 75%-87%) across the three treatment modalities, respectively (Figure 5).

Figure 4 Forest diagrams for 5-year OS

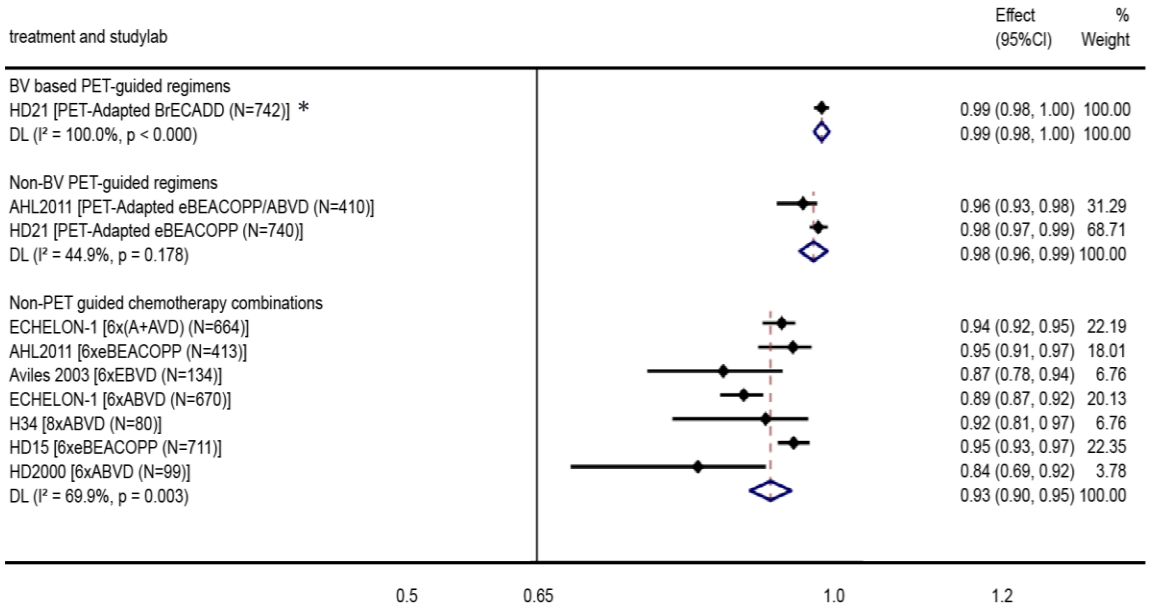
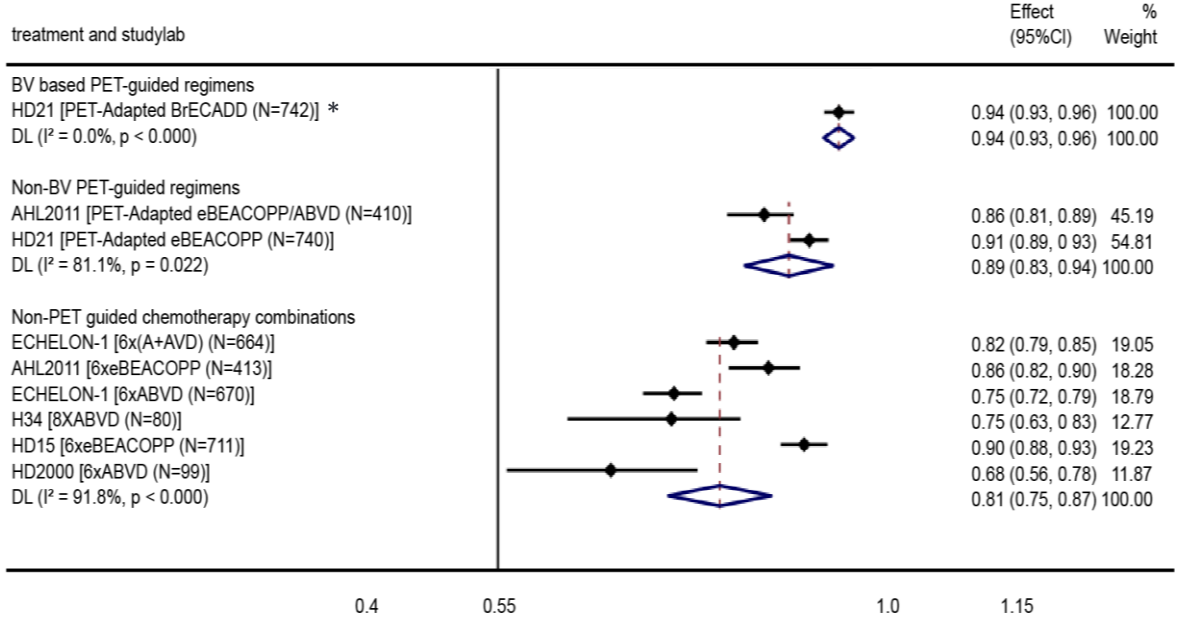


Figure 5 Forest diagrams for 5-year PFS



* During this meta-analysis, 4-year data was used in place of 5-year for HD21.

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Limitations and Author's Conclusions

Limitations

- The use of proportional meta-analysis, which focuses on pooled single-arm proportions, may itself contribute to substantial heterogeneity due to differences in baseline risk and study design.
- The absence of real-world data may restrict generalizability to everyday clinical practice.

Author's Conclusions

- This systematic review and meta-analysis of frontline studies in advanced stage cHL patients further supports the effectiveness of BV-based PET-regimens in achieving favorable 3- and 5-year OS and PFS rates. This meta-analysis integrates high-quality RCTs data across multiple international and national databases, covering a large sample of advanced-stage cHL patients.
- Based on the observed heterogeneity in efficacy, this study highlights the importance of individualized, PET-guided treatment strategies in advanced-stage cHL patients. Patients with high relapse risk—such as those with poor interim PET response or adverse baseline features—may benefit from treatment intensification using BV-based regimens, which demonstrated superior PFS and OS.
- Future research should focus on integrating prognostic indicators, PET response, and toxicity data into adaptive treatment frameworks to optimize therapeutic benefit while minimizing harm.

Li DH et al. Abstract PF865. Presented at the 2025 European Hematology Association Annual Meeting | June 12-15, 2025 | Milan, Italy

References, Acknowledgements, & Disclosures

References

1. Ansell SM, Radford J, Connors JM, et al. Overall Survival with Brentuximab Vedotin in Stage III or IV Hodgkin's Lymphoma. The New England journal of medicine. 2022;387(4):310-320.
2. Avilés A, Cleto S, Neri N, et al. Treatment of advanced Hodgkin's disease: EBVD versus intensive brief chemotherapy. Leuk Lymphoma. 2003;44(8):1361-1365.
3. Avilés A, Delgado S, Talavera A, González JL, Díaz Maqueo JC. Malignancy: Adjuvant Radiotherapy to Initial Bulky Disease in Patients with Advanced Stage Hodgkin's Disease. Hematology. 2000;4(6):479-485.
4. Bakemeier RF, Anderson JR, Costello W, et al. BCVPP chemotherapy for advanced Hodgkin's disease: evidence for greater duration of complete remission, greater survival, and less toxicity than with a MOPP regimen. Results of the Eastern Cooperative Oncology Group study. Ann Intern Med. 1984;101(4):447-456.
5. Borchmann P, Ferdinandus J, Schneider G, et al. Assessing the efficacy and tolerability of PET-guided BrECADD versus eBEACOPP in advanced-stage, classical Hodgkin lymphoma (HD21): a randomised, multicentre, parallel, open-label, phase 3 trial. The Lancet. 2024;404(10450):341-352.
6. Casasnovas RO, Bouabdallah R, Brice P, et al. PET-adapted treatment for newly diagnosed advanced Hodgkin lymphoma (AHL2011): a randomised, multicentre, non-inferiority, phase 3 study. Lancet Oncol. 2019;20(2):202-215.
7. Damaschin C, Goergen H, Kreissl S, et al. Brentuximab vedotin-containing escalated BEACOPP variants for newly diagnosed advanced-stage classical Hodgkin lymphoma: follow-up analysis of a randomized phase II study from the German Hodgkin Study Group. Leukemia. 2022;36(2):580-582.
8. Engert A, Haverkamp H, Kobe C, et al. Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin's lymphoma (HD15 trial): a randomised, open-label, phase 3 non-inferiority trial. Lancet. 2012;379(9828):1791-1799.
9. Evens AM, Connors JM, Younes A, et al. Older patients (aged ≥60 years) with previously untreated advanced-stage classical Hodgkin the phase lymphoma: III ECHELON-1 a detailed study analysis from the phase III ECHELON-1 study. Haematologica. 2022;107(5):1086-1094.
10. Federico M, Luminari S, Iannitto E, et al. ABVD compared with BEACOPP compared with CEC for the initial treatment of patients with advanced Hodgkin's lymphoma: results from the HD2000 Gruppo Italiano per lo Studio dei Linfomi Trial. J Clin Oncol. 2009;27(5):805-811.
11. Gordon LI, Hong F, Fisher RI, et al. Randomized phase III trial of ABVD versus Stanford V with or without radiation therapy in locally extensive and advanced-stage Hodgkin lymphoma: an intergroup study coordinated by the Eastern Cooperative Oncology Group (E2496). J Clin Oncol. 2013;31(6):684-691.
12. Hoskin PJ, Lowry L, Horwich A, et al. Randomized comparison of the stanford V regimen and ABVD in the treatment of advanced Hodgkin's Lymphoma: United Kingdom National Cancer Research Institute Lymphoma Group Study ISRCTN 64141244. J Clin Oncol. 2009;27(32):5390-5396.
13. Johnson PW, Radford JA, Cullen MH, et al. Comparison of ABVD and alternating or hybrid multidrug regimens for the treatment of advanced Hodgkin's lymphoma: results of the United Kingdom Lymphoma Group LY09 Trial (ISRCTN97144519). J Clin Oncol. 2005;23(36):9208-9218.
14. Mounier N, Brice P, Bologna S, et al. ABVD (8 cycles) versus BEACOPP (4 escalated cycles ≥ 4 baseline): final results in stage III-IV low-risk Hodgkin lymphoma (IPS 0-2) of the LYSA H34 randomized trial. Ann Oncol. 2014;25(8):1622-1628.
15. Pinto A, Corazzelli G, Evangelista A, et al. FRONTLINE INTENSIFIED ABVD DEMONSTRATES SUPERIOR EFFICACY THAN PET-ADAPTED ABVD IN ADVANCED HODGKIN LYMPHOMA: THE FIL-ROUGE PHASE 3 TRIAL BY THE FONDAZIONE ITALIANA LINFOMI. Hematological Oncology. 2023;41(S2):31-33.
16. Radford J, Bartlett N, Straus D, et al. Brentuximab vedotin plus chemotherapy for stage III/IV classical Hodgkin lymphoma: 4-year update of the ECHELON-1 study. British journal of haematology. 2020;189((Radford J.) University of Manchester, Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom):101-102.
17. Straus DJ, Długosz-Danecka M, Alekseev S, et al. Brentuximab vedotin with chemotherapy for stage III/IV classical Hodgkin lymphoma: 3-year update of the ECHELON-1 study. Blood. 2020;135(10):735-742.
18. Straus DJ, Dlugosz-Danecka M, Connors JM, et al. Brentuximab vedotin with chemotherapy for stage III or IV classical Hodgkin lymphoma (ECHELON-1): 5-year update of an international, open-label, randomised, phase 3 trial. Lancet Haematology. 2021;8(6):E410-E421.

