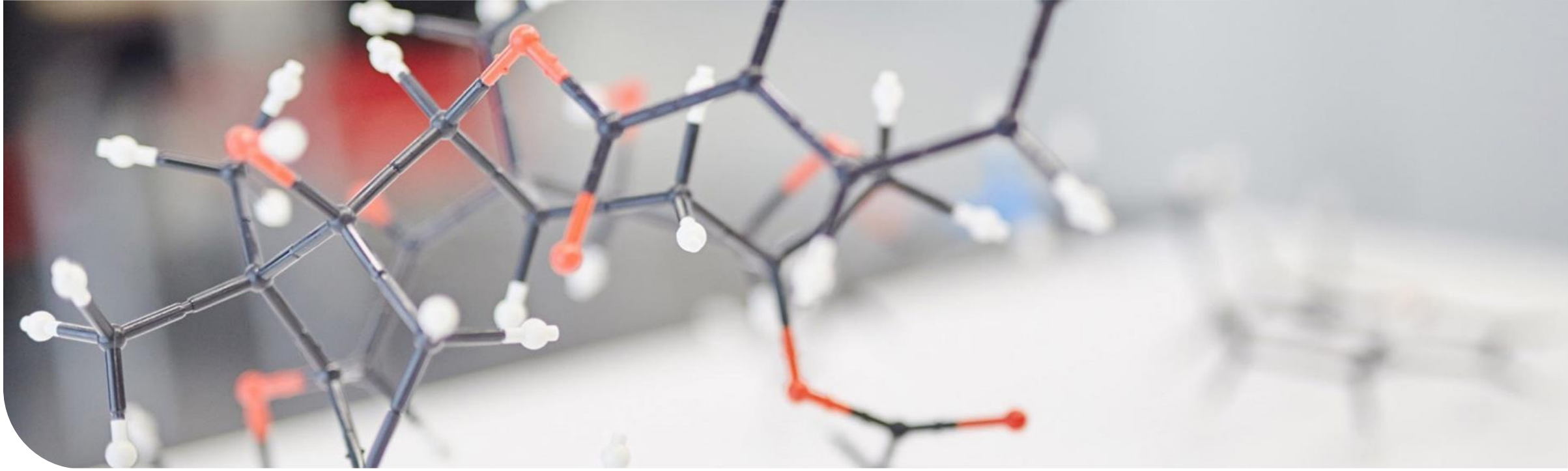


Brentuximab Vedotin 2024 Post-Congress Deck

VV-MEDMAT-113242

January 2025

Better Health, Brighter Future

Disclaimers

- Diese Folien sind zur reaktiven Verwendung durch Medical Affairs im wissenschaftlichen Austausch mit Angehörigen der Fachkreise (nach §2 HWG) als Antwort auf unaufgeforderte Informationsanfragen zu den hierin enthaltenen Themen zugelassen.
- Die Antworten müssen eng auf die unaufgeforderte Anfrage zugeschnitten sein und einen angemessenen Kontext enthalten.
- Folien, die Daten aus extern gesponserten Studien enthalten, dürfen ohne Genehmigung des Hauptprüfers und/oder des Hauptautors nicht hinzugefügt oder verändert werden.
- Einige der in dieser Präsentation beschriebenen Verwendungen sind nicht von den Aufsichtsbehörden zugelassen.
- Bitte beachten Sie die Fachinformation für ADCETRIS (Brentuximab Vedotin) verfügbar unter https://www.takeda-produkte.de/system/files/produkt-info/fachinformation-adcetrisr-50-mg-pulver-fur-ein-konzentrat-zur-herstellung-einer-infusionslosung.pdf.
- Diese Folien dürfen nicht mit Sales geteilt oder durch Sales verwendet werden.
- **Diese Folien dürfen nicht zurückgelassen und nicht außerhalb von Takeda weitergegeben werden.**
    - Wenn Global Medical Information eine unaufgeforderte Anfrage nach den in diesem Deck enthaltenen Daten erhält, wird die Original-Kongresspräsentation (Poster oder Folien) von Global Medical Information mit Genehmigung des Autors geteilt, oder das Abstract wird weitergegeben, wenn keine Genehmigungen eingeholt werden können. Die in dieser Präsentation enthaltenen Folien dürfen nicht versendet werden.

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

Table of contents I

Presentation title	Authors	Presented at	Abstract Code	Type
Seven-year overall survival analysis from ECHELON-1 study of A+AVD versus ABVD in patients with previously untreated stage III/IV classical Hodgkin lymphoma	Ansell S.M, et al.	ASCO 2024	Abstract 7053	Company – Sponsored
Phase 2 trial of brentuximab vedotin (BV) with pembrolizumab (pembro) in patients with previously treated metastatic non-small cell lung cancer (NSCLC) or cutaneous melanoma (SGN35-033): overall survival	Zakharia Y. et al.		Abstract 2617	Pfizer – Sponsored*
Frontline brentuximab vedotin and cyclophosphamide, doxorubicin, and prednisone in patients with peripheral T-cell lymphoma with less than 10% CD30 expression: results from the phase 2 SGN35-032 study	Swaminathan P.I, et al.		Abstract 7069	Pfizer – Sponsored*
Brentuximab vedotin in combination with lenalidomide and rituximab in patients with relapsed/refractory diffuse large B-cell lymphoma: results from the phase 3 ECHELON-3 study	Kim J. et al.		Abstract LBA7005	Pfizer – Sponsored*
Favorable, Contemporary, Real-World Outcomes of Brentuximab Vedotin as Post-ASCT Consolidation in RRHL: A Systematic Review and Meta-Analysis	Sureda A, et al.	EHA 2024	Abstract P1101	Company – Sponsored
Treatment Effects of BrECADD on health-related Quality of Life: An Analysis of Patient Reported Outcomes in the randomized international Phase III German Hodgkin Study Group HD21 trial	Ferdinandus J, et al.		Abstract P1100	Takeda IIR*
Gonadal Function Recovery and Fertility in the Phase III German Hodgkin Study Group HD21 trial	Ferdinandus J, et al.		Abstract S228	Takeda IIR*
The randomized study GHSG HD21 shows superior tolerability and efficacy of BrECADD versus BEACOPP in advanced stage classical Hodgkin lymphoma	Borchmann P,et al.		Abstract S225	Takeda IIR*

Click here for additional brentuximab vedotin data

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

ASCO, American Society of Clinical Oncology; EHA, European Hematology Association

A+AVD, brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; ASCT, autologous stem cell transplant;BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; RRHL, relapsed or refractory Hodgkin lymphoma

Table of contents II

Presentation title	Authors	Presented at	Abstract Code	Type
Real-world evidence study of brentuximab vedotin retreatment in patients with cutaneous T-cell lymphoma	Mitteldorf C, et al.	EORTC-CLTG 2024	Abstract A-133	Company – Sponsored
Sub-analysis of the BELIEVE STUDY: Effectiveness and safety for re-treatment with Brentuximab-vedotin in relapsed/refractory (R/R) Cutaneous T Cell Lymphoma (CTCL): a retrospective medical chart review study in Spain. NCT:04998331	Sureda A, et al.		Abstract A-111	Company – Sponsored
The BELIEVE Study: Effectiveness and Safety for Re-treatment with Brentuximab-Veodtin in Relapsed/Refractory (R/R) Hodgkin Lymphoma: A Retrospective Medical Chart Review in Spain	Sureda A, et al.	ISHL 2024	Abstract P134	Company – Sponsored
Brentuximab Vedotin (BV) Exposure and Long-Term Efficacy Analysis in Patients (pts) With Classical Hodgkin Lymphoma (cHL): Analysis of the Phase 3 ECHELON-1 (E1) Study	Zhang Z, et al.		Abstract P008	Pfizer – Sponsored*
PET-Guided BrECADD in Older Patients with Advanced-Stage Classic Hodgkin Lymphoma: Results from a Phase 2 Part of the GHSG HD21 Trial	Ferdinandus, et al.		Abstract T076	Takeda IIR*
Brentuximab Vedotin - ESHAP Significantly Increases the Metabolic Complete Remission Rate versus ESHAP in Relapsed Classical Hodgkin's Lymphoma. Final Results of the BRESELIBET Prospective Trial	Sureda A, et al.		T104	Takeda IIR*
EORTC-1537-COBRA: Very early FDG-PET-response adapted targeted therapy for advanced Hodgkin lymphoma: A single-arm phase II study	Hutchings, et al.		T003	Takeda IIR*

Click here for additional brentuximab vedotin data

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

EORTC-CLTG, European Organisation for Research and Treatment of Cancer – Cutaneous Lymphoma Tumours Group; ISHL, International Symposium on Hodgkin Lymphoma

BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; ESHAP, etoposide, methylprednisolone, cytosine, arabinose, cisplatin; (FDG)-PET, (fluorodeoxyglucose)-positron emission tomography; GHSG, German Hodgkin Study Group

Table of contents III

Presentation title	Authors	Presented at	Abstract Code	Type
Impact of Treatment-Related Morbidities on Health-Related Quality of Life in Advanced-Stage Classical Hodgkin Lymphoma Receiving Multiagent Therapy: Findings from the HD21 Study	Kristo F, et al.	ASH 2024	Abstract 4426	Company – Sponsored
Estimation of Health State Utility Values for Patients Undergoing First-line Treatment of Advanced Stage Classical Hodgkin Lymphoma in the HD21 Trial	Pelligra CG, et al.		Abstract 2346	Company – Sponsored
Patient-Reported Chemotherapy-Induced Peripheral Neuropathy (CIPN) in Advanced Hodgkin Lymphoma Patients Treated with BrECADD and eBEACOPP in the HD21 Trial	Kristo F, et al.		Abstract 1662	Company – Sponsored
Effectiveness and Safety for Re-Treatment with Brentuximab-Vedotin in Patients with Relapsed/Refractory (R/R) CD30+ Malignancies: A Retrospective Medical Chart Review Study in Spain. The BELIEVE Study. NCT:04998331	García-Sanz R, et al.		Abstract 2376	Company – Sponsored
BV-CHP in Previously Untreated Patients with CD30-Positive Adult T-Cell Leukemia-Lymphoma: A Multicenter Real-World Retrospective Study	Makiyama J, et al.		Abstract 4435	Company – Sponsored
Brentuximab Vedotin, Cyclophosphamide, Doxorubicin and Prednisone (BCAP) First-Line Treatment of Advanced-Stage Hodgkin Lymphoma in Older Patients: Final Results of the GHSG-NLG Phase II BVB Trial	Brockelmann PJ, et al.		Abstract 3054	Takeda IIR*
PET-Guided BrECADD in Older Patients with Advanced-Stage Classic Hodgkin Lymphoma: Results from a Phase 2 Part of the GHSG HD21 Trial	Ferdinandus J, et al.		Abstract 568	Takeda IIR*

Click here for additional brentuximab vedotin data

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

ASH, American Society of Hematology

BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; BV-CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisolone; eBEACOPP, escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone

Seven-year overall survival analysis from ECHELON-1 study of A+AVD versus ABVD in patients with previously untreated stage III/IV classical Hodgkin lymphoma

Ansell S.M, et al. ASCO 2024
Abstract #7053

Stephen M. Ansell,[1] David J. Straus,[2] Joseph M. Connors,[3] Wojciech Jurczak,[4] Won-Seog Kim,[5] Andrea Gallamini,[6] Radhakrishnan Ramchandren,[7] Jonathan W. Friedberg,[8] Ranjana Advani,[9] Martin Hutchings,[10] Andrew M. Evens,[11] Kerry J. Savage,[3] Hyeon-Seok Eom,[12] Tatyana Feldman,[13] Jeremy S. Abramson,[14] Cassie Dong,[15] Bipin Savani,[15] Athanasios Zomas,[16] Keenan Fenton,[17] and John Radford[18]

[1]Division of Hematology, Mayo Clinic, Rochester, MN, USA; [2]Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]BC Cancer, Centre for Lymphoid Cancer, Vancouver, Canada; [4]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [5]Division of Hematology-Oncology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]Research and Innovation Department, Antoine-Lacassagne Cancer Center, Nice, France; [7]University of Tennessee Graduate School of Medicine, Knoxville, TN, USA; [8]Wilmot Cancer Institute, University of Rochester, Rochester, NY, USA; [9]Department of Medicine, Division of Oncology, Stanford University, Stanford, CA, USA; [10]Department of Hematology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; [11]Division of Blood Disorders, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [12]Department of Hematology-Oncology, Center for Hematologic Malignancy, National Cancer Center, Goyang, Republic of Korea; [13]John Theurer Cancer Center, Hackensack Meridian Health, Hackensack, NJ, USA; [14]Massachusetts General Hospital, Boston, MA, USA; [15]Takeda Development Center Americas, Inc. (TDCA), Lexington, MA, USA; [16]Takeda Pharmaceuticals International AG, Zurich, Switzerland; [17]Pfizer Inc., Bothell, WA, USA; [18]University of Manchester and the Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Introduction

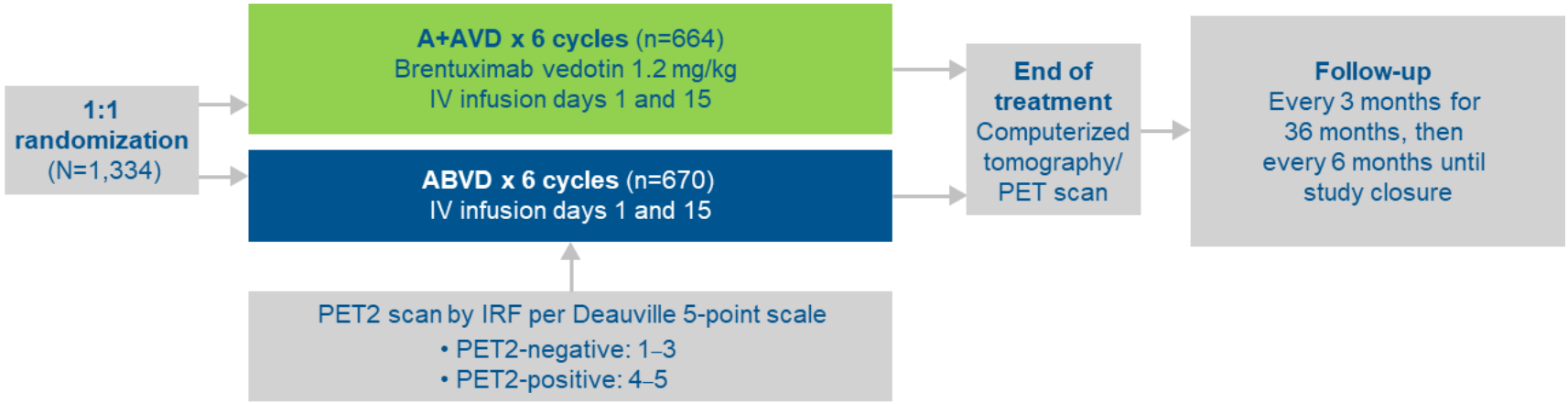
- The standard-of-care for the treatment of advanced-stage classical Hodgkin lymphoma (cHL) has been first-line treatment with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) for over 30 years
  - However, a significant proportion of patients with Stage III/IV cHL either relapse or are refractory to ABVD
- Although various approaches including positron emission tomography (PET)-adapted strategies and bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP)-based regimens have succeeded in improving disease control or tolerability versus ABVD, none show a meaningful overall survival (OS) advantage
- After a 6-year follow-up of the phase 3 ECHELON-1 study (NCT01712490), analyses demonstrated a long-term OS and progression-free survival (PFS) benefit with first-line brentuximab vedotin + doxorubicin, vinblastine, and dacarbazine (A+AVD) versus ABVD
- Here we report an updated analysis of PFS, OS, and safety for patients in the ECHELON-1 study after a median follow-up of 7 years