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Disclosures

TR is member of advisory council/committees for Takeda;

LDH, ZWH, DY, TR receive Honoraria of Takeda;

WJL is employee of Takeda

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This study was funded by Takeda (China) International Trading Co., Ltd., an affiliation of Takeda Pharmaceutical company.

EHA – Abstract #PS1863

Metabolic Tumor Volume in Older Patients with Advanced-Stage Classic Hodgkin Lymphoma: Results from the GHSG HD21 Trial

Paul J. Bröckelmann[1] , Justin Ferdinandus[1] , Helen Kaul[1], Dominic Ufton[2], Katrin Roth[2], Alexander Fossa[3], Andreas Hüttmann[4], Felix Keil[5], Yon-Dschun Ko[6], Felicitas Hitz[7], Mark Hertzberg[8], Wolfram Klapper[9], Christian Baues[10], Hans-Theodor Eich[11], Stefanie Kreissl[13], Michael Fuchs[1], Gundolf Schneider[1], Hishan Tharmaseelan[1], Dennis A. Eichenauer[1], Bastian von Tresckow[1,4], Peter Borchmann[1], Carsten Kobe[2]

[1]University of Cologne, Faculty of Medicine and University Hospital of Cologne, Department I of Internal Medicine, and Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf (CIO ABCD), and German Hodgkin Study Group (GHSG), Cologne, Germany [2] Department of Nuclear Medicine, University Hospital of Cologne, and German Hodgkin Study Group (GHSG), Cologne, Germany. [3] Department of Oncology, Oslo University Hospital, Oslo, Norway; Nordic Lymphoma Group [4] Department of Hematology and Stem Cell Transplantation, West German Cancer Center and German Cancer consortium (DKTK partner site Essen), University Hospital Essen, University of Duisburg-Essen, Essen, Germany [5] Department of Hematology, Hanusch Krankenhaus, Vienna, Austria [6] Oncological Center, Johanniter Hospital, Bonn, Germany [7] Department of Medical Oncology/Hematology, Kantonsspital St.Gallen, St.Gallen, Switzerland [8] Prince of Wales Hospital Department of Haematology and University NSW, Sydney, and Australasian Leukaemia & Lymphoma Group (ALLG), Melbourne, Australia [9] Pathology, Hematopathology Section and Karl Lennert-Cancer Center, University Hospital Schleswig-Holstein, Kiel, Germany [10] Dept. of Radiation Oncology, University Hospital of Ruhr-Universität Bochum, Marien Hospital Herne, Herne, Germany [11]Department of Radiotherapy, University Hospital of Muenster, Muenster, Germany [12] Ordensklinikum Linz Elisabethinen, Linz, Austria

Introduction

- In the phase 2 cohort of the GHSG HD21 trial,[1] PET-guided treatment with 4-6x brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine and dexamethasone (BrECADD) was feasible and highly effective in older patients with advanced-stage Hodgkin lymphoma (AS-cHL) >60 years of age.[2]
- We previously demonstrated absence of residual metabolic tumor volume (MTV) after two cycles of chemotherapy in a majority of younger patients with AS-cHL, which was associated with favorable outcome.[3]
- Here, we analyze the metabolic tumor volume (MTV) at baseline and during treatment of patients in the HD21 older cohort.

Methods

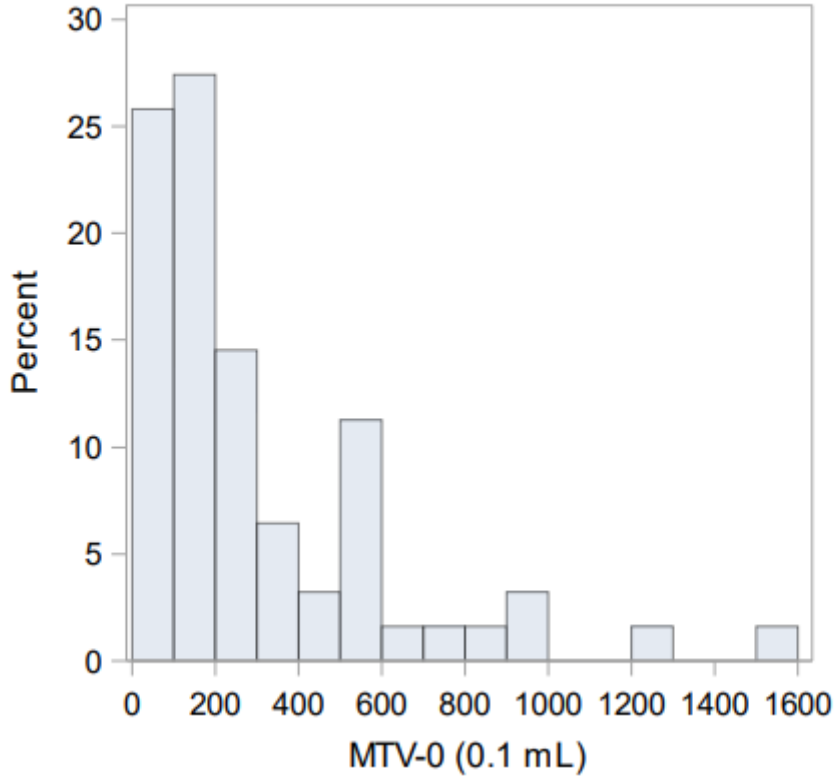
- Patients with AS-cHL aged 61-75 years were enrolled in a phase II single-arm cohort of the HD21 trial (NCT02661503).
- Patients with negative PET/CT, i.e. Deauville score (DS) 1-3, after 2x BrECADD received a total of 4x BrECADD, while PET2-positive patients received 6x BrECADD.
- We centrally measured MTV before treatment (MTV-0) and after 2x BrECADD (MTV-2) encompassing all sites of disease visible in PET with a standard uptake value above 4 (MTV4.0).
- Analyses were done using descriptive statistics. Kaplan-Meier analyses were used to analyze progression-free (PFS) and disease-specific survival (DSS), and Cox regressions were used to quantify associations of MTV.

Brockelmann PJ, et al. Abstract PS1863. Presented at the 2025 European Hematology Association Annual Meeting | June 12-15, 2025 | Milan, Italy

Results

- MTV-0 was measurable in 62 (75%) of the 83 patients included in the intention-to-treat cohort. MTV-2 could be measured in 79 of 80 patients with centrally reviewed PET2. Both MTV-0 and MTV-2 were measured in 60 patients.
- Median MTV-0 was 195 mL (range 5-1525; Figure 1). Patients with a complete response after 2x BrECADD had a median MTV-0 of 165 mL (range 5-1525) and patients with partial response (PR) a median of 198 mL (56-1238). MTV0 was not predictive of response at interim or end of treatment in this small cohort.