PFS, progression-free survival; OS, overall survival; PET, positron emission tomography; A+AVD, brentuximab vedotin[b] + doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; BEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; cHL, classical Hodgkin Lymphoma

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Methods and Study Design

- In the open-label, randomized, phase 3 ECHELON-1 study, patients with previously untreated Stage III/IV cHL were randomized 1:1 to receive 6 cycles of A+AVD or ABVD
- PET scan after cycle 2 (PET2) evaluation was mandatory
- Primary endpoint: Modified PFS per independent review facility (IRF; previously reported)
- Key secondary endpoint: Alpha-controlled, event-driven analysis of OS
- Safety outcomes include:
  - Second malignancies
  - Adverse events
  - Outcomes of pregnancy among patients and their partners
  - Peripheral neuropathy (PN) resolution and improvement rates
- P-values are descriptive only



PFS, progression-free survival; OS, overall survival; PET, positron emission tomography; A+AVD, brentuximab vedotin[b] + doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; cHL, classical Hodgkin Lymphoma; PN, peripheral neuropathy; IRF, independent review facility; IV, intravenous

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results

Patient Demographics and Disease Characteristics

- In total, 1,334 patients were randomized to receive A+AVD (n=664) or ABVD (n=670)
- Median follow-up was 89.3 months (95% confidence interval [CI]: 87.0–90.2)
- Baseline demographics and disease characteristics were well balanced between the two treatment arms and have been described previously

OS and PFS

- The clinical benefit of A+AVD was maintained compared to ABVD
- 7-year OS rates: A+AVD 93.5% (95% confidence interval [CI]: 91.1–95.2); ABVD 88.8% (95% CI: 85.8–91.1); hazard ratio (HR) 0.617 (95% CI: 0.423–0.899); P=0.011
- Median OS has not been reached in either treatment arm
- Consistent with previous PFS analysis in ECHELON-1, 7-year PFS rates with A+AVD versus ABVD were 82.3% (95% CI: 79.1–85.0) versus 74.5% (95% CI: 70.8–77.7); HR 0.677 (95% CI: 0.532–0.863); P=0.001
- OS benefit was generally consistent across subgroups, including in the age <40 years and Stage IV disease subgroups

PFS, progression-free survival; OS, overall survival; Aprednisone; +AVD, brentuximab vedotinb + doxorubicin,a vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; HR, hazard ratio; CI, confidence interval

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online,May 31-June 4, 2024

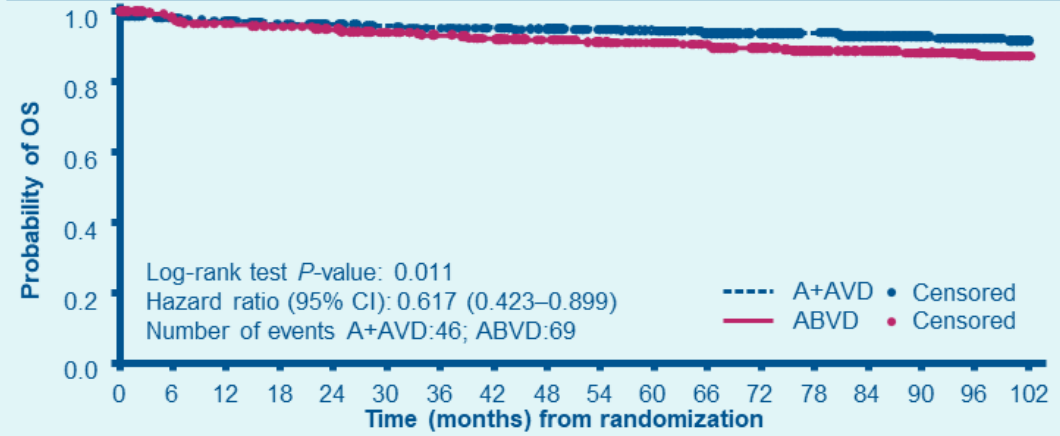
Results

Question	Is the benefit seen with A+AVD versus ABVD in the ECHELON-1 study at 6 years' follow-up maintained after 7 years?			
Study design	**NCT01712490** open-label, RCT, phase 3	**A+AVD or ABVD** 6 cycles, intravenous (IV) infusion days 1 and 15	**Endpoints** PFS and OS	**Current analysis** Data cut-off March 11, 2023

Key take aways

At 7-year median follow-up, patients with Stage III/IV cHL who received A+AVD continued to show a sustained PFS and OS benefit versus ABVD

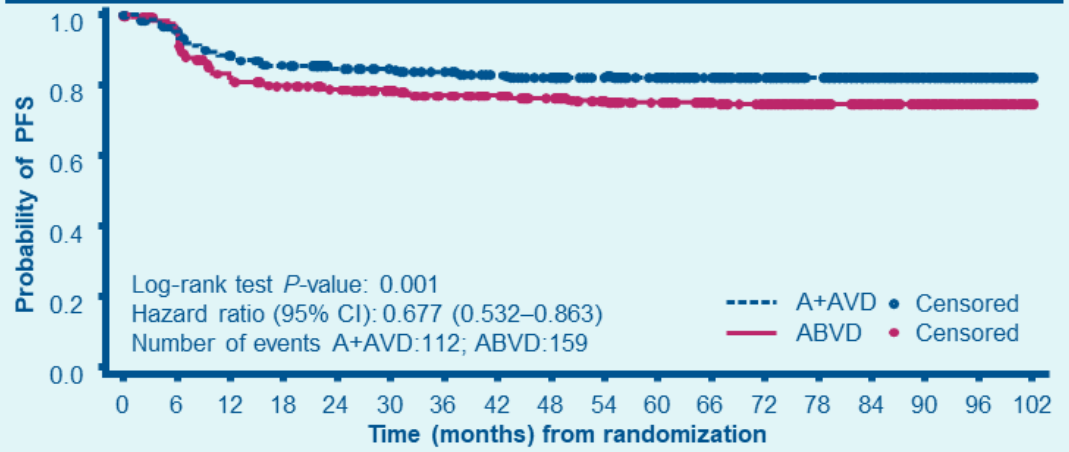
Figure 1: OS



Number of patients at risk

A+AVD	664	638	626	612	598	584	572	557	538	517	494	472	443	416	378	310	200	117
ABVD	670	634	614	604	587	567	545	527	505	479	455	426	398	372	340	268	178	97

Figure 2: PFS



Number of patients at risk

A+AVD	664	619	563	537	520	508	496	480	463	446	426	405	384	362	332	273	177	101
ABVD	670	612	519	500	484	464	441	430	412	389	369	348	321	301	278	220	146	78

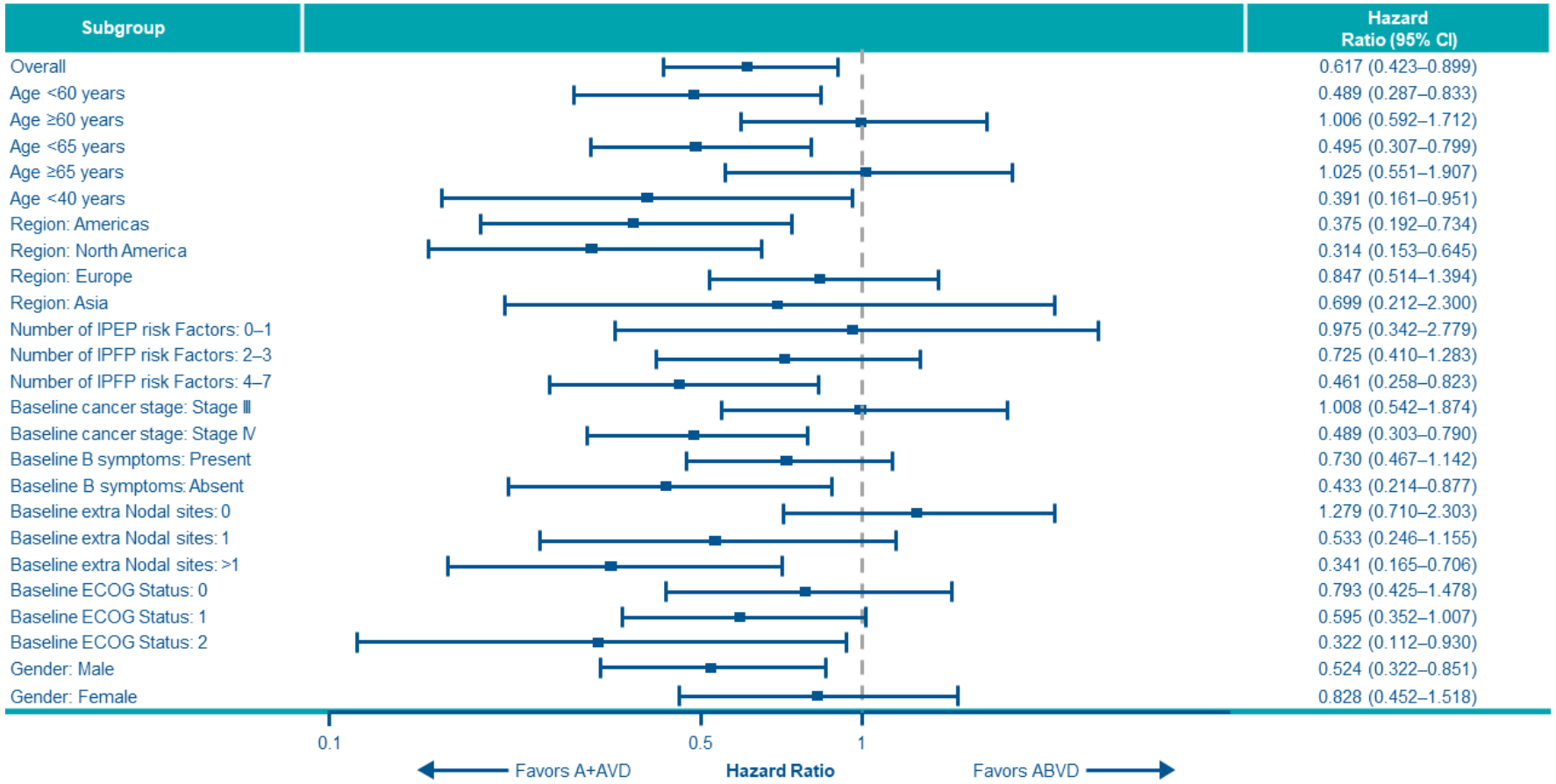
- 7-year OS rates: A+AVD 93.5% (95% confidence interval [CI]: 91.1–95.2); ABVD 88.8% (95% CI: 85.8–91.1); hazard ratio (HR) 0.617 (95% CI: 0.423–0.899); *P*=0.011
- Consistent with previous PFS analysis in ECHELON-1, 7-year PFS rates with A+AVD versus ABVD were 82.3% (95% CI: 79.1–85.0) versus 74.5% (95% CI: 70.8–77.7); HR 0.677 (95% CI: 0.532–0.863); P=0.001

PFS, progression-free survival; OS, overall survival; A+AVD, brentuximab vedotin[b] + doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; HR, hazard ratio; CI, confidence interval; RCT, randomized controlled trial

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results

Figure 4: OS benefit across subgroups



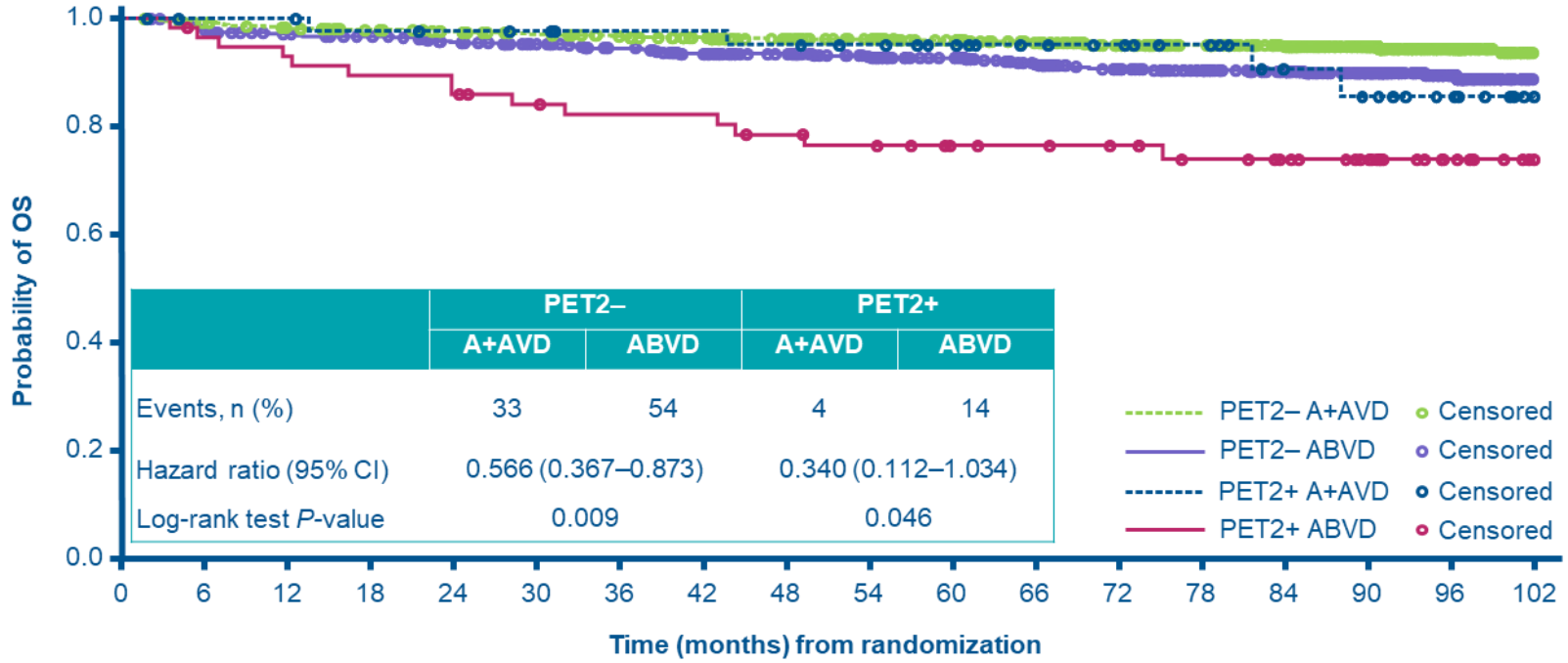
- OS benefit was generally consistent across subgroups, including in the age <40 years and Stage IV disease subgroups

OS, overall survival; A+AVD, brentuximab vedotin[b] + doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; HR, hazard ratio; CI, confidence interval; IPFP, International Prognostic Factors Project; ECOG, Eastern Cooperative Oncology Group

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results

Figure 5: OS by PET2 status



	PET2–		PET2+	
	A+AVD	ABVD	A+AVD	ABVD
Events, n (%)	33	54	4	14
Hazard ratio (95% CI)	0.566 (0.367–0.873)		0.340 (0.112–1.034)	
Log-rank test *P*-value	0.009		0.046	

Number of patients at risk

A+AVD	588	580	569	557	545	533	524	510	493	474	456	439	412	388	358	293	187	110
ABVD	577	566	550	542	527	510	490	472	453	430	410	382	357	337	311	248	168	93
A+AVD	47	45	45	43	42	41	39	39	38	36	33	29	27	24	18	16	12	6
ABVD	58	55	53	51	49	46	44	44	41	39	35	34	32	28	25	20	10	4

- Seven-year OS rates were improved with A+AVD compared to ABVD in patients with both PET2– (95.0% versus 90.2%; HR 0.57; 95% CI: 0.37–0.87; *P*=0.009) and PET2+ (90.7% versus 74.0%; HR 0.34; 95% CI: 0.11–1.03; *P*=0.046) status, respectively

OS, overall survival; PET, positron emission tomography; A+AVD, brentuximab vedotin[b] + doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; HR, hazard ratio; CI, confidence interval

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results – Mortality

Causes of death

- In the A+AVD and ABVD treatment arms, 46 (22 disease-related) and 69 (30 disease-related) deaths were reported, respectively **(Table 1)**

Table 1: Summary of deaths

Cause of death	A+AVD (n=662)	ABVD (n=659)
All deaths, n (%)	46 (7)	69 (10)
Disease related, n (%)	22 (3)	30 (5)
Not disease related, n (%)	24 (4)	38 (6)
Unknown, n (%)	0	1 (<1)
Deaths >30 days after last dose of frontline therapy, n (%)	37 (6)	56 (8)
Disease related, n (%)	19 (3)	26 (4)
Not disease related*, n (%)	18 (3)	29 (4)
Unknown, n (%)	2 (<1)	7 (1)
Deceased, n (%)	3 (<1)	0
Cardiac arrest, n (%)	2 (<1)	0

*Causes of death in ≥2 patients in either arm

A+AVD, brentuximab vedotin[b] +doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results – Safety Profile

Second Malignancies

- The rate of second malignancies was similar between arms; 33 (5%) in patients who received A+AVD and 39 (6%) in patients who received ABVD

Pregnancy

- A total of 92 patients reported pregnancies in the A+AVD arm (55 female patients and 37 males with pregnant partners); in the ABVD arm 73 patients reported pregnancies (31 female patients and 42 males with pregnant partners)
- Of these pregnancies, 1 or more live births were reported in 84/92 patients and their partners treated with A+AVD (91%) and 59/73 treated with ABVD (81%)
- No stillbirths were reported in either treatment arm

Peripheral Neuropathy

- In patients with PN receiving A+AVD and ABVD:
  - Treatment-emergent PN resolved or improved in 86% (381/443) and 87% (249/286) of patients, respectively
  - Median (range) time to resolution was 16 (0–373) weeks with A+AVD and 10 (0–343) weeks with ABVD
  - Median (range) time to improvement was 42 (2–182) weeks with A+AVD and 19 (15–142) weeks with ABVD
- PN was ongoing in 28% of A+AVD (122/443; 12% grade ≥2) and 20% of ABVD (58/286; 7% grade ≥2) patients

A+AVD, brentuximab vedotin[b] + doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; PN, peripheral neuropathy

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Authors' Conclusions

- At 7-year median follow up, patients with Stage III and IV cHL who received A+AVD showed a sustained PFS and OS benefit vs ABVD, with fewer lymphoma-related deaths and PFS rates suggesting potential curability
- Based on these data, A+AVD should be considered a preferred first-line treatment option for patients with previously untreated Stage III or IV cHL

PFS, progression-free survival; OS, overall survival; A+AVD, brentuximab vedotin[b] + doxorubicin,[a] vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; cHL, classical Hodgkin Lymphoma

Ansell S.M, et al. Poster Presentation 7053. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Phase 2 trial of brentuximab vedotin (BV) with pembrolizumab (pembro) in patients with previously treated metastatic non-small cell lung cancer (NSCLC) or cutaneous melanoma (SGN35-033): overall survival

Zakharia Y , et Al.
Abstract #2617

Yousef Zakharia,[1] Sylvia Lee,[2] Robert M. Jotte,[3,4] Amanda Gillespie-Twardy,[4,5] Inderjit Mehmi,[6] Sunandana Chandra,[7] Omid Hamid,6 Graham Watson,[4,8] Patrick J. Ward,[4,9] Marya F. Chaney,[10] Hailing Lu,[11] Jason Berndt,[11] Kapil Rathi,[11] Anu Gupta,[11] C. Lance Cowey[4,12]

1University of Iowa, Iowa City, IA; 2Fred Hutchinson Cancer Center, Seattle, WA; 3Rocky Mountain Cancer Centers, Lone Tree, CO; 4US Oncology Network, The Woodlands, TX*; 5Blue Ridge Cancer Care, Roanoke, VA; 6The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, CA; 7Northwestern University, Chicago, IL; 8Virginia Oncology Associates, Norfolk, VA; 9Oncology Hematology Care, Cincinnati, OH; 10Merck & Co., Inc., Rahway, NJ; 11Pfizer Inc., Bothell, WA; 12Texas Oncology – Baylor Charles A. Sammons Cancer Center, Dallas, TX *US Oncology Network is now partnered with Sarah Cannon Research Institute (SCRI), Nashville, TN

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Background

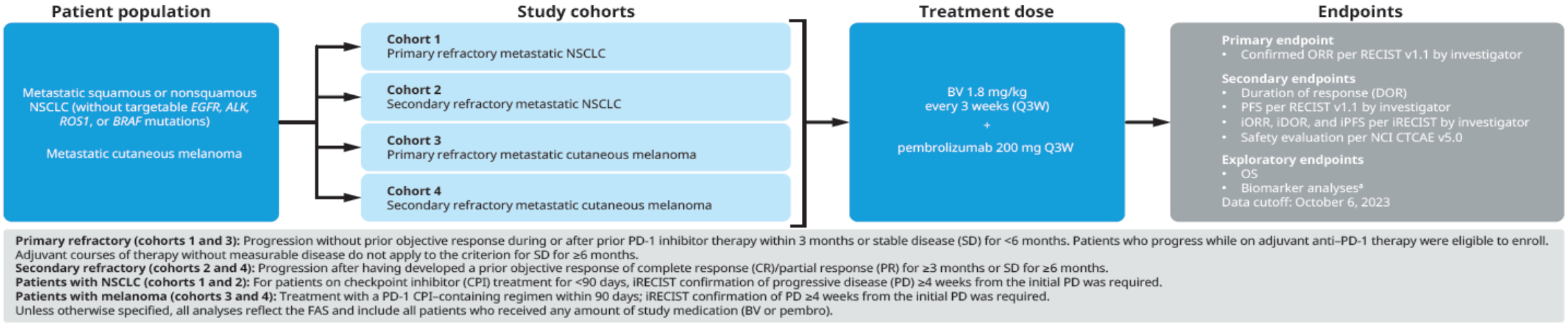
- BV is composed of a CD30-directed monoclonal antibody conjugated to the potent microtubule-disrupting agent monomethyl auristatin E
- BV may selectively deplete a subset of regulatory T cells that express CD30 and re-sensitize tumors to anti–programmed cell death 1 protein (PD-1) therapy
- SGN35-033 is an ongoing, phase 2, multicohort, multicenter, open-label trial evaluating the efficacy and safety of BV + pembro in patients with anti–PD-1 refractory solid tumors
    - It was previously reported that BV + pembro was associated with an overall response rate (ORR) of 8% to 22%, a disease control rate (DCR) of 67% to 80%, and CD8+ T-cell infiltration in on-treatment biopsies of responding patients
- OS data for the combination of BV + pembro in patients with anti–PD-1–refractory solid tumors enrolled in the SGN35-03 (NCT04609566) study are reported here

BV, brentuximab vedotin; CD30, cluster differentiation 30; DCR, disease control rate; ORR, overall response rate; OS; overall survival; PD-1, programmed cell death 1 protein; pembro, pembrolizumab

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Study Design

Figure 1: Study design

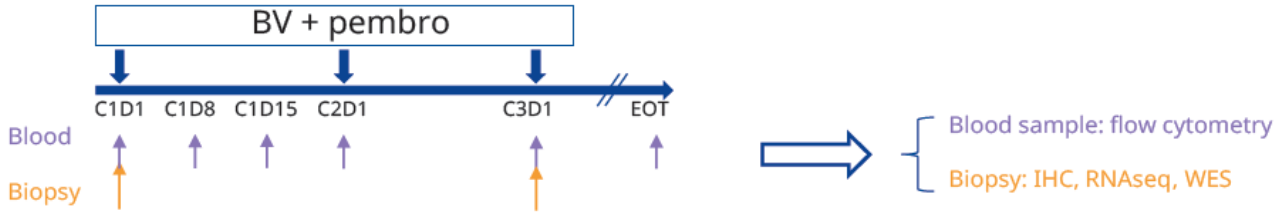


Primary refractory (cohorts 1 and 3): Progression without prior objective response during or after prior PD-1 inhibitor therapy within 3 months or stable disease (SD) for <6 months. Patients who progress while on adjuvant anti–PD-1 therapy were eligible to enroll. Adjuvant courses of therapy without measurable disease do not apply to the criterion for SD for ≥6 months.
Secondary refractory (cohorts 2 and 4): Progression after having developed a prior objective response of complete response (CR)/partial response (PR) for ≥3 months or SD for ≥6 months.
Patients with NSCLC (cohorts 1 and 2): For patients on checkpoint inhibitor (CPI) treatment for <90 days, iRECIST confirmation of progressive disease (PD) ≥4 weeks from the initial PD was required.
Patients with melanoma (cohorts 3 and 4): Treatment with a PD-1 CPI–containing regimen within 90 days; iRECIST confirmation of PD ≥4 weeks from the initial PD was required.
Unless otherwise specified, all analyses reflect the FAS and include all patients who received any amount of study medication (BV or pembro).

CTCAE, Common Terminology Criteria for Adverse Events; NCI, National Cancer Institute; RECIST, Response Evaluation Criteria in Solid Tumours. [a] Biomarker analysis at baseline and during treatment, including T cells in peripheral blood by flow cytometry, regulatory T (Treg) and CD8 T cells by immunohistochemistry (IHC) in tumor biopsies, and gene expression profiles by RNA sequencing (RNAseq) in tumor biopsies.

- Whole blood was collected at baseline and different time points during treatment (C1D8, C1D15, C2D1, C3D1, and end of treatment [EOT]) to evaluate for potential changes in Treg level in peripheral blood
- Tumor biopsies were collected at baseline and C3D1 for evaluation of potential changes in the tumor microenvironment by IHC (CD30, PD-L1, CD8, Foxp3) and RNAseq/whole exome sequencing (WES)

Figure 2: Collection of biomarker samples



IHC, immunohistochemistry

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results – Patient Characteristics

- In total, 55 patients with metastatic NSCLC and 58 patients with metastatic cutaneous melanoma received treatment
- Among all patients, 63% were men, 57% were aged ≥65 years, and 54% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0
- A total of 81% of patients with cutaneous melanoma received prior ipilimumab/anti–CTLA-4 therapy; 4% of patients with metastatic NSCLC received prior docetaxel

Table 1: Patient characteristics

	Metastatic NSCLC			Metastatic cutaneous melanoma		
	Primary refractory (n=12)	Secondary refractory (n=43)	Total (N=55)	Primary refractory (n=17)	Secondary refractory (n=41)	Total (N=58)
Median age (range), years	67.5 (49-80)	67.0 (55-86)	67.0 (49-86)	59.0 (23-83)	65.0 (25-86)	64.5 (23-86)
Sex, n (%)						
Male	11 (92)	24 (56)	35 (64)	11 (65)	25 (61)	36 (62)
Female	1 (8)	19 (44)	20 (36)	6 (35)	16 (39)	22 (38)
ECOG performance status, n (%)						
0	6 (50)	16 (37)	22 (40)	13 (76)	26 (63)	39 (67)
1	6 (50)	27 (63)	33 (60)	4 (24)	15 (37)	19 (33)
Time from initial diagnosis to first dose, mo						
n	12	40	52	14	34	48
Median (range)	15.5 (5-41)	22.4 (8-138)	20 (5-138)	32.3 (6-132)	59.7 (8-259)	44.1 (6-259)
Prior lines of systemic therapy received						
Median (range)	1.5 (1-5)	2.0 (1-3)	2.0 (1-5)	1.0 (1-5)	3.0 (1-7)	2.0 (1-7)
Prior systemic therapy, n (%)						
Platinum	10 (83)	36 (84)	46 (84)	0	2 (5)	2 (3)
Docetaxel	0	2 (5)	2 (4)	0	0	0
Ipilimumab/anti–CTLA-4	0	6 (14)	6 (11)	15 (88)	32 (78)	47 (81)

CLTA-4, cytotoxic T-lymphocyte associated protein 4, NSCLC, non-small cell lung cancer

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results - Efficacy

- The ORR ranged from 8% to 22% across cohorts
  - Patients with secondary refractory tumors had numerically higher response rates than those with primary refractory tumors (14% vs 8% in NSCLC, 22% vs 18% in melanoma)

Table 2: Objective response per RECIST 1.1

	Metastatic NSCLC			Metastatic cutaneous melanoma		
	Primary refractory (n=12)	Secondary refractory (n=43)	Total (n=55)	Primary refractory (n=17)	Secondary refractory (n=41)	Total (n=58)
Confirmed ORR (CR+PR; 95% CI), %	8 (0.2-38.5)	14 (5.3-27.9)	13 (5.3-24.5)	18 (3.8-43.4)	22 (10.6-37.6)	21 (11.2-33.4)
Complete response, n (%)	0	1 (2)	1 (2)	0	1 (2)	1 (2)
Partial response, n (%)	1 (8)	5 (12)	6 (11)	3 (18)	8 (20)	11 (19)
Stable disease, n (%)	7 (58)	25 (58)	32 (58)	8 (47)	22 (54)	30 (52)
Progressive disease, n (%)	4 (33)	7 (16)	11 (20)	5 (29)	8 (20)	13 (22)
Not applicable, n (%)[a]	0	5 (12)	5 (9)	1 (6)	2 (5)	3 (5)
Disease control rate (CR+PR+SD; 95% CI), %	67 (34.9-90.1)	72 (56.3-84.7)	71 (57.1-82.4)	65 (38.3-85.8)	76 (59.7-87.6)	72 (59.1-83.3)
Median duration of response (95% CI), mo[b]	3.6 (NE-NE)	19.1 (4.6-NE)	19.1 (3.6-NE)	4.2 (4.2-NE)	4.3 (2.9-NE)	4.2 (3.9-6.8)