Figure 1: Metabolic tumor volume at baseline (MTV-0)



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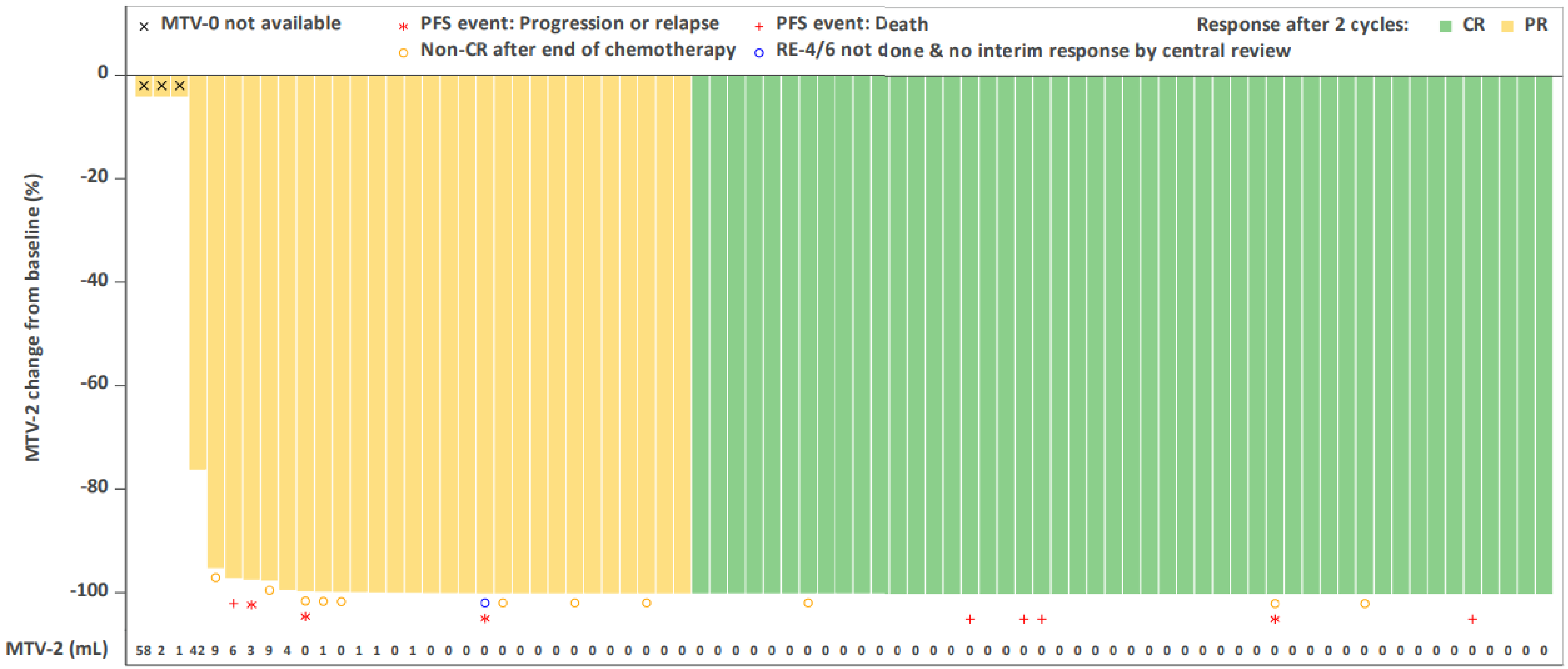
Results

- In total, 60/79 (76%) patients had no residual MTV-2 (Figure 2). Among 31 patients with PR, 12 (39%) had no measurable MTV-2.
- The 2-year PFS estimates for patients with and without measurable MTV-2 were 89% (CI95: 75-100) and 92% (CI95: 84-100), respectively, with a hazard ratio of 1.63 (95%CI: 0.41-6.53). The 2-year DSS estimates for patients with and without measurable MTV-2 were 91% (95%CI: 74-100) and 98% (CI95: 95-100), respectively, with a hazard ratio of 3.26 (95%CI: 0.20-52.12).

Figure 2: Metabolic tumor volume (MTV4.0) after two cycles of BrECADD (MTV-2): Change from baseline and outcome correlation



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Author’s Conclusions

- PET-guided BrECADD achieves early deep remissions in older patients with AS-cHL, irrespective of initial lymphoma burden.
- Most patients had no measurable MTV-2, including many patients with PR according to Deauville criteria.
- The observed high PFS and DSS rates in this group encourage the evaluation of MTV-2 to guide individualized treatment also in older patients with AS-cHL.

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References, Acknowledgements, & Disclosures

References

1. Borchmann P, … Diehl V. *Lancet* 2024
2. Ferdinandus J, …, Bröckelmann PJ ASH 2024
3. Ferdinandus J, …. Kobe C ASH 2024

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Potential Conflicts of Interest

PJB is an advisor or consultant for Hexal, Merck Sharp & Dohme (MSD), Need Inc., Stemline and Takeda; holds stock options in Need Inc., has received honoraria from AstraZeneca, BeiGene, Bristol-Myers Squibb/Celgene (BMS), Eli Lilly, MSD, Need Inc., Stemline and Takeda and reports research funding to institution from BeiGene, BMS, MSD and Takeda. He reports an Excellence Stipend of the Else-Kröner-Fresenius Foundation (EKFS).

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ELEVATED SERUM TARC AFTER ONE CYCLE OF BV-AVD PREDICTS POOR OUTCOME DESPITE BRECADD ESCALATION IN ADVANCED HODGKIN LYMPHOMA: EORTC-1537-COBRA ANALYSIS

Sophie Teesink, Lydia Visser, Laure Musekera, Anna Sureda, Susanna Carvalho, Andrey Vranovsky, Annika Loft, Anne Arens, Sanne Tonino, Ward Sents, Cédric Mallien, Berthe Aleman, Walter Noordzij, Catherine Fortpied, Martin Hutchings, Arjan Diepstra and Wouter Plattel

EHA 2025. Milan, Italy, 12 June 2025, abstract s229

Disclosures

- Nothing to disclose

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Background

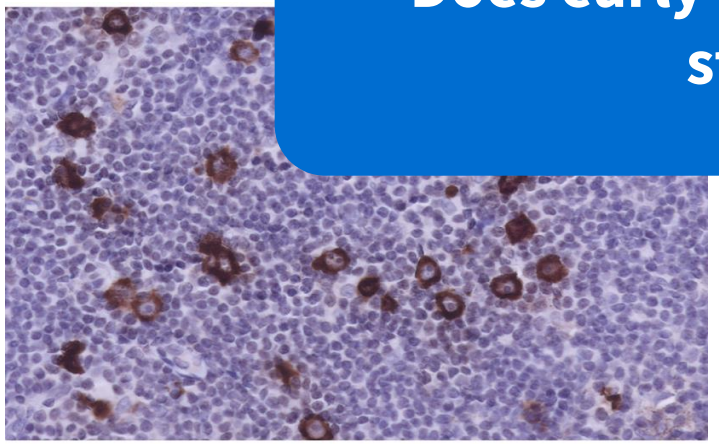
- In cHL golden standard: interim FDG-PET response adapted treatment [1-4]
- Limitations
  - Nonspecific
  - Limited positive predictive value
- Room for biomarkers

1. Gallamini A. et al. J Clin Oncol. 2007
2. Johnson PW. et al. N Engl J Med 2016
3. Borchmann P. et al. Lancet 2017
4. Andre MPE et al. J. Clin Oncol 2017

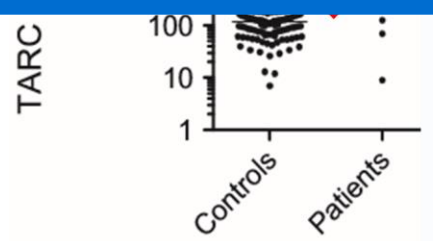
Background

- Thymus and Activation related chemokine (TARC, or CCL17)
  - Excreted by Hodgkin-Reed Sternberg cells
  - Elevated in >90% of patients at baseline

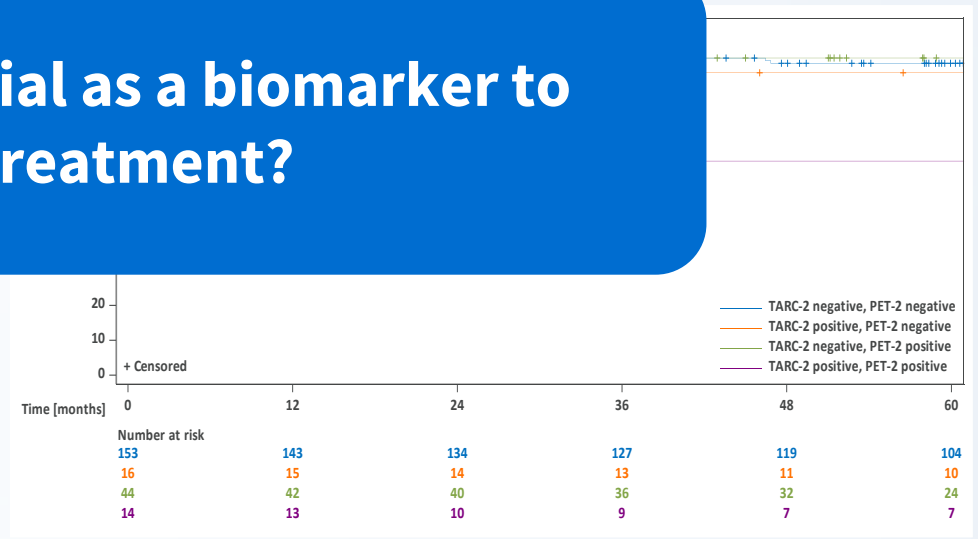
Does early interim sTARC have potential as a biomarker to stratify patients and guide treatment?



Kilsdonk M et al. Histopathology 2022



Plattel WJ et al. Br J Haematology, 2016



Plattel WJ et al. *Presented at EHA2024*

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Aim

Does early interim sTARC have potential as a biomarker to stratify patients and guide treatment?