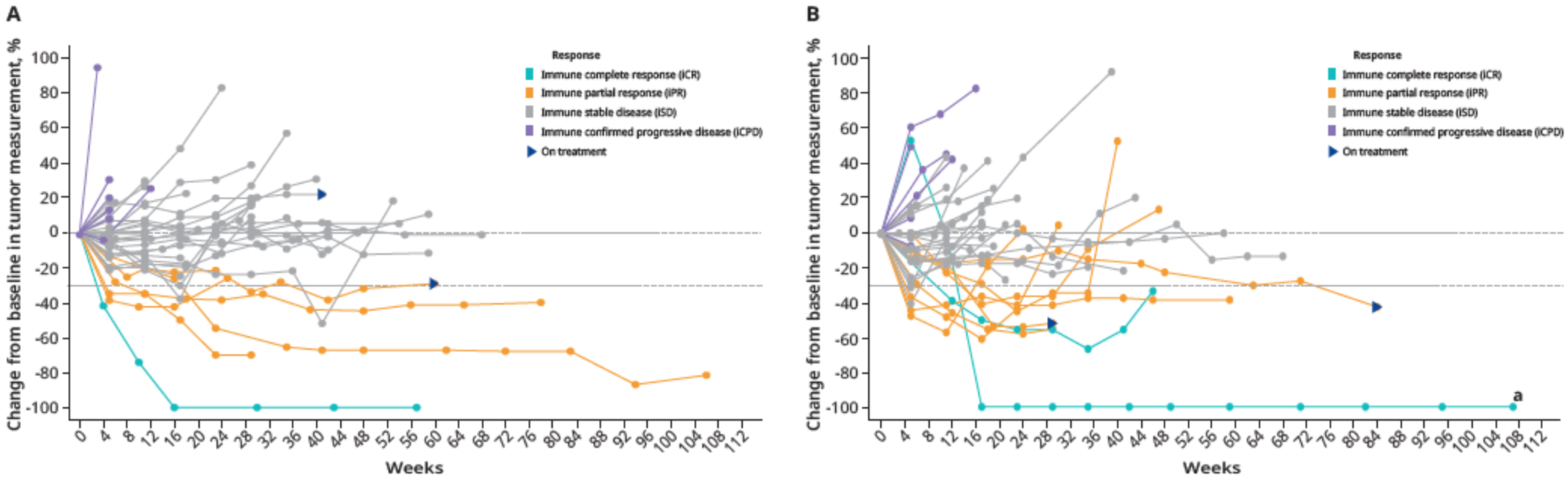
[a] Not applicable includes the patients who discontinued the treatment with no postbaseline response assessment. [b] As estimated using Kaplan-Meier method.

CR, complete response; NE, not evaluable; NSCLC, non-small cell lung cancer; ORR, overall response rate; PR, partial response; SD, stable disease

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results - Efficacy

Figure 3: Best overall response per iRECIST for patients with secondary refractory metastatic NSCLC (A) and cutaneous melanoma (B)



[a] Patient with iCR after pseudoprogression presented in biomarker analysis **Figure 7B**.

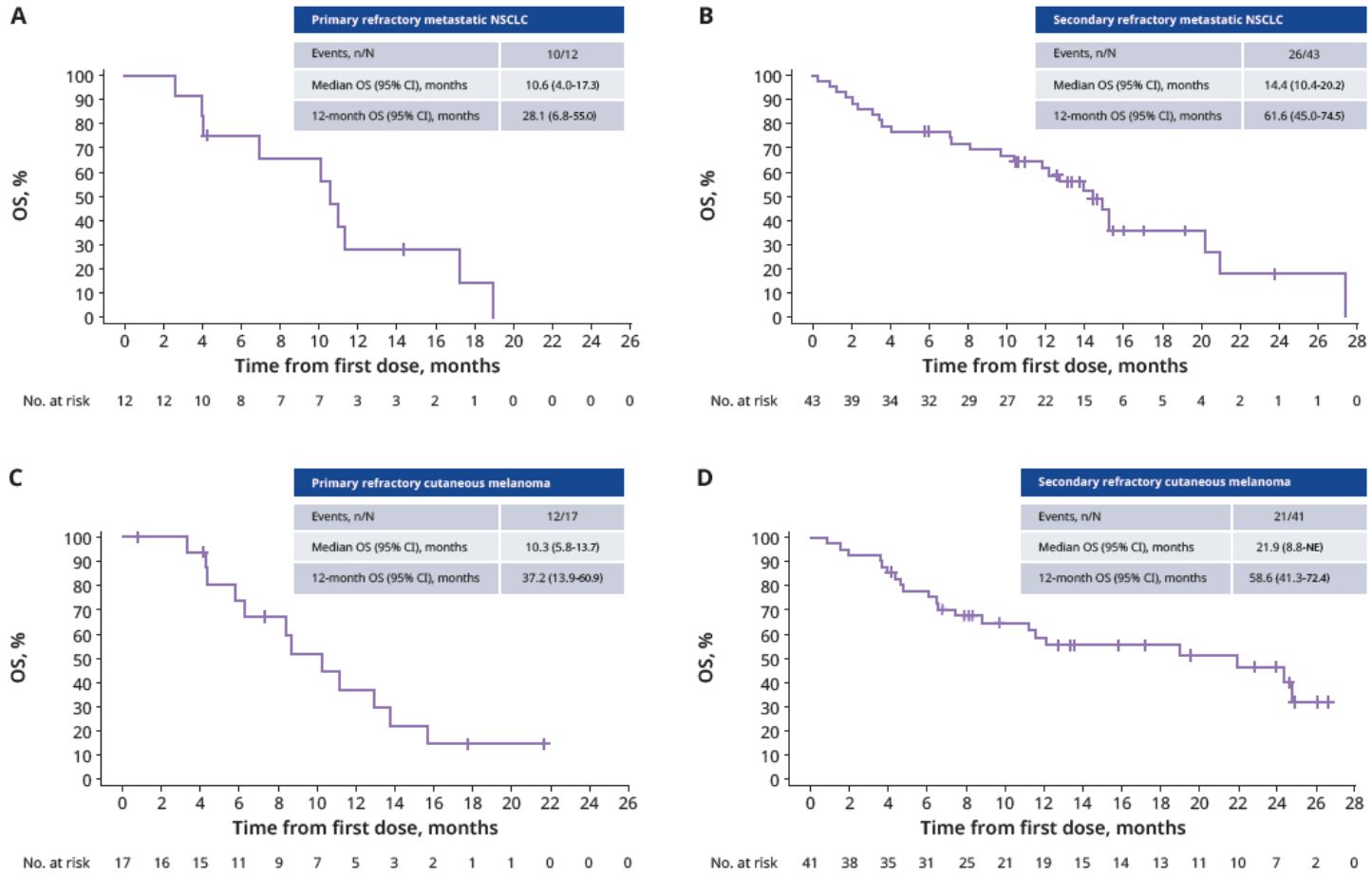
iRECIST, immune response evaluation criteria in solid tumors; NSCLC, non-small cell lung cancer

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results - Efficacy

- The median OS was 12.7 months in patients with metastatic NSCLC and 12.9 months in patients with metastatic cutaneous melanoma
- The estimated OS rates in patients with metastatic NSCLC and cutaneous melanoma were 76.4% and 76.8% at 6 months, and 54.1% and 52.4% at 12 months, respectively
    - OS outcomes were better in the secondary refractory cohorts than primary refractory cohorts for both NSCLC and cutaneous melanoma

Figure 4: Kaplan-Meier curves for OS for primary (A) and secondary refractory (B) metastatic NSCLC and primary (C) and secondary refractory (D) cutaneous melanoma



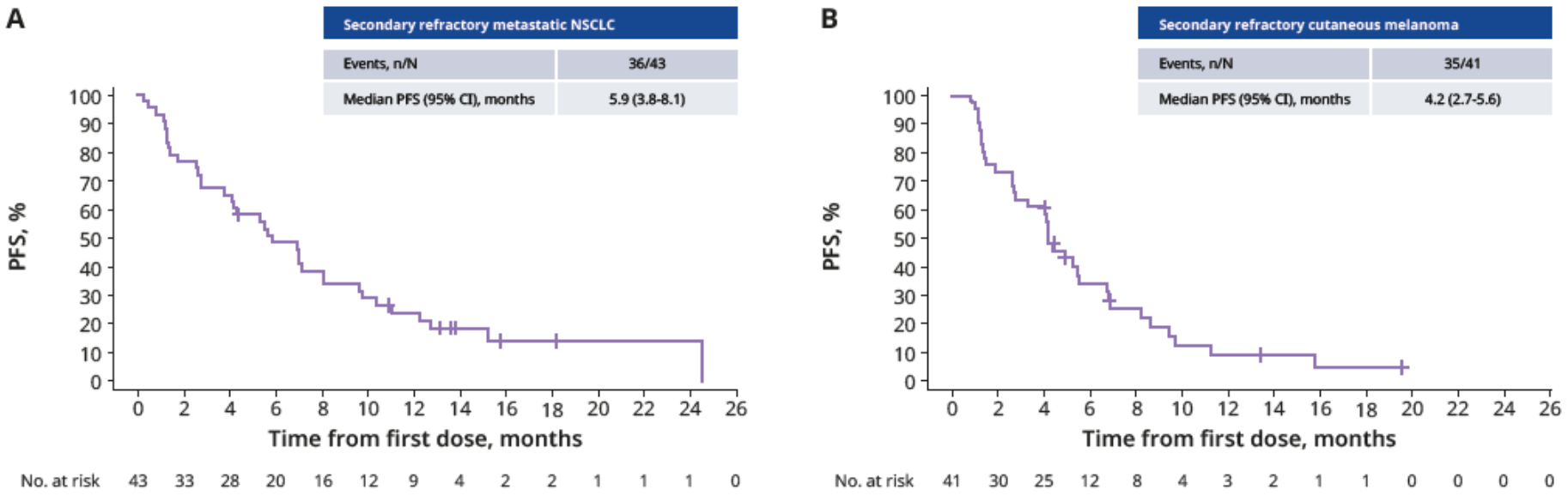
NSCLC, non-small cell lung cancer; OS, overall survival

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results - Efficacy

- The median PFS was 4.2 months in patients with metastatic NSCLC and 4.1 months in patients with metastatic cutaneous melanoma
  - The estimated PFS rate at 6 months was 37.8% in patients with metastatic NSCLC and 29.8% in patients with cutaneous melanoma

Figure 5: Kaplan-Meier curves for PFS for secondary refractory metastatic NSCLC (A) and cutaneous melanoma (B)



NSCLC, non-small cell lung cancer; PFS, progression free survival

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results – Safety

- No new safety signals were identified and no deaths due to treatment-related treatment-emergent adverse events (TEAEs) were reported
  - The most frequently reported TEAEs of any grade were fatigue (46%), nausea (42%), peripheral sensory neuropathy (38%), and diarrhea (30%)
- Grade ≥3 TEAEs were reported in 56% and 55% of patients with metastatic NSCLC and cutaneous melanoma, respectively
- Treatment-emergent serious adverse events (TESAEs) were reported in 33% and 50% of patients with metastatic NSCLC and cutaneous melanoma, respectively
  - Across all cohorts, the most frequently reported grade ≥3 TEAEs were fatigue (5%) and neutropenia (5%), and the most frequently reported TESAEs were vomiting (4%), acute kidney injury (3%), and cerebrovascular accident (3%)
- Treatment-emergent immune-mediated AEs were reported in 25% of patients across all cohorts, and treatment-emergent peripheral neuropathy (per a standardized MedDRA query) was reported in 48% of patients
- Any TEAEs leading to treatment discontinuation of either study treatment were reported in 17% of patients

Table 3: Incidence of TEAEs occurring at ≥20% frequency and grade ≥3 TEAEs occurring at ≥5% frequency

	Metastatic NSCLC (N=55)		Metastatic cutaneous melanoma (N=58)	
	Any grade (≥20%)	Grade ≥3 (≥5%)	Any grade (≥20%)	Grade ≥3 (≥5%)
Any TEAEs	51 (93)	31 (56)	56 (97)	32 (55)
Fatigue	28 (51)	3 (5)	24 (41)	3 (5)
Nausea	28 (51)	3 (5)	20 (34)	2 (3)
Peripheral sensory neuropathy	20 (36)	0	23 (40)	0
Diarrhea	16 (29)	0	18 (31)	0
Constipation	15 (27)	1 (2)	17 (29)	0
Decreased appetite	13 (24)	3 (5)	10 (17)	0
Dyspnea	17 (31)	1 (2)	5 (9)	0
Vomiting	11 (20)	1 (2)	10 (17)	2 (3)
Pruritus	11 (20)	0	5 (9)	0
Neutropenia	3 (5)	3 (5)	3 (5)	3 (5)
Hypokalemia	4 (7)	0	6 (10)	4 (7)
Acute kidney injury	3 (5)	3 (5)	1 (2)	0
Aspartate aminotransferase increased	5 (9)	3 (5)	3 (5)	0
Hepatitis	0	0	3 (5)	3 (5)

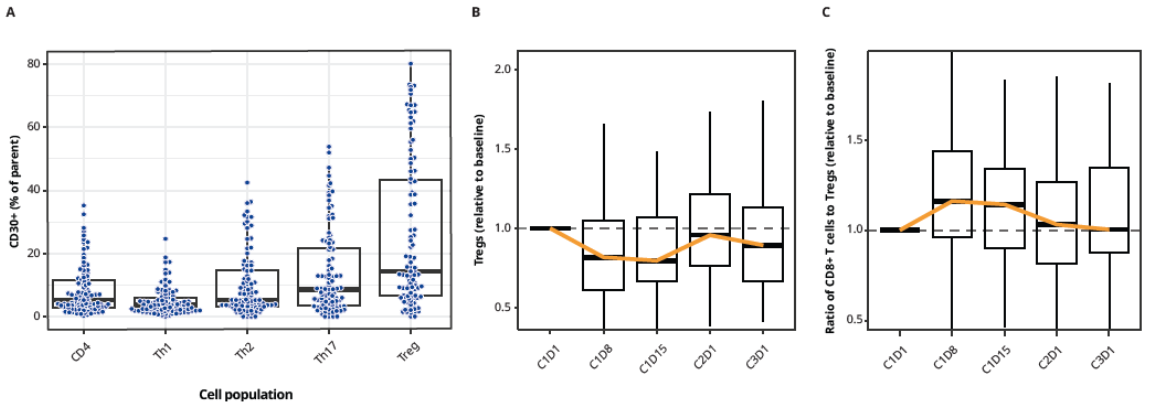
AE, adverse event; NSCLC, non-small cell lung cancer; TEAE, treatment-emergent adverse event; TESEA; treatment-emergent serious adverse event

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Results – Biomarker Analysis

- Tregs express higher levels of CD30 and are selectively depleted by treatment with BV + pembro
  - Tregs express higher levels of CD30 compared with other T-cell subsets
  - Treg levels in blood decreased and the ratio of CD8/Treg increased transiently during cycle 1 of treatment with BV + pembro

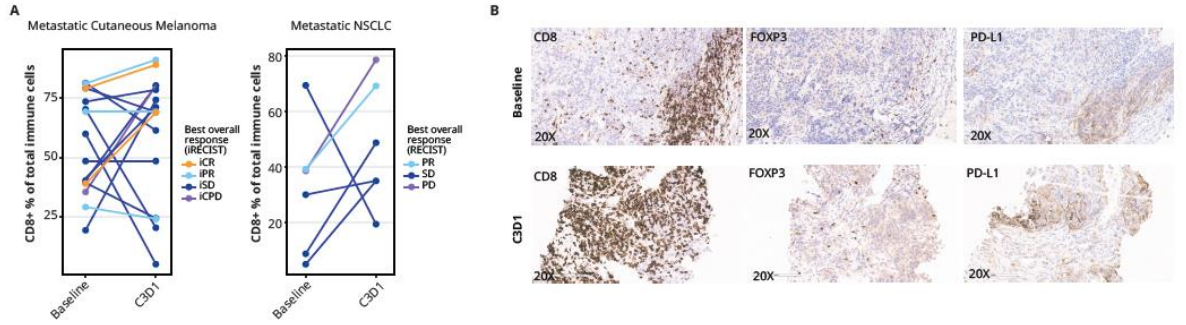
Figure 6: Percentage of CD30-positive-cells out of total or subsets of CD4 T cells (A) and the absolute numbers of Tregs (B) and ratios of CD8 to Tregs (C) at baseline and throughout treatment



Each dot represents baseline data from an individual patient (**Figure 6A**); numbers of Tregs (**Figure 6B**) and ratios of CD8 T cells to Tregs (**Figure 6C**) were normalized to baseline (C1D1) values. The y-axis has been cropped to show the central 95% of observations across time points.

- There was an overall trend of increased CD8 T-cell infiltration after treatment with BV + pembro
- One patient with cutaneous melanoma who had CR after pseudoprogression demonstrated higher CD8 T-cell infiltration and increased PD-L1 expression

Figure 7: CD8 T-cell infiltration in paired tumor biopsies by IHC (A) and representative[a] IHC micrographs (B) at baseline and after treatment with BV + pembro



iCPD, immune confirmed progressive disease; iPR, immune partial response; iSD, immune stable disease.
[a] Representative IHC pictures in baseline and C3D1 biopsies are from a patient with melanoma who had iCR after pseudoprogression, as indicated by an asterisk in **Figure 3B**.

BV, brentuximab vedotin; CD, cluster differentiation; CR, complete response; PD-1, programmed cell death-ligand 1; pembro, pembrolizumab

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Author’s Conclusion

- Treatment with BV in combination with pembrolizumab resulted in encouraging overall survival (OS) and progression-free survival (PFS) rates that support the hypothesis that this combination is active in patients with metastatic solid tumor malignancies refractory to prior PD-1 treatment
- Enhanced antitumor activity was observed in secondary refractory cohorts compared with primary refractory cohorts
- The safety profile of this combination was tolerable, with no new safety signals reported
- Biomarker data showing Treg depletion and a trend of increases in CD8 T-cell infiltration are consistent with the hypothesized immunomodulatory effects of BV

BV, brentuximab vedotin; CD30, cluster differentiation 30; OS; overall survival; PD-1, programmed cell death-ligand 1; PFS, progression free survival

Zakharia, et al. Poster Presentation 2617. Presented at Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024

Frontline brentuximab vedotin and cyclophosphamide, doxorubicin, and prednisone in patients with peripheral T-cell lymphoma with less than 10% CD30 expression: results from the phase 2 SGN35-032 study

Swaminathan P.I, et Al.
Abstract #7069

Swaminathan P. Iyer,[1] Deepa Jagadeesh,[2] Eva Domingo Domenech,[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 Catala 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

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Background

- Brentuximab vedotin is a CD30-directed ADC approved for multiple cancer types, including previously untreated systemic ALCL and CD30-expressing PTCL
- A+CHP was evaluated in the phase 3 ECHELON-2 study (NCT01777152) in patients with ALCL and other PTCL types with ≥10% CD30 expression
  - Compared with patients receiving conventional frontline therapy, those treated with A+CHP had a survival benefit (HR, 0.72; 95% CI, 0.53-0.99; *P*=.0424) and a 30% reduced risk of progression (stratified HR, 0.70; 95% CI, 0.53-0.91; *P*=.0077)
- Since no correlation was assessed between CD30 expression and efficacy in the ECHELON-2 study, the SGN35-032 study is investigating the efficacy and safety of frontline A+CHP in patients with non-systemic ALCL PTCL with <10% CD30 expression

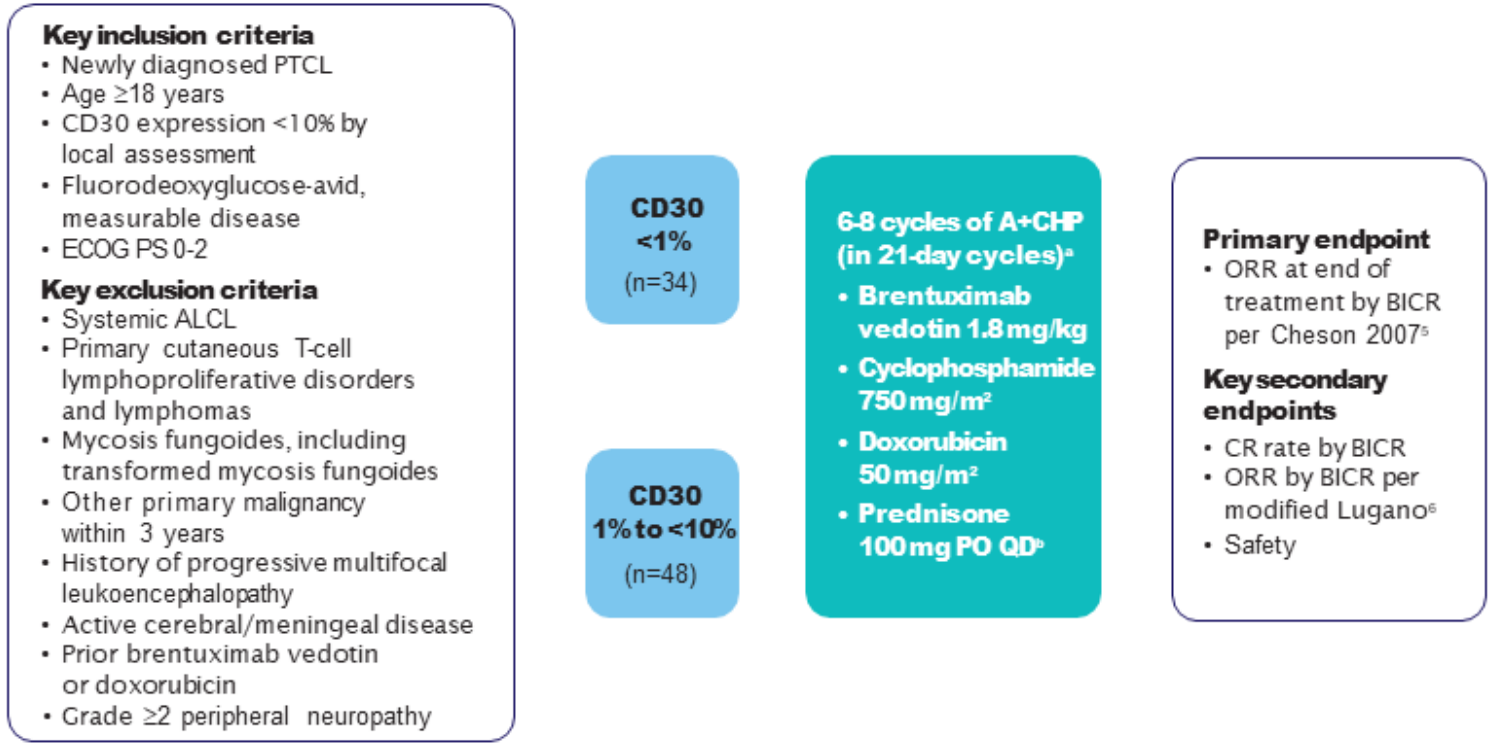
ADC, antibody-drug conjugate; ALCL, Anaplastic large cell lymphoma; PTCL, Peripheral T-cell lymphoma; A+CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; HR, hazard ratio; CI, confidence interval;

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Methods

- SGN35-032 (NCT04569032; EudraCT 2020-002336-74) is an ongoing, open-label, dual-cohort, global, multicenter, phase 2 study **(Figure 1)**
- Patients with newly diagnosed non-systemic ALCL PTCL with <10% CD30 expression (by standard immunohistochemistry by local pathology assessment) were enrolled
  - Patients were assigned to the 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 of ORR at end of treatment was assessed by blinded independent central review (BICR) per Cheson 2007

Figure 1: Study design



a) Brentuximab vedotin, cyclophosphamide, and doxorubicin were administered via intravenous infusion on day 1 of each cycle b) Prednisone was administered orally on days 1 to 5 of each cycle

ALCL, Anaplastic large cell lymphoma; PTCL, Peripheral T-cell lymphoma; A+CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; BICR, blinded independent central review; ORR, objective response rate; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PO, "by mouth"; QD, "every day"

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Demographics

- A total of 82 patients with newly diagnosed non-systemic ALCL PTCL were enrolled into the CD30 <1% (n=34) and CD30 1% to <10% (n=48) cohorts
- At the data cutoff of January 31, 2024, 45 of 82 (55%) patients were still in follow-up; median follow-up time was 11.65 months
- Baseline characteristics were similar between the 2 cohorts **(Table 1)**

Table 1: Demographics and baseline disease characteristics

	CD30 <1% (n=34)[a]	CD30 1% to <10% (n=48)[a]	Total (N=82)
Age, median (range), years	63.0 (24-78)	64.0 (32-80)	63.5 (24-80)
Age category, n (%)			
<65 years	19 (56)	28 (58)	47 (57)
≥65 years	15 (44)	20 (42)	35 (43)
Race, n (%)			
White	26 (76)	37 (77)	63 (77)
Asian	2 (6)	4 (8)	6 (7)
Black or African American	2 (6)	2 (4)	4 (5)
Other/unknown/not reportable	4 (12)	5 (10)	9 (11)
ECOG performance status, 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)
Diagnosis, n (%)			
PTCL not otherwise specified	18 (53)	19 (40)	37 (45)
Angioimmunoblastic T-cell lymphoma	8 (24)	18 (38)	26 (32)
Nodal PTCL with T-follicular helper phenotype	4 (12)	4 (8)	8 (10)
Follicular T-cell lymphoma	1 (3)	4 (8)	5 (6)
Other	3 (9)	3 (6)	6 (7)
Baseline IPI score, n (%)[c]			
0	2 (6)	1 (2)	3 (4)
1	4 (12)	10 (21)	14 (17)
2	12 (35)	17 (35)	29 (35)
3	10 (29)	16 (33)	26 (32)
4	4 (12)	2 (4)	6 (7)
5	1 (3)	1 (2)	2 (2)
Missing	1 (3)	1 (2)	2 (2)

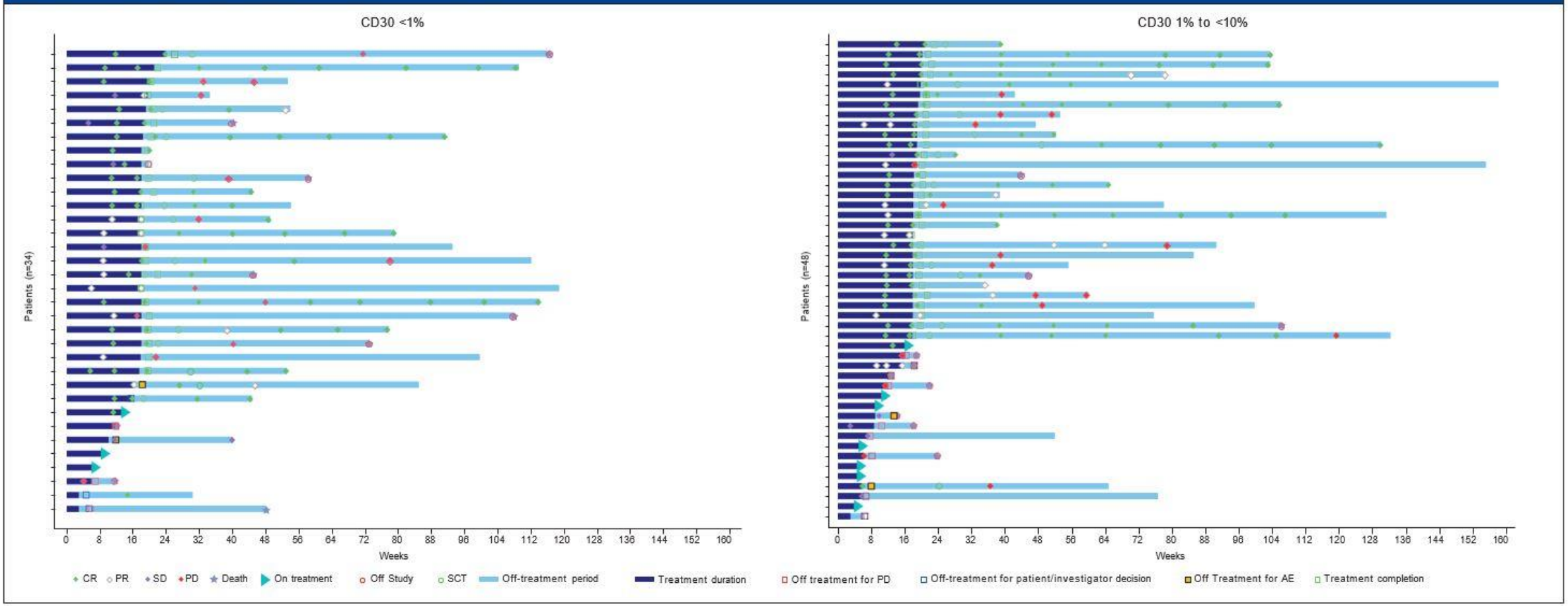
a) CD30 expression per local testing b) The last non-missing value before or on the day of first study treatment c) The International Prognostic Index score aids in predicting the patient's prognosis

ALCL, Anaplastic large cell lymphoma; PTCL, Peripheral T-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IPI, International Prognostic Index