Main aim:

- Correlation of early interim sTARC with interim PET after one cycle BV-AVD

- Prognostic value of interim sTARC, PET and combination

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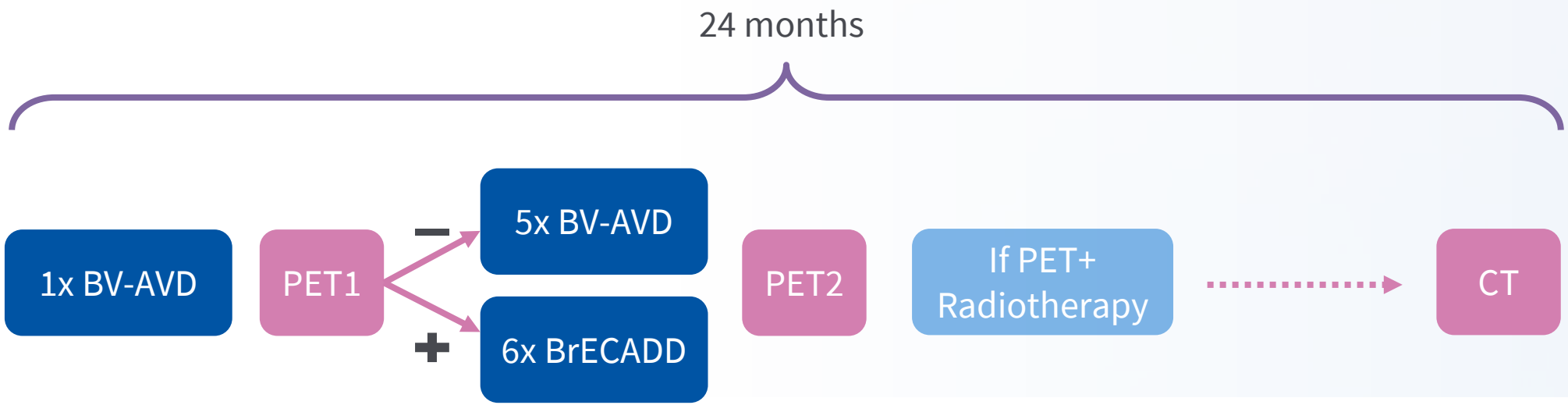
EORTC-COBRA trial - Background

- COBRA study (very early PET response adapted)
- Advanced stage cHL
  - 145 eligible patients at PET1



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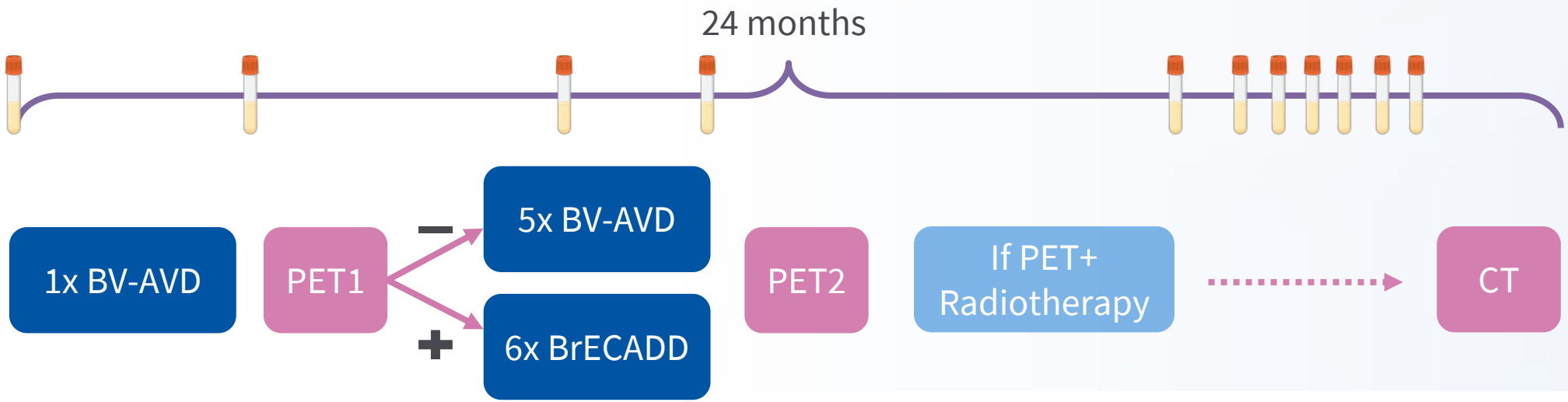
Methods

- Preplanned sTARC → baseline & one cycle
  - Measured by ELISA blinded for clinical characteristics and outcome
  - Predefined cut-off >1000 pg/ml
    - Outcome analysis only pts with both sTARC positive baseline (95%) + available sample over time (n = 127)



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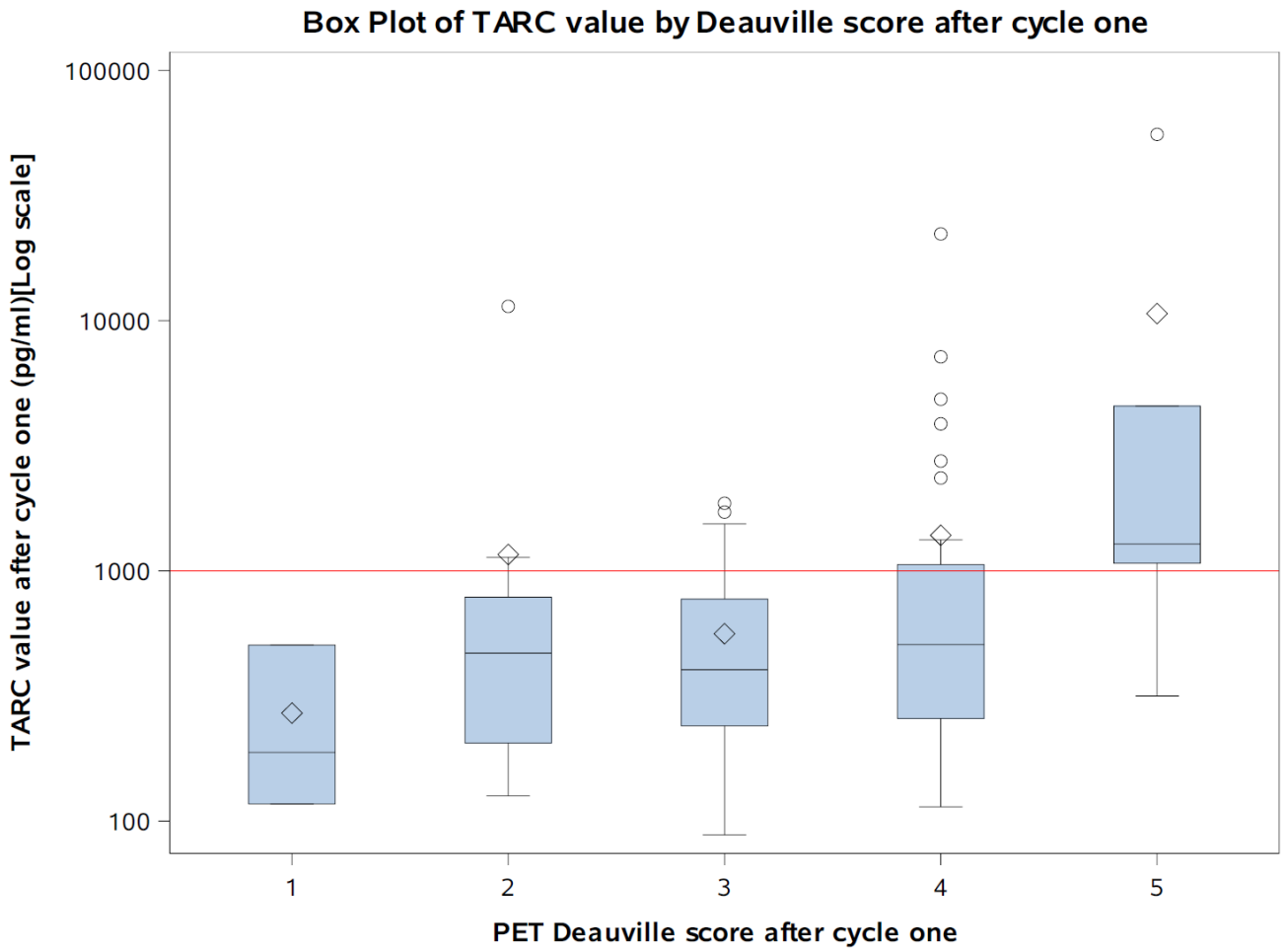
Very early response: PET1 vs sTARC



36/53 (68%) of PET1+ patients is sTARC1 negative

Odds of elevated sTARC 2.3x higher in PET+ patients

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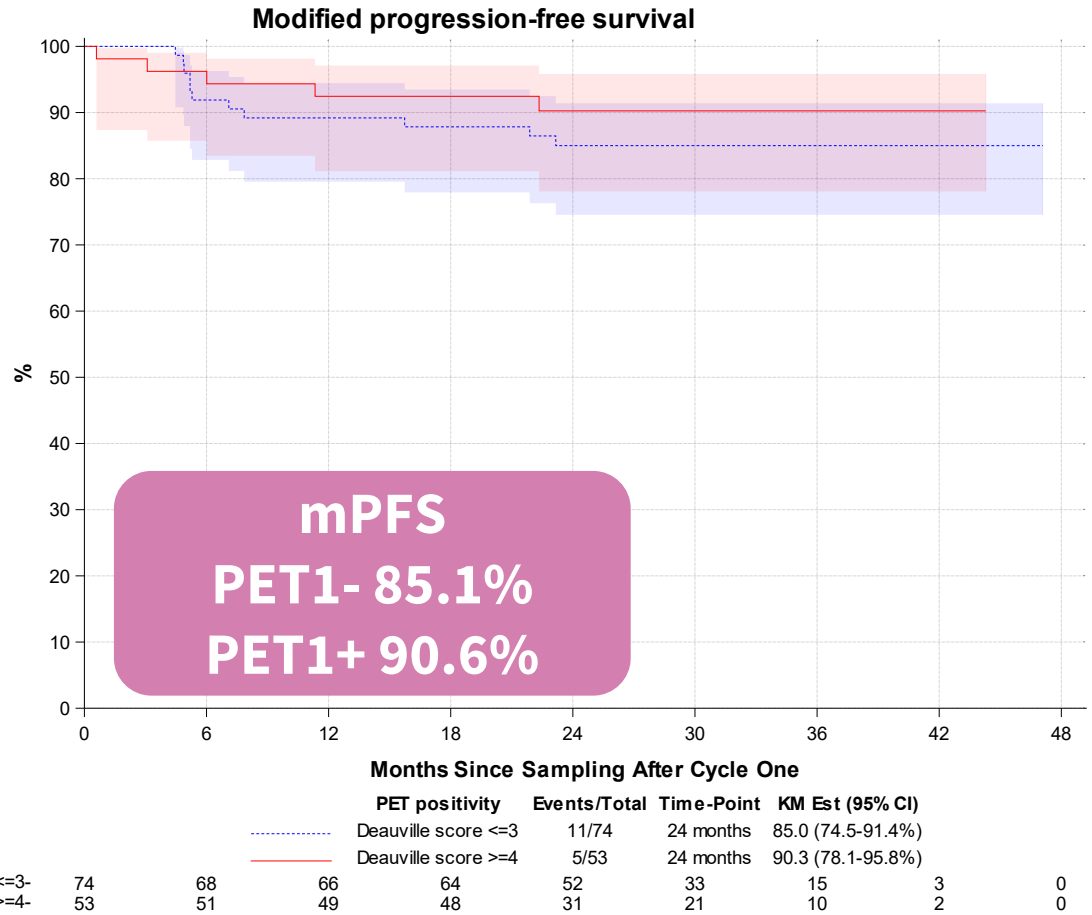
Outcome PET

- Complete metabolic response rate at end of treatment all patients: **91.0%**
- 16 PFS events

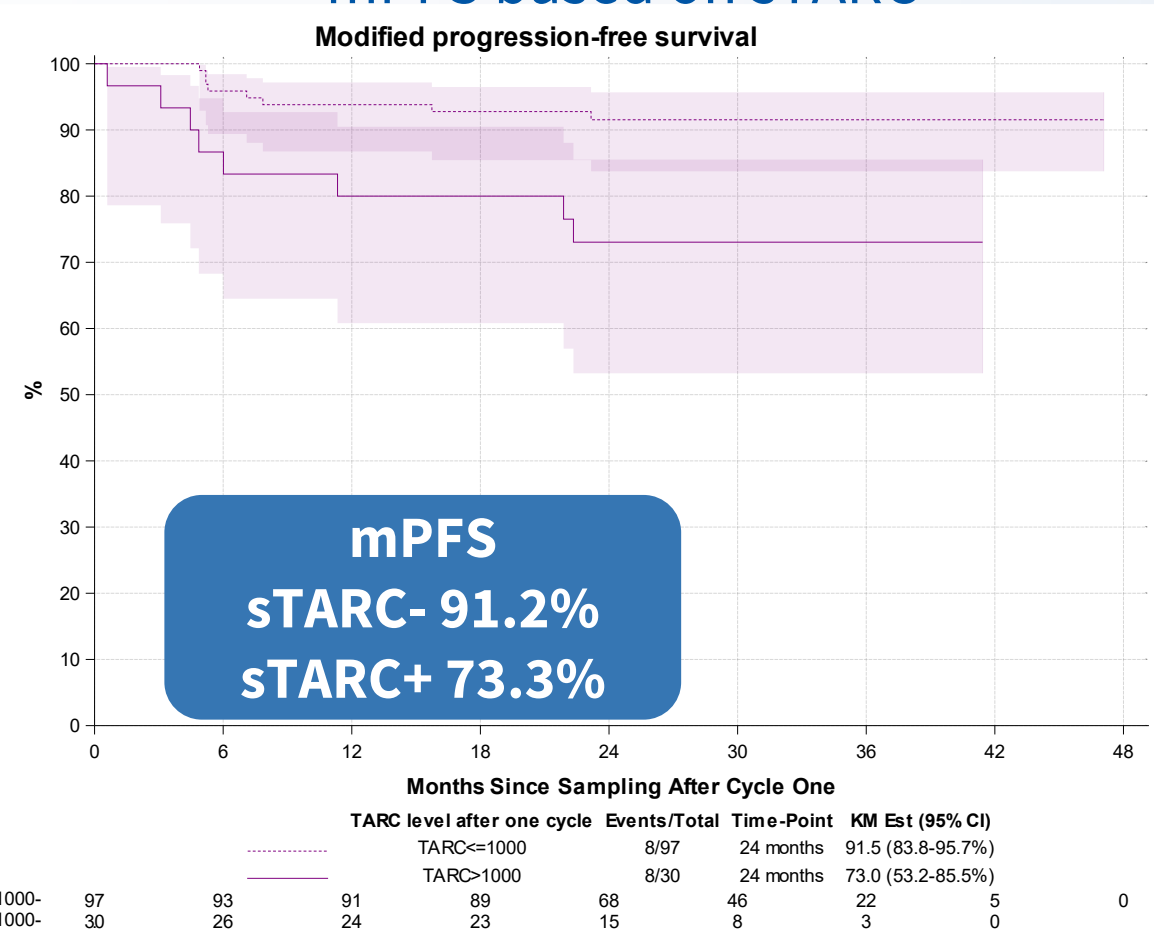
Progression free survial

While adapted based on PET1!

mPFS based on PET1



mPFS based on sTARC



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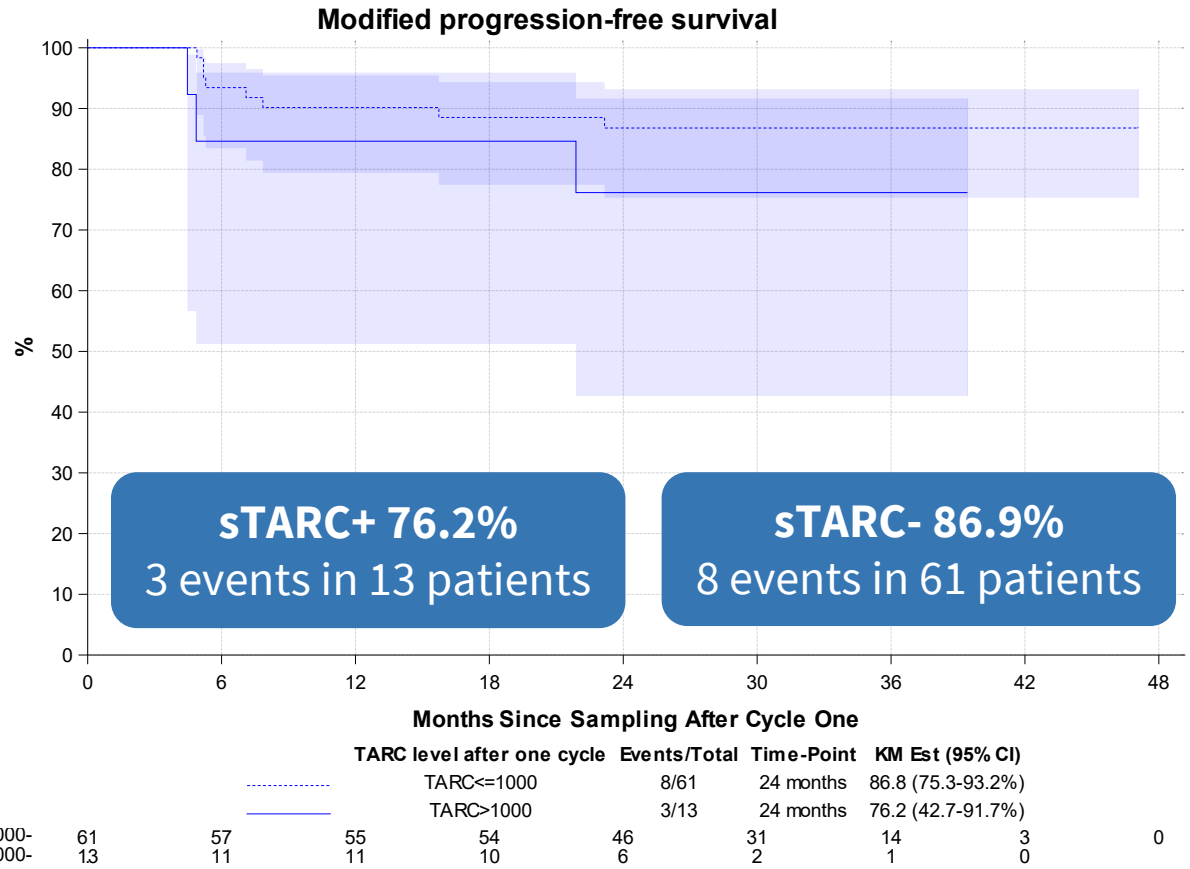
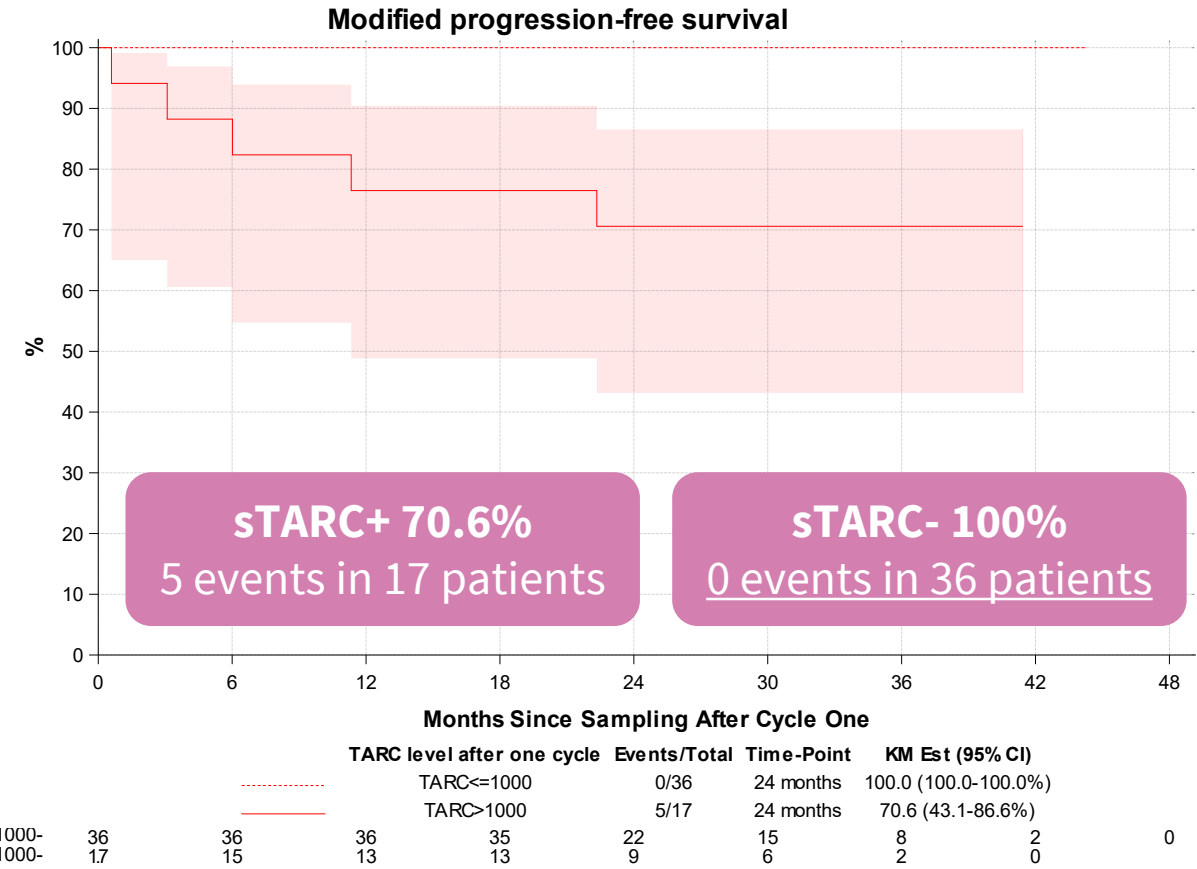
PET1 negative: 5x BV-AVD (n=74)