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Results

Figure 2: Treatment and response per BICR by local CD30 assessment



The median treatment duration was 18.0 weeks (range, 3-24 weeks)

BICR, blinded independent central review; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; AE, adverse event; SCT, stem cell transplantation

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Results - Efficacy

Table 2: ORR by BICR by CD30 status			
	CD30 <1%	**CD30 1% to <10%**	**Total**
Per local CD30[a]	**n=32**	**n=42**	**n=74**
Best overall response, n (%)[b]			
CR	19 (59)	28 (67)	47 (64)
PR	7 (22)	5 (12)	12 (16)
SD	1 (3)	4 (10)	5 (7)
PD	1 (3)	3 (7)	4 (5)
NE[c]	4 (13)	2 (5)	6 (8)
CR rate (95% CI), %[d]	59 (40.6-76.3)	67 (50.5-80.4)	64 (51.5-74.4)
ORR (95% CI), %[d]	81 (63.6-92.8)	79 (63.2-89.7)	80 (68.8-88.2)
Per central CD30[a]	**n=20**	**n=28**	**n=74[e]**
Best overall response, n (%)[b]			
CR	11 (55)	19 (68)	47 (64)
PR	2 (10)	4 (14)	12 (16)
SD	1 (5)	2 (7)	5 (7)
PD	4 (20)	0	4 (5)
NE[c]	2 (10)	3 (11)	6 (8)
CR rate (95% CI), %[d]	55 (31.5-76.9)	68 (47.6-84.1)	64 (51.5-74.4)
ORR (95% CI), %[d]	65 (40.8-84.6)	82 (63.1-93.9)	80 (68.8-88.2)

Among the 74 response-evaluable patients, the ORR was 80% (95% CI, 68.8%-88.2%) per BICR

- *Analysis performed among the response-evaluable set, which is a subset of all treated patients with postbaseline response assessment or those who discontinued treatment.*
- *Complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) per Cheson 2007 per independent assessor. CR, PR, SD, PD, and not evaluable (NE) are mutually exclusive.*
- *NE includes patient with no postbaseline response assessments.*
- *Two-sided 95% exact confidence interval computed using the Clopper-Pearson method.*
- *Per central testing, 26 patients either had CD30 expression*
- *≥10% or were missing CD30 results.*

BICR, blinded independent central review; ORR, objective response rate; CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Results – Safety Profile

Table 3: Summary of AEs

	CD30 <1%[a] (n=34)	CD30 1% to <10%[a] (n=48)	Total (N=82)
Grade ≥3 TEAEs (≥10% of total patients)			
Patients with any event, n (%)	21 (62)	25 (52)	46 (56)
Neutropenia	4 (12)	11 (23)	15 (18)
Febrile neutropenia	6 (18)	8 (17)	14 (17)
Treatment-related TEAEs (≥10% of total patients)[b]			
Patients with any event, n (%)	25 (74)	40 (83)	65 (79)
Peripheral sensory neuropathy	10 (29)	15 (31)	25 (30)
Diarrhea	7 (21)	13 (27)	20 (24)
Nausea	6 (18)	13 (27)	19 (23)
Neutropenia	4 (12)	12 (25)	16 (20)
Febrile neutropenia	6 (18)	8 (17)	14 (17)
Anemia	4 (12)	9 (19)	13 (16)
Vomiting	2 (6)	7 (15)	9 (11)
Alopecia	2 (6)	6 (13)	8 (10)
Decreased appetite	3 (9)	5 (10)	8 (10)
Fatigue	4 (12)	4 (8)	8 (10)
Treatment-emergent serious AEs (≥5% of total patients)			
Patients with any serious AE, n (%)	15 (44)	16 (33)	31 (38)
Febrile neutropenia	6 (18)	9 (19)	15 (18)
Pyrexia	4 (12)	1 (2)	5 (6)
Diarrhea	2 (6)	2 (4)	4 (5)

a) CD30 expression per local testing b) Treatment relatedness is per investigator determination of relatedness to any study drug

- Grade ≥3 treatment-emergent adverse events (TEAEs) were experienced by 46 patients (56%)
- Six patients (7%) discontinued study treatment due to TEAEs
- There were 2 (2%) treatment-related deaths: 1 patient died due to decreased appetite, and 1 patient died due to general physical health deterioration

TEAE, treatment-emergent adverse evet; AE, adverse event

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Authors' Conclusions

- The anti-CD30 antibody–drug conjugate (ADC) brentuximab vedotin combined with cyclophosphamide, doxorubicin, and prednisone (A+CHP) appears effective as a frontline treatment in patients with non-systemic anaplastic large cell lymphoma (ALCL) peripheral T-cell lymphoma (PTCL) with <10% CD30 expression
- Per local CD30 assessment, efficacy of A+CHP was similar in patients in the CD30 <1% cohort and CD30 1% to <10% cohort, with an objective response rate (ORR) of 81% and 79%, respectively, and a complete response (CR) rate of 59% and 67%
- No new safety signals were observed, and the data were consistent with the known safety profile of A+CHP
- This study is ongoing and updated results will be shared in the future

ADC, antibody-drug conjugate; ALCL, Anaplastic large cell lymphoma; PTCL, Peripheral T-cell lymphoma; A+CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; ORR, objective response rate; CR, complete response

Swaminathan P.I, et al. Poster Presentation 7069. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Brentuximab vedotin in combination with lenalidomide and rituximab in patients with relapsed/refractory diffuse large B-cell lymphoma: results from the phase 3 ECHELON-3 study

Kim J, et Al.
Abstract #LBA7005

Jeong-A Kim,[1] Uwe Hahn,[2] Won-Seog Kim,[3] Isabelle Fleury,[4] Kamel Laribi,[5] Juan Miguel Bergua Burgues,[6] Krimo Bouabdallah,[7] Nicholas Forward,[8] Fontanet Bijou,[9] David MacDonald,[10] Craig A. Portell,[11] Herve Ghesquieres,[12] Grzegorz S. Nowakowski,[13] Christopher A. Yasenchak,[14] Evelyn Rustia,[15] Michelle Fanale,[15] Fei Jie,[15] Nancy L. Bartlett[16]

[1]St. Vincent's Hospital, The Catholic University of Korea, Suwon, South Korea; [2]Haematology Unit, Royal Adelaide Hospital, Adelaide, Australia; [3]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, South Korea; [4]Hôpital Maisonneuve-Rosemont, Institut Universitaire d'hématologie-oncologie et de Thérapie Cellulaire, Université de Montréal, Montréal, QC, Canada; [5]Department of Hematology, Centre Hospitalier Le Mans, Le Mans, France; [6]Hospital San Pedro de Alcantara, Cáceres, Spain; [7]Service d'hematologie Clinique et Therapie Cellulaire, CHU Haut-Leveque, Pessac, France; [8]Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; [9]Centre de Lutte Contre le Cancer (CLCC) - Institut Bergonié, Bordeaux, France; [10]Division of Hematology, The Ottawa Hospital, Ottawa, ON, Canada; [11]UVA Comprehensive Cancer Center, University of Virginia, Charlottesville, VA, USA; [12]Hopital Lyon Sud - HCL, Pierre-Bénite, France; [13]Division of Hematology, Mayo Clinic, Rochester, MN, USA; [14]Willamette Valley Cancer Institute and Research Center/US Oncology Research, Eugene, OR, USA; [15]Pfizer Inc., Bothell, WA, USA; [16]Siteman Cancer Center, Washington University School of Medicine, St Louis, MO, USA

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

Key Takeaways

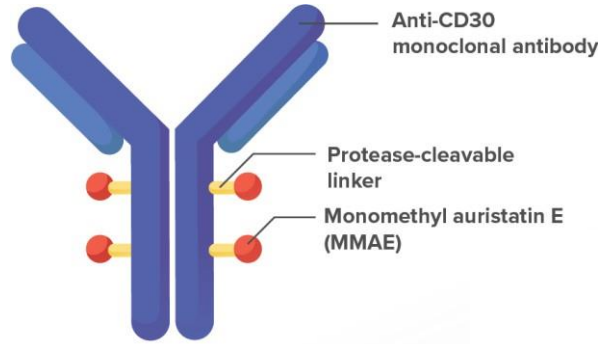
- ECHELON-3 is the first randomized, placebo-controlled, phase 3 study to demonstrate overall survival benefit in a contemporary population of patients with R/R DLBCL who have received ≥2 prior lines of systemic therapy
- This study met its primary objective of demonstrating a significant improvement in overall survival for BV+Len+R compared to placebo+Len+R
- Key secondary endpoints of PFS and ORR were also significantly improved by BV+Len+R vs placebo+Len+R
- Consistent benefit of BV+Len+R for OS, PFS, and ORR was observed in tumors with or without CD30 expression
- This triplet combination, with its promising OS benefit, has the potential to address the high unmet need in patients with R/R DLBCL, particularly those who are not able to receive CAR T-cell therapy or bispecific antibodies or have R/R disease following these treatments

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; DLBCL, diffuse large B-cell lymphoma; CAR, chimeric antigen receptor; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, rituximab; R/R, relapsed or refractory.

Background and Rationale

- BV is an antibody-drug conjugate targeting CD30[1]
- In patients with R/R DLBCL:
  - ORR with BV (n=49) was **44%**[2]
  - ORR with BV+R (n=13) was **46%**[2]
  - ORR with Len+R (n=32) was **28%**[3]
  - ORR with BV+Len (n=37) was **57%,** and CR rate was 35%[4]
    - Responses were observed in patients regardless of CD30 status



Brentuximab vedotin

- Despite recent advances including T-cell directed therapies, there remains a high unmet need for readily available and tolerable regimens for patients with later line DLBCL
  - Real-world data has shown that rwOS in the 3L+ setting is less than a year[5,6]
- ECHELON-3 (NCT04404283) is a randomized, double-blind, placebo-controlled, active comparator, multicenter, phase 3 study comparing BV or placebo in combination with Len+R (BV+Len+R vs placebo+Len+R) in patients with R/R DLBCL[7,8]
- Here we report safety and efficacy results from the interim analysis of the ECHELON-3 study

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; Len, lenalidomide; ORR, objective response rate; R, rituximab; rwOS, real world overall survival; R/R, relapsed or refractory.

1. Makita S, et al. Onco Targets Ther. 2020;13:5993-6009. 2. Jacobsen ED, et al. Blood. 2015;125(9):1394-1402. 3. Wang Y, et al. Blood. 2015;126(23):3969. 4. Ward JP, et al. Blood. 2022;139(13):1999-2010.;
5. Ip A et al. Adv Ther. 2024;41(3):1226-1244.; 6. Sineshaw HM, et al. Cancer Med. 2024;13(7)e7173.; 7. Bartlett NL, et al. Hemasphere. 2022;6(suppl):1064-1065. 8. ClinicalTrials.gov. Accessed April 2, 2024. https://www.clinicaltrials.gov/study/NCT04404283.

ECHELON-3 Trial Design

Phase 3 in Relapsed/Refractory Diffuse Large B-Cell Lymphoma

Key inclusion criteria

- R/R DLBCL with eligible subtypes[a]
- Age ≥18 years
- **≥2 prior lines of therapy**
- **Ineligibility for or disease relapse following HSCT or CAR T-cell therapy**
- ECOG PS 0-2
- FDG-avid, measurable disease

Key exclusion criteria

- Prior BV or Len
- Active cerebral/meningeal disease
- Grade ≥2 peripheral neuropathy

Randomization 1:1

Treatment groups[c]

BV+Len+R (n=112)

BV 1.2 mg/kg IV Q3W + Len 20 mg PO QD + R 375 mg/m^2 IV Q3W[b]

Placebo+Len+R (n=118)

Placebo IV Q3W + Len 20 mg PO QD + R 375 mg/m^2 IV Q3W[b]

Primary endpoint

- OS in ITT population

Secondary endpoints

- PFS_{INV} and ORR_{INV} using the response criteria per Lugano 2014 in ITT population
- $CR\ rate_{INV}$
- DOR_{INV}
- OS in CD30-positive population
- Safety and tolerability

Stratification

- CD30 status (≥1% vs <1%)
- Cell of origin (GCB or non-GCB)
- Prior treatment with CAR-T therapy (received or not)
- Prior treatment with SCT (received or not)

- Per protocol, G-CSF prophylaxis was required

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

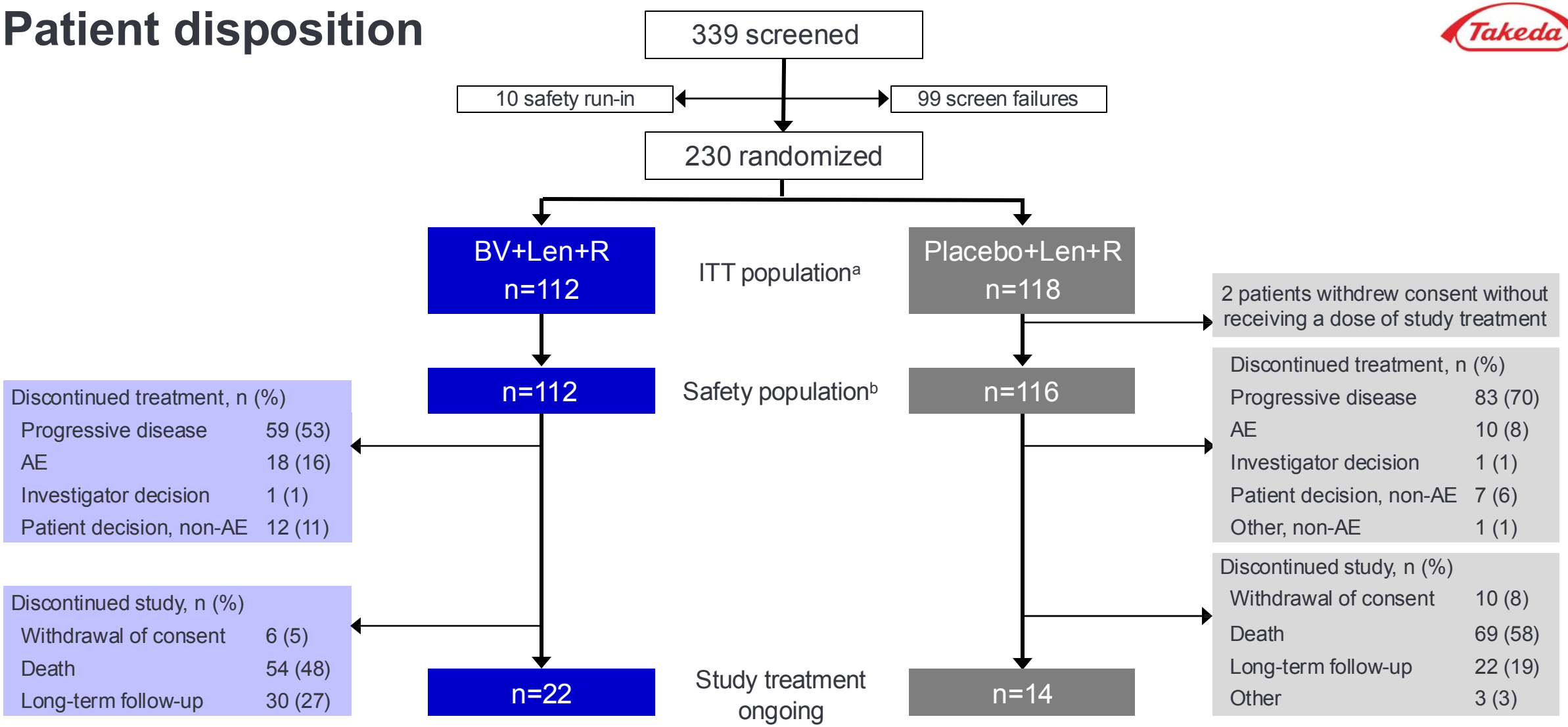
BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; GCB, germinal center B cell; HSCT, hematopoietic stem cell transplant; INV, investigator; ITT, intention to treat; IV, intravenous; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, oral; Q3W, every 3 weeks; QD, once daily; R, rituximab; R/R, relapsed or refractory; SCT, stem cell transplant; G-CSF, granulocyte colony-stimulating factor

[a] Eligible subtypes include but are not limited to transformed DLCBL, high-grade double-/triple-hit lymphoma, and not otherwise specified.