PET1 positive: 6x BrECADD (n=53)

68% of patients sTARC-



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Conclusion

- **Early normalisation of sTARC predicts excellent outcome despite PET positivity**
  - ➢**Most of PET1+ patients are sTARC- (68%)**

- **Double positive patients (interim sTARC & PET) are at increased risk of treatment failure despite treatment intensification**

sTARC has a significant prognostic value very early during treatment and can be used in treatment guidance

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Central PET review panel:

Anne Arens, Annika Loft, Walter Noordzij

Radiotherapy QC panel:

Berthe Aleman, Richard van der Maazen, Paul Meijnders

EORTC HQ team:

Catherine Fortpied, Laure Musekera*, Ward Sents, Cedric Mallien, Emanuel Buhrer, Sarah Nuyens, Shani De Coster, Hazal Erkol, Bette Stofs

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EHA – Abstract #PF870

Consolidation treatment with brentuximab vedotin after allogeneic stem-cell transplantation for relapsed Hodgkin Lymphoma: Analyisis of the GHSG phase 2 BV-ALLO trial

Christof Scheid[1], Janina Jablonski[2], Andrea Kerkhoff[4], Matthias Stelljes[4], Karolin Trautmann-Grill[5], Martin Bornhäuser[5], Johanna Maria Tischer[6], Michael von Bergwelt[6], Francis Ayuk[7], Nicolaus Kröger[7], Udo Holtick[1], Michael Fuchs[12], Peter Borchmann[12], Paul J. Bröckelmann[1-3]

[1]University of Cologne, Faculty of Medicine and University Hospital Cologne, Department of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD), Cologne, Germany. [2]German Hodgkin Study Group (GHSG), Cologne, Germany. [3]Max Planck Research Group Mechanisms of DNA Repair, Max Planck Institute for Biology of Ageing, Cologne, Germany. [4]University Hospital Münster, Germany. [5]University Hospital Carl Gustav Carus, TU Dresden, Germany. [6]University Hospital, Ludwig-Maximilians-University, Munich, Germany. [7]University Hospital Eppendorf, Hamburg, Germany.

Introduction & Aim

Introduction

- Allogeneic stem cell transplantation (alloSCT) is potentially curative in patients with relapsed or refractory classic Hodgkin Lymphoma (rrHL).
- However, relapse occurs in about 50% of patients within the first 2 years after alloSCT (Sureda et al. Haematologica 2012).
- Brentuximab vedotin (BV) is an antibody drug-conjugate targeting CD30 and approved as consolidation treatment after autologous SCT.
- Feasibility and efficacy after alloSCT have, however, not yet been studied prospectively.

Aim

- To investigate the safety and efficacy of BV consolidation after alloSCT
- To reduce the risk of relapse within the first year after alloSCT

Scheid C, et al. Abstract PF870. Presented at the 2025 European Hematology Association Annual Meeting | June 12-15, 2025 | Milan, Italy

Methods

Study Design:

- Prospective multicenter single-arm GHSG phase II trial (NCT03652441)

Recruitment:

- 11/2019– 9/2022, 5 German centers

Study treatment:

- BV was administered at 1.8 mg/kg every 3 weeks for up to 16 doses and a maximum of 12 months
- Start between days +30 to +45 after alloSCT
- Maximum interruption allowed: 12 weeks

Primary endpoint:

- Cumulative incidence of relapse (CIR) at 12 months

Secondary endpoints: included safety, feasibility, progression-free (PFS) and overall survival (OS)

Scheid C, et al. Abstract PF870. Presented at the 2025 European Hematology Association Annual Meeting | June 12-15, 2025 | Milan, Italy

Results

13 patients with Hodgkin lymphoma

- **Sex:** male 69% female 31%
- **Age:** median 33 years (range 19-61)

Prior treatment:

- median 4 prior (range: 2-17)
- prior BV: 11 (85%)
- prior anti-PD1: 13 (100%)

Response prior alloSCT:

CR: 4 (31%), PR: 8 (61%), SD 1 (8%)

Median BV treatment duration:

21 weeks (range: 6-58) after alloSCT,

Median number of BV doses:

5 (range: 1-15)

Reasons for BV discontinuation: treatment interruption >12 weeks: 5, toxicity: 3, other disease incl. GvHD: 3, PD: 2, non-relapse mortality: 1

GvHD: acute GvHD: 9 (69%), grade 3-4: 5 (39%) chronic GvHD: 2 (15%)

Scheid C, et al. Abstract PF870. Presented at the 2025 European Hematology Association Annual Meeting | June 12-15, 2025 | Milan, Italy

Results

Figure 1. Cumulative incidence of relapse

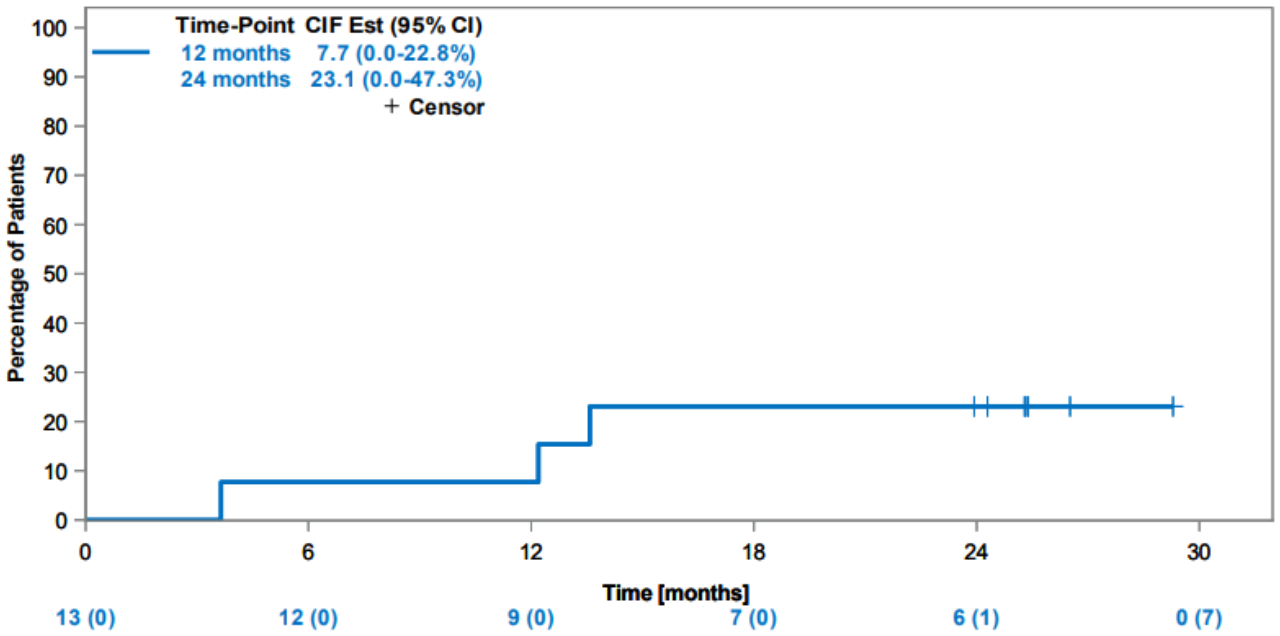
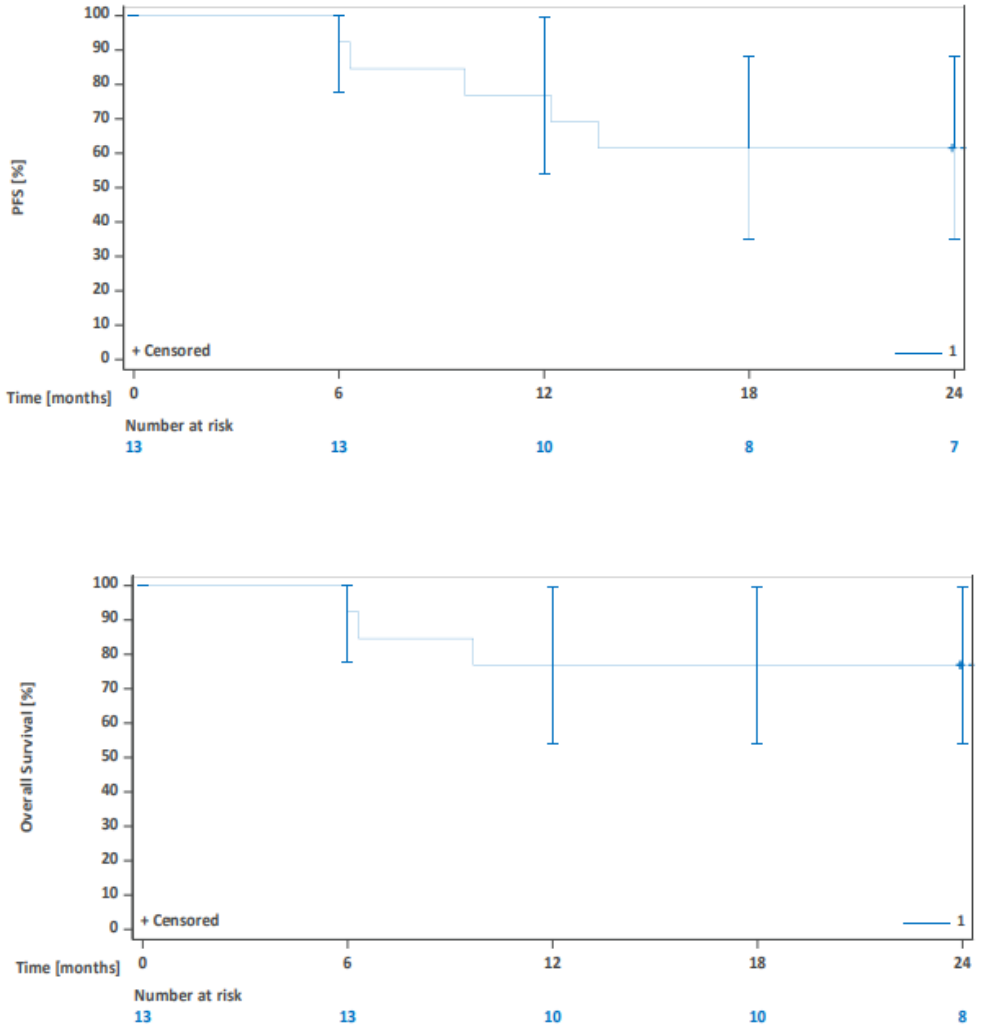


Figure 2. PFS (top) and OS (bottom)



Best response after alloSCT: CR 11/13 patients (85%), 1 no change, 1 unknown

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Results

Table 1. Toxicity unrelated to alloSCT

	all Grades	Grade 3-4	Grade 1	Grade 2	Grade 3	Grade 4
Alopecia	1 (8%)	.	.	1	.	.
Anaphylactic reactions	2 (15%)	.	1	1	.	.
Anemia	4 (31%)	1 (8%)	1	2	1	.
Gastrointestinal disorders	3 (23%)	.	.	3	.	.
Hepatobiliary disorders	2 (15%)	1 (8%)	1	.	.	1
Impairment of organ function	4 (31%)	.	2	2	.	.
Infection	4 (31%)	1 (8%)	3	.	1	.
Leukopenia	5 (39%)	2 (15%)	2	1	.	2
Mucositis	1 (8%)	.	.	1	.	.
Nausea/vomiting	5 (39%)	.	3	2	.	.
Neutropenia	5 (39%)	4 (31%)	1	.	1	3
Sensory polyneuropathy	10 (77%)	1 (8%)	6	3	1	.
Thrombopenia	3 (23%)	.	2	1	.	.

Table 2. Toxicity related to alloSCT

	all Grades	Grade 3-4	Grade 1	Grade 2	Grade 3	Grade 4
Anemia	6 (46%)	3 (23%)	1	2	3	.
Bleeding	1 (8%)	.	1	.	.	.
Febrile neutropenia	1 (8%)	1 (8%)	.	.	1	.
Gastrointestinal disorders	1 (8%)	1 (8%)	.	.	1	.
Haemorrhagic cystitis	1 (8%)	1 (8%)	.	.	1	.
Hepatobiliary disorders	4 (31%)	3 (23%)	.	1	3	.
Impairment of organ function	1 (8%)	.	1	.	.	.
Infection	3 (23%)	.	.	3	.	.
Leukopenia	3 (23%)	1 (8%)	1	1	1	.
Mucositis	.	.	.	.	.	.
Nausea/vomiting	2 (15%)	.	1	1	.	.
Neutropenia	3 (23%)	2 (15%)	.	1	1	1
Thrombopenia	5 (39%)	3 (23%)	1	1	2	1

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Author’s Conclusions

- Combining BV consolidation with alloSCT resulted in a high complete remission rate and cumulative incidence of relapse of less than 10% at 12 months.
- For a HL patient cohort with mostly active disease at alloSCT, this compares favourably with previous results.
- However, treatment interruption and discontinuation were common due to alloSCT related complications and toxicities.
- Therefore, BV consolidation is an effective treatment option post alloSCT, but needs to be adapted to the clinical complexity and increased vulnerabilities in this setting.

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ICML – Abstract #354

A matching-adjusted indirect treatment comparison (MAIC) of BrECADD vs N+AVD in populations with advanced Hodgkin lymphoma (aHL) treated in the Front-Line (FL) setting

Thomas Melchardt, MD,[1] **Alexa Molinari**, PharmD, MS,[2] Fjoralba Kristo, MD, MPH,[3] Zhiyi Lan, MSc,[4] Zijiao Yuan, MSc,[4] Athanasios Zomas, MD,[5] Vanessa Stache, PhD, MS,[5] Abbey Poirier, MSc,[4] Victoria Federico Paly, MHS[2]

[1]Paracelsus Medical University, Salzburg, Austria; [2]Takeda Pharmaceuticals America, Inc., Lexington, MA, USA; [3]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [4]Cytel Inc., Cambridge, MA, USA; [5]Takeda Pharmaceuticals International AG, Zurich, Switzerland

Question

What is the comparative effectiveness of BrECADD vs N+AVD with regards to progression-free survival (PFS) in patients aged 18–60, 18–75, and 61–75 years with aHL?

Methods

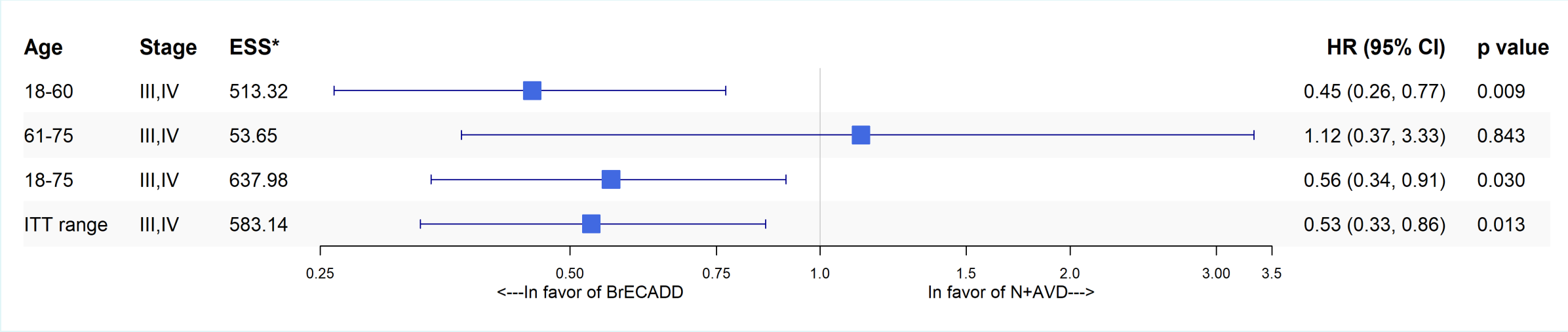
A feasibility assessment and a MAIC were conducted to compare PFS in patients with aHL treated with BrECADD vs N+AVD.

Key take aways

BrECADD was associated with significantly improved PFS in comparison to N+AVD in patients with aHL aged 18–60 and 18–75.

Results

Figure 1: Cox regression results for base case scenario PFS



*ESS (effective sample size) calculated represents the adjusted BrECADD patient sample after weighting. BrECADD unweighted sample sizes were originally 18–60 years n=751, 61–75 n=85, and 18–75 n=836. N+AVD sample sizes were 18–60 years n=319, 61–75 n=50, 18–75 n=365, and ITT n=487.

Background & Objective

- In the HD21 trial, PET-guided brentuximab vedotin, etoposide, cyclophosphamide, adriamycin/doxorubicin, dacarbazine, dexamethasone (BrECADD) demonstrated improved PFS over PET-guided escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone (eBEACOPP) among patients with aHL aged 18–60 years.[1] Patients aged 61–75 years were treated in a single-arm, nonrandomized, phase 2 cohort with BrECADD exclusively. [1]
- SWOG S1826 evaluated nivolumab (N) + adriamycin/doxorubicin, vinblastine, and dacarbazine (AVD) against brentuximab vedotin (BV) + AVD in patients with Stage III/IV aHL, and N+AVD was found to be superior in PFS with a 25.2-month median follow-up.[2]
- No head-to-head comparisons have been conducted between these regimens in patients with aHL to date.