[b] Starting with cycle 2, R can be administered intravenously or subcutaneously (1400 mg subcutaneously Q3W).

[c] Treatment was allowed to continue until disease progression or unacceptable toxicity.

Patient disposition



- Median duration of treatment was 3.6 months (range: 0.5-26.4) for BV+Len+R and 2.0 months (range: 0.1-26.6) for placebo+Len+R

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

AE, adverse event; BV, brentuximab vedotin; ITT, intention to treat; Len, lenalidomide; R, rituximab.

a Includes all randomized patients regardless of actual treatment received.

b Patients who received ≥1 dose of study treatment. Patients who received any BV dose were put in the experimental group. Patients who did not receive BV but received either Len or R were put into the control group

Patient characteristics were well balanced between groups

	BV+Len+R (n=112)	Placebo+Len+R (n=118)
Patient characteristics		
Age, median (range), years	74.0 (29-87)	70.0 (21-89)
Age		
≥65 years, n (%)	79 (71)	76 (64)
≥80 years, n (%)	23 (21)	15 (13)
Male, n (%)	60 (54)	70 (59)
ECOG PS 2, n (%)[a]	12 (11)	13 (11)
Race, n (%)		
White	65 (58)	56 (47)
Asian	28 (25)	32 (27)
Other or unknown	19 (17)	30 (25)
Prior treatments		
Lines of systemic therapies, median (range)	3 (2-8)	3 (2-7)
Systemic therapies received, n (%)		
Previous anthracycline	110 (98)	115 (97)
Previous anti-CD20 antibody	110 (98)	114 (97)
CAR T-cell therapy	32 (29)	35 (30)
Bispecific antibody	14 (13)	20 (17)
HSCT	10 (9)	18 (15)

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; HSCT, hematopoietic stem cell transplant; Len, lenalidomide; R, rituximab.

a Values presented are the last non-missing value on or before the first dose date. If a subject did not receive any dose, the randomization/enrollment date is used in place of the first dose date.

Disease characteristics were well balanced between groups

n (%)	BV+Len+R (n=112)	Placebo+Len+R (n=118)
DLBCL NOS	63 (56)	64 (54)
Transformed DLBCL	32 (29)	27 (23)
Cell of origin[a]		
GCB	51 (46)	54 (46)
Non-GCB	61 (54)	64 (54)
CD30 status[b]		
≥1%	36 (32)	38 (32)
<1%	76 (68)	80 (68)
Other disease characteristics		
Ann Arbor stage III/IV at study entry[c]	83 (74)	98 (83)
IPI score ≥3 at time of enrollment	67 (60)	71 (60)
Primary refractory, n (%)[c]	64 (57)	64 (54)
Refractory to last prior DLBCL therapy, n (%)[c]	98 (88)	96 (81)

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CD, cluster of differentiation; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B cell; IPI, International Prognostic Index; Len, lenalidomide; NOS, not otherwise specified; R, rituximab.

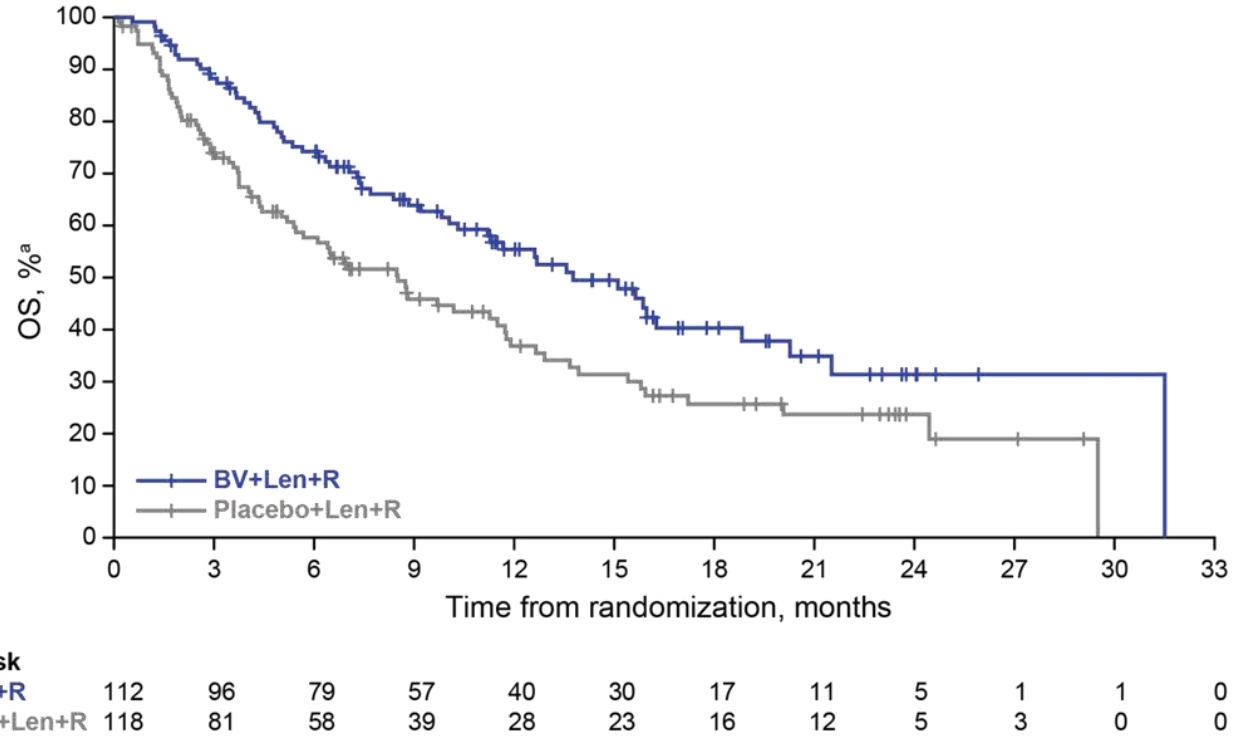
[a] Based on post randomization corrected values.

[b] CD30 status per central result. When central result is not available, local result is used.

[c] Relapsed or refractory status is derived from prior therapy data. Refractory was defined as no response or a response lasting <6 months from the last treatment end date. Relapsed was defined as a response lasting ≥6 months from the last treatment end date

Primary endpoint met with significant improvement in Overall Survival

BV+Len+R reduces risk of death by 37% compared to placebo+Len+R



	BV+Len+R (n=112)	Placebo+Len+R (n=118)
OS, median (95% CI), months	**13.8** (10.3-18.8)	**8.5** (5.4-11.7)
Hazard ratio (95% CI)[b]	0.629 (0.445-0.891)	
Log-rank *P* value[c]	.0085	
Events (deaths)	58	76
Follow-up, median (95% CI), months	15.5 (12.2-18.1)	18.9 (12.2-23.2)

- BV+Len+R prolonged median OS by 5.3 months compared with placebo+Len+R
- Prespecified O'Brien-Fleming efficacy boundary was crossed at this interim analysis

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CD, cluster of differentiation; GCB, germinal center B cell; Len, lenalidomide; OS, overall survival; R, rituximab; CI, confidence interval

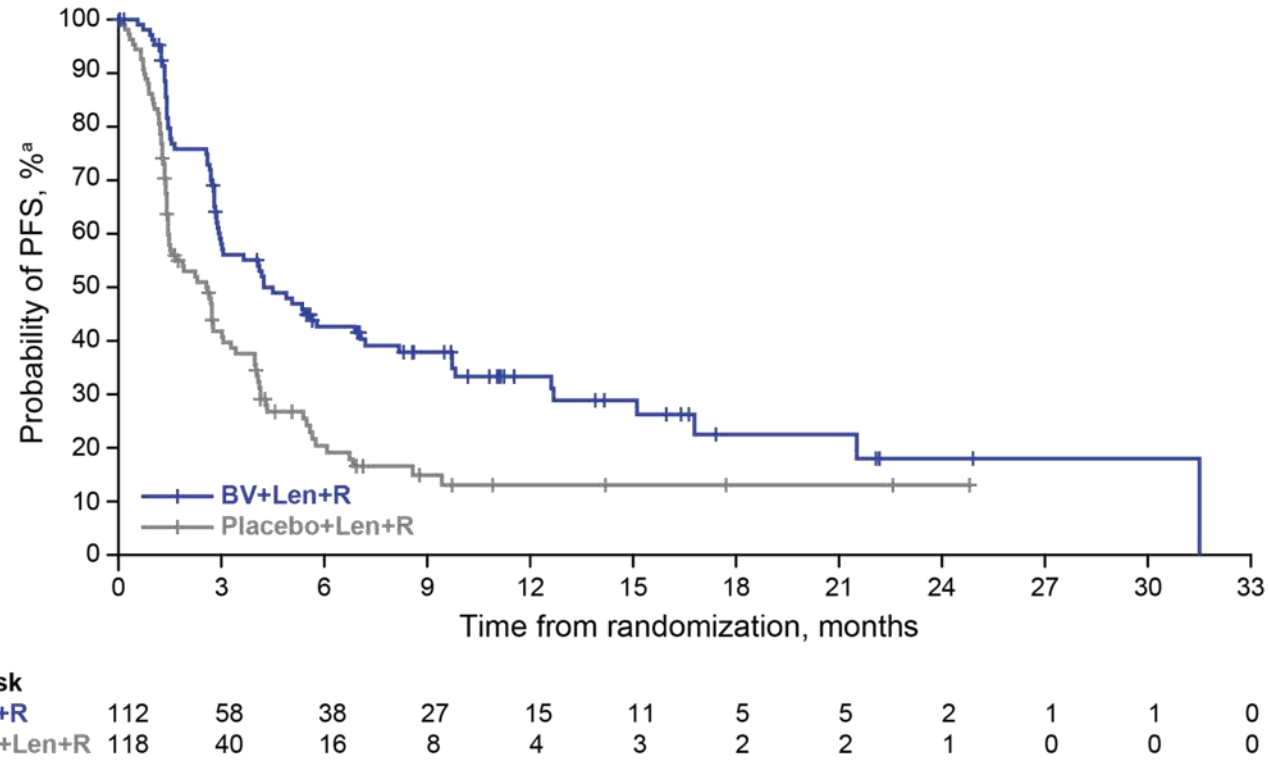
[a] OS is time from randomization to death due to any cause. OS is estimated using Kaplan-Meier method.

[b] Hazard ratio and 95% CI are based on a stratified Cox regression model with stratification factors (GCB or non-GCB) and CD30 status (≥1% or <1%) at randomization. Hazard ratio of <1 favors BV+Len+R. Nonbinding futility boundary hazard ratio is 1.1.

[c] Two-sided *P* value from a stratified log-rank test with stratification factors of cell origin and CD30 status at randomization. O'Brien-Fleming efficacy boundary 2-sided *P* value is .0232.

Key secondary endpoint met with significant improvement in PFS

BV+Len+R reduces risk of disease progression or death by 47% compared to placebo+Len+R



	BV+Len+R (n=112)	Placebo+Len+R (n=118)
PFS, median (95% CI), months	**4.2** (2.9-7.1)	**2.6** (1.4-3.1)
Hazard ratio (95% CI)[b]	0.527 (0.380-0.729)	
Log-rank *P* value[c]	<.0001	
Events	71	85
Follow-up, median (95% CI), months	11.1 (8.6-14.2)	8.8 (6.9-10.9)

- PFS was an alpha controlled key secondary endpoint

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CD, cluster of differentiation; GCB, germinal center B cell; Len, lenalidomide; PFS, progression-free survival; R, rituximab; CI, confidence interval

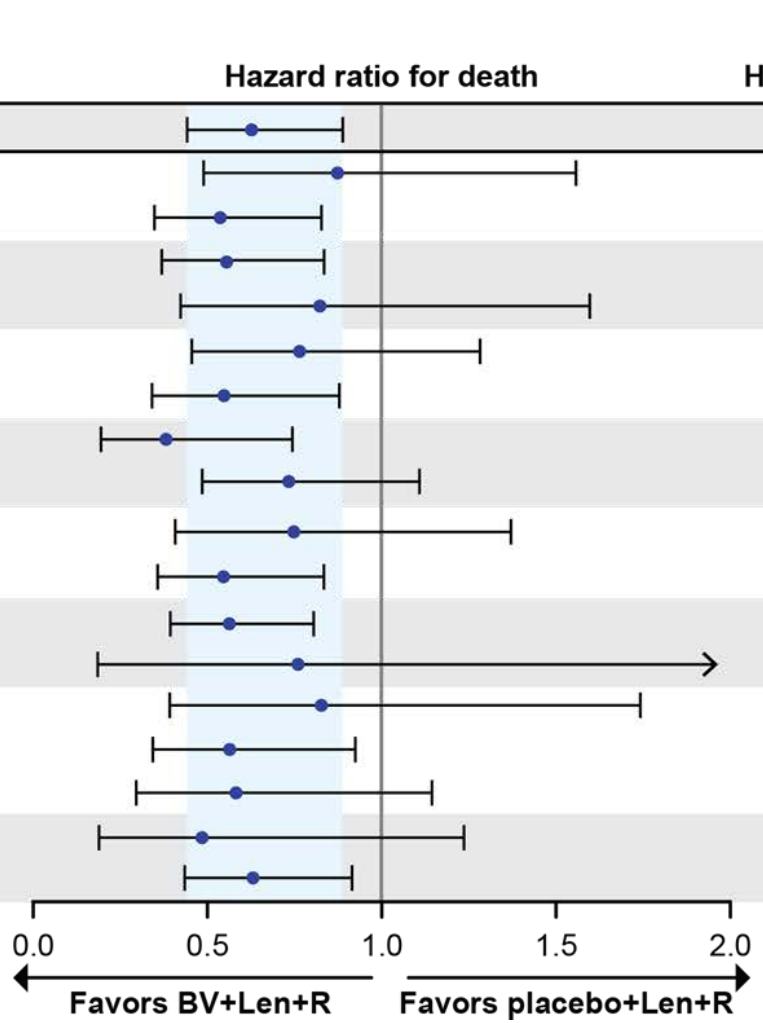
[a] PFS is time from randomization to earliest occurrence or progressive disease per Lugano 2014 or death. PFS is estimated using Kaplan-Meier method.