Objective: In the absence of head-to-head comparisons, this set of analyses assessed the comparative effectiveness of first-line BrECADD versus N+AVD with regards to PFS in the 18–60, 18–75, and 61–75 years old populations and the SWOG S1826 intention-to-treat (ITT) (age 12+) population with Stage III/IV aHL.

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Methods

Data sources

- Baseline characteristics and efficacy data for SWOG S1826 were sourced from conference presentations and published reports.[2–4]
- Patient-level data pooled for the randomized and nonrandomized cohorts (R+nR) from HD21 were weighted for comparison with aggregate data from SWOG S1826 using a MAIC approach.
- The HD21 median follow-up (mFU) was 53.0 months for the randomized cohorts and 27.1 months for the nonrandomized cohort, while the mFU for SWOG S1826 was 25.2 months.

Effect modifiers and prognostic factors

- Potential treatment effect modifiers (TEMs) and prognostic variables (PVs) were identified through interviews with practicing hematologists across EU countries for each cohort and statistical significance based on analysis of HD21 IPD. These TEMs and PVs were used to inform the scenario analyses conducted.

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Methods

MAIC analysis methods

- The time-to-event outcome data in SWOG S1826 were recreated via digitization based on available PFS curves for the overall ITT (age 12+), age 18–60, age 18–75, and age 61–75 years populations.
- Analyses were adjusted for age, sex, international prognostic score (IPS), stage, and B symptoms at baseline to inform the base case (BC) comparisons. Please see **Table 1** below for a list of scenario analyses conducted. The best case (BC) conditions are highlighted in purple and represent the analyses presented in **Figure 1.**
- Weighted Cox regression was employed to generate hazard ratios (HRs) with 95% confidence intervals (CIs). Scenario analyses were conducted to assess the implications of covariate combinations and various censoring cutoff timepoints.

Table 1: Scenarios for analysis

Analysis	Matching Variables	Rationale
Base case ("BC"):	Age, sex, IPS, stage, B symptoms	All available matching variables included
Scenario 1 (S1) – Significant variables	Age, sex, IPS	Limit to matching variables identified as statistically significant per analysis of HD21 IPD
Scenario 2 (S2) – Clinically-relevant variable adjustment	Age, stage, B symptoms	Limit to matching variables deemed relevant per interviews with practicing hematologists
Scenario 3 (S3) – Age sensitivity	Age, sex, IPS, stage, B symptoms	Implement age as continuous vs categorical
Scenario 4 (S4) – Adjustment without age	Sex, IPS, stage, B symptoms	Explore the potential impact of adjusting for all BC variables except age
Additional scenarios for 18+, pooled HD21 R+nR analyses only	**Time horizon censoring**	**Rationale**
Base Case ("BC 30")	30 months	In the pooled analysis (HD21 + HD21 elderly), considering the potential censoring bias due to different follow-up times for the two cohorts, different time cutoffs were tested to assess the robustness of results
Scenario 1 ("SC-24"): Censoring at 24 months	24 months	
Scenario 2 ("SC-36"): Censoring at 36 months	36 months	
Scenario 3 ("SC-all"): No time cutoff	Full follow-up	

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Results

- Patient characteristics were well-balanced between trials after MAIC reweighting.

Base case results

- BrECADD demonstrated significantly improved PFS compared to N+AVD in the overall 18–75 aHL population (HD21 R+nR) with a HR=0.56 (95% CI: 0.34–0.91, *P*=0.030) and in the 18–60 population (HD21 R): HR=0.45 (95% CI: 0.26–0.77, *P*=0.009). Among the 61–75 aHL population, a non-significant trend in favor of N+AVD was observed (HR=1.12; 95% CI: 0.37–3.33, *P*=0.843). When compared to the SWOG S1826 ITT population (age 12+), BrECADD (HD21 R+nR, 18–75) demonstrated significant benefit in PFS (HR=0.53; 95% CI: 0.33–0.86, *P*=0.013). Figure 1 above depicts all BC results.

Scenario analysis results

- Additional scenario analyses also demonstrated benefit in favor of BrECADD regardless of variable adjustment or censoring timepoint cutoff applied for the 18–60 and 18–75 cohorts. These results are presented in Figure 2 below and display the robustness of the analyses as the findings remained consistent with the BC results.

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Results

Figure 2: Cox regression results for PFS: Additional scenarios

Comparison	Scenario	ESS*	HR (95% CI)	p value
Age 18-60; Stage III/IV	Naïve	631	0.48 (0.29, 0.80)	0.004
HD21 younger vs SWOG S1826 younger	BC	513.32	0.45 (0.26, 0.77)	0.009
	S1	533.69	0.43 (0.25, 0.75)	0.007
	S2	533.28	0.44 (0.25, 0.77)	0.008
	S3	358.68	0.36 (0.19, 0.68)	0.003
	S4	579.51	0.50 (0.29, 0.85)	0.019
Age 61-75; Stage III/IV	Naïve	82	0.96 (0.36, 2.60)	0.941
HD21 elderly vs SWOG S1826 elderly	BC	53.65	1.12 (0.37, 3.33)	0.843
	S1	81.8	0.95 (0.35, 2.59)	0.914
	S2	55.15	1.22 (0.41, 3.62)	0.728
	S3	50.58	0.97 (0.32, 2.92)	0.958
	S4	54.25	1.13 (0.38, 3.41)	0.824
Age 18-75; Stage III/IV	Naïve (30)	713	0.56 (0.35, 0.90)	0.016
HD21 pooled vs SWOG S1826 adult	BC (30)	637.98	0.56 (0.34, 0.91)	0.030
	S1 (30)	674.87	0.54 (0.34, 0.88)	0.023
	S2 (30)	654.09	0.55 (0.34, 0.89)	0.025
	S3 (30)	531.96	0.46 (0.27, 0.78)	0.007
	S4 (30)	650.26	0.59 (0.36, 0.96)	0.046
	SC-24	637.98	0.52 (0.31, 0.88)	0.023
	SC-36	637.98	0.54 (0.33, 0.88)	0.021
	SC-All	637.98	0.50 (0.31, 0.81)	0.009
Age ITT range; Stage III/IV	Naïve (30)	713	0.59 (0.38, 0.92)	0.019
HD21 pooled vs SWOG S1826 ITT	BC (30)	583.14	0.53 (0.33, 0.86)	0.013
	S1 (30)	605.86	0.52 (0.33, 0.83)	0.010
	S2 (30)	597.95	0.52 (0.32, 0.85)	0.011
	S3 (30)	412.99	0.40 (0.22, 0.71)	0.002
	S4 (30)	668.29	0.61 (0.39, 0.96)	0.040
	SC-24	583.14	0.56 (0.34, 0.93)	0.031
	SC-36	583.14	0.52 (0.32, 0.84)	0.010
	SC-All	583.14	0.52 (0.32, 0.82)	0.007

Note Unadjusted analyses are otherwise denoted as “naïve” in the scenarios above. BC is to communicate the “base case” scenario which are fully adjusted for all mutually available/reported variables. SC1through SC-All are the scenario analyses ran according to *Table 1.*

*ESS (effective sample size) calculated represents the adjusted BrECADD patient sample after weighting. BrECADD unweighted sample sizes were originally 18–60 years n=751, 61–75 n=85, and 18–75 n=836. N+AVD sample sizes were 18–60 years n=319, 61–75 n=50, 18–75 n=365, and ITT n=487.

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Limitations & Author's Conclusions

Limitations

- There are limitations to consider when interpreting the results from these unanchored MAICs, including:
  - All variables identified as TEMs or PVs were not available for matching in all included studies. In the presence of residual confounding, unanchored comparisons are more susceptible to bias and systematic error from improper model specification.
  - The HD21 nR cohort (the elderly cohort, 61–75) had a relatively short median follow-up time of 27.1 months and a small sample size, which limited the power of any analysis involving these data and prompts the need for further analysis.
  - There are substantial differences in regional location, patient populations, and follow-up time between studies and cohorts compared.
  - These analyses were limited to PFS and did not include indirect comparison of overall survival due to the immaturity of the data for that outcome.

Author's Conclusions

- Among patients aged 18–60 and 18–75 years with aHL, BrECADD was robustly associated with significantly improved PFS in comparison to N+AVD. Results for the 61–75 years old population deliver additional evidence but are limited by small sample size and number of events. These findings can aid healthcare decision-makers where head-to-head data are unavailable.

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References, Acknowledgements, & Disclosures

References

1. Borchmann P, Ferdinandus J, Schneider G, et al. Lancet. 2024;404:341–52
2. Castellino SM, Li H, Herrera HF, et al. Hemasphere. 2024;8:e70012. Abstract T087
3. Herrera AF, LeBlanc M, Castellino SM, et al. N Eng J Med. 2024;391:1379–89
4. Rutherford S, Li H, Herrera AF, et al. Hemasphere. 2024;8:e70012. Abstract T077

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Disclosures

TM: consulting fees from Takeda and MSD. AM, FK, AZ, VS, VP: employment with and ownership of stock/shares in Takeda Pharmaceuticals. ZL, ZY, AP: employment with Cytel, Inc

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- Real world patient characteristics, treatment patterns, and outcomes for Chinese patients with CD30-positive peripheral T-cell lymphoma. Yan X, et al. ICML 2025. *Hematol. Oncol.* 2025;43(S3); **abstract 754**