[b] Hazard ratio and 95% CI are based on a stratified Cox regression model with stratification factors (GCB or non-GCB) and CD30 status (≥1% or <1%) at randomization. Hazard ratio of <1 favors BV + Len + R.

[c] Two-sided *P* value from a stratified log-rank test based on stratification factors cell of origin (GCB or non-GCB) and CD30 status (≥1% or <1%) at randomization.

Median OS was longer with BV+Len+R across subgroups[a]

Subgroups		Median OS, months (events/n) BV+Len+R	Placebo+Len+R	Hazard ratio (95% CI)
All patients		**13.8 (58/112)**	**8.5 (76/118)**	**0.63 (0.44-0.89)**
Age	<65 Years	11.2 (20/33)	8.7 (28/42)	0.88 (0.49-1.56)
	≥65 Years	15.9 (38/79)	8.5 (48/76)	0.54 (0.35-0.83)
CD30 expression	<1%	15.6 (42/76)	6.5 (55/80)	0.56 (0.37-0.84)
	≥1%	13.6 (16/36)	11.7 (21/38)	0.83 (0.43-1.60)
Cell of origin	GCB	13.6 (28/51)	8.5 (32/54)	0.77 (0.46-1.29)
	Non-GCB	18.8 (30/61)	8.5 (44/64)	0.55 (0.34-0.88)
Prior CAR-T	Received	15.6 (16/32)	4.4 (25/35)	0.38 (0.20-0.75)
	Not received	13.8 (42/80)	9.7 (51/83)	0.74 (0.49-1.11)
Baseline IPI score	<3	18.8 (20/45)	15.4 (24/47)	0.75 (0.41-1.37)
	≥3	11.7 (38/67)	5.2 (52/71)	0.55 (0.36-0.84)
Status after last prior therapy	Refractory	11.7 (55/98)	5.5 (70/96)	0.57 (0.40-0.81)
	Relapsed	NA (3/13)	20.1 (6/21)	0.76 (0.19-3.09)
Region	North America	15.1 (18/30)	11.8 (12/19)	0.83 (0.39-1.74)
	Europe	11.3 (26/50)	6.5 (42/60)	0.57 (0.35-0.93)
	Asia-Pacific	20.3 (14/32)	11.3 (22/39)	0.58 (0.30-1.15)
Double-/triple-hit lymphoma	Yes	16.3 (8/15)	4.4 (10/14)	0.49 (0.19-1.24)
	No	13.6 (50/97)	8.7 (66/104)	0.63 (0.44-0.92)



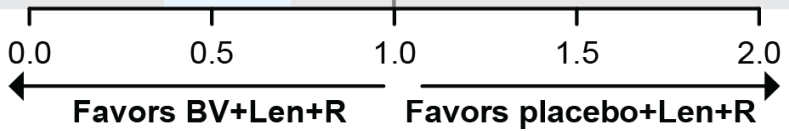
Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; GCB, germinal center B cell; IPI, International Prognostic Index; Len, lenalidomide; NA, not available; OS, overall survival; R, rituximab; CI, confidence interval

[a] The subgroups shown here had a hazard ratio of <1.

Median PFS was longer with BV+Len+R across subgroups[a]

Subgroups		Median PFS, months (events/n) BV+Len+R	Placebo+Len+R	Hazard ratio (95% CI)
All patients		**4.2 (71/112)**	**2.6 (85/118)**	**0.53 (0.38-0.73)**
Age	<65 Years	2.9 (25/33)	1.4 (33/42)	0.69 (0.41-1.17)
	≥65 Years	5.7 (46/79)	2.8 (52/76)	0.48 (0.32-0.72)
CD30 expression	<1%	3.1 (49/76)	1.9 (57/80)	0.57 (0.38-0.84)
	≥1%	6.9 (22/36)	2.7 (28/38)	0.49 (0.28-0.86)
Cell of origin	GCB	4.2 (33/51)	2.8 (38/54)	0.55 (0.34-0.89)
	Non-GCB	4.5 (38/61)	1.9 (47/64)	0.52 (0.33-0.80)
Prior CAR-T	Received	3.0 (21/32)	1.4 (25/35)	0.41 (0.22-0.76)
	Not received	5.1 (50/80)	2.8 (60/83)	0.58 (0.40-0.85)
Baseline IPI score	<3	5.4 (29/45)	2.8 (32/47)	0.60 (0.36-1.00)
	≥3	3.6 (42/67)	1.5 (53/71)	0.49 (0.32-0.73)
Status after last prior therapy	Refractory	4.1 (66/98)	1.5 (74/96)	0.51 (0.36-0.71)
	Relapsed	15.1 (5/13)	5.6 (10/21)	0.29 (0.08-0.98)
Region	North America	4.1 (22/30)	1.4 (12/19)	0.65 (0.32-1.34)
	Europe	3.6 (31/50)	1.5 (44/60)	0.48 (0.30-0.77)
	Asia-Pacific	9.7 (18/32)	3.0 (29/39)	0.50 (0.28-0.91)
Double-/triple-hit lymphoma	Yes	4.1 (9/15)	1.5 (9/14)	0.36 (0.13-0.97)
	No	4.5 (62/97)	2.6 (76/104)	0.56 (0.40-0.78)



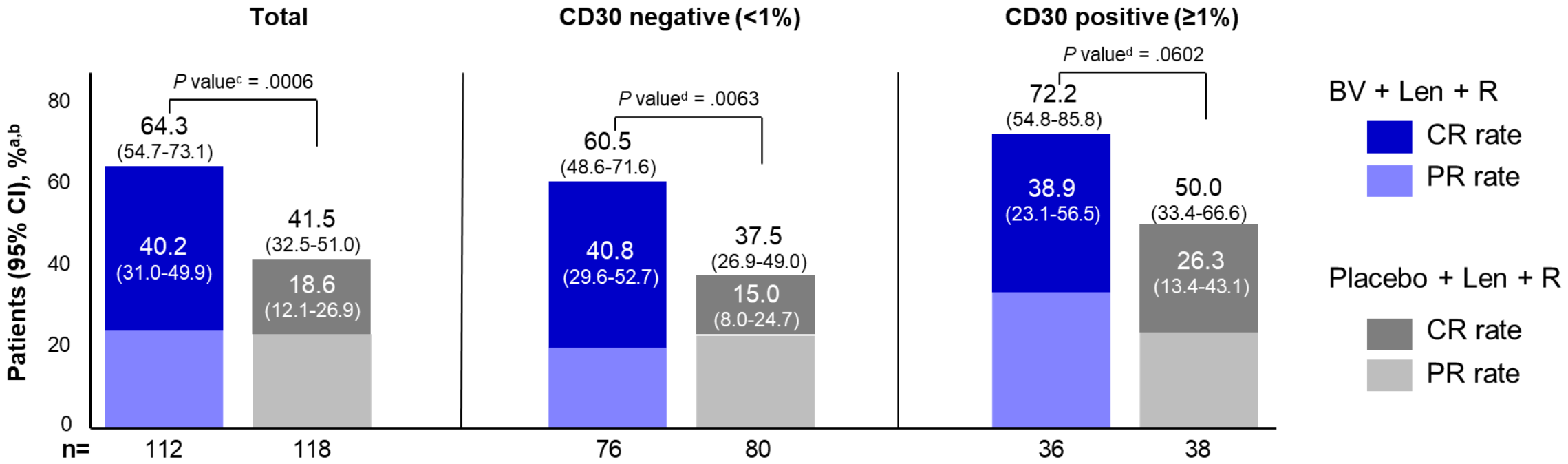
Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; GCB, germinal center B cell; IPI, International Prognostic Index; Len, lenalidomide; PFS, progression-free survival; R, rituximab; CI, confidence interval

[a] The subgroups shown here had a hazard ratio of <1.

Overall Response Rate was significantly higher with BV+Len+R

40% CR rate with BV+Len+R and ORR improvement regardless of CD30 expression



- In the total population, the median DOR (95% CI) was longer with BV+Len+R: 8.3 months (4.2-15.3 months) vs 3.0 months (2.8-5.4 months)
  - In patients who had a CR, the median DOR (95% CI) was 18.9 months (11.1 months-NR) with BV+Len+R and NR (2.8 months-NR) with placebo+Len+R
  - The median time to CR onset (range) was 1.58 months (1.2-7.3 months) with BV+Len+R and 1.61 months (0.7-4.6 months) with placebo+Len+R

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CD, cluster of differentiation; CR, complete response; DOR, duration of response; GCB, germinal center B cell; Len, lenalidomide; NR, not reached; ORR, objective response rate; PR, partial response; R, rituximab; CI, confidence interval

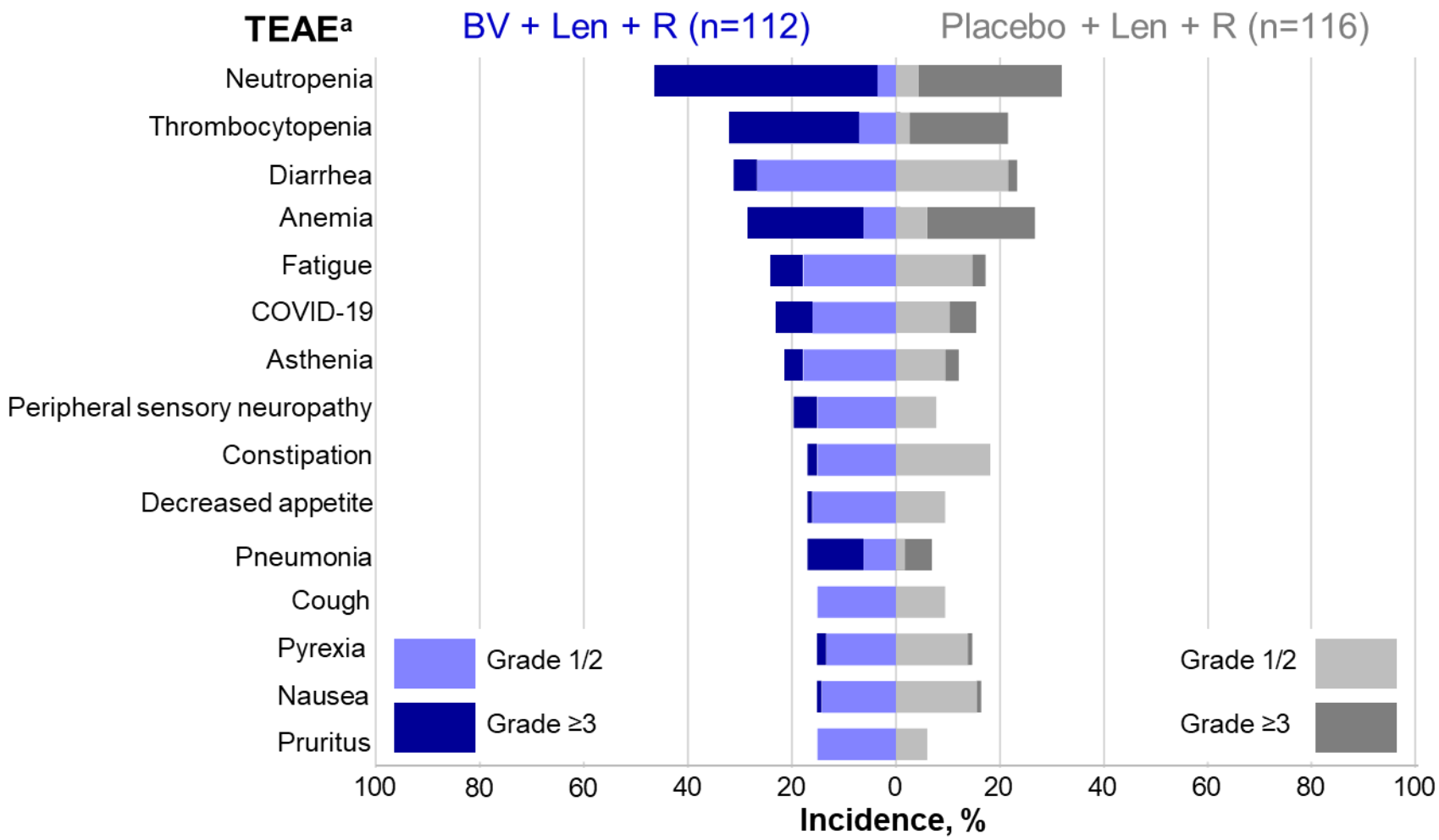
[a] Exact 95% CI computed using the Clopper-Pearson method (Clopper 1934).

[b] Best response per Lugano 2014 by investigator assessment. Includes metabolic and nonmetabolic response. Response assessments after progressive disease or start of new anticancer therapy are excluded.

[c] Two-sided *P* value based on Cochran-Mantel-Haenszel test controlling for stratification factors cell of origin (GCB or non-GCB) and CD30 status (≥1% or <1%) at randomization.

[d] Two-sided *P* value based on Fisher exact test.

No new safety signals were observed with addition of BV to Len+R



- TEAEs of any grade occurred in 97% of patients with each treatment
- Grade ≥3 TEAEs:
  - 88% with BV+Len+R
  - 77% with placebo+Len+R
  - 9% febrile neutropenia in each group
- Grade 5 TEAEs:
  - 12% with BV+Len+R
  - 8% with placebo+Len+R
- Any grade peripheral neuropathy TEAEs
  - 31% with BV+Len+R
  - 24% with placebo+Len+R
- Relative dose intensity
  - 94.4% for BV
  - 99.7% for placebo

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; Len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

[a] TEAEs listed are those occurring in ≥15% of patients on either arm. TEAEs are newly occurring or worsening within the safety reporting period (after first dose of study treatment and within 30 days after last dose of BV or Len or 110 days after last dose of R, whichever is later). TEAEs are organized by decreasing frequency in the BV+Len+R group.

Subsequent anticancer therapies received were balanced across both arms

n (%)	BV+Len+R (n=112)	Placebo+Len+R (n=116)
Received any subsequent therapy[a]	38 (34)	55 (47)
For progressive disease	30 (27)	44 (38)
For relapsed disease	6 (5)	5 (4)
Secondary malignancy	0	2 (2)
Other	5 (4)	8 (7)
Subsequent therapies		
Anti-CD20	9 (8)	10 (9)
Antibody-drug conjugate	7 (6)	6 (5)
Bispecific	5 (4)	10 (9)
CAR T-cell therapy	5 (4)	5 (4)
Tafasitamab	4 (4)	1 (1)
Other	12 (11)	27 (23)

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; Len, lenalidomide; R, rituximab.

[a] Patients receiving multiple therapies were counted once for each type of therapy and specific therapy received.

Summary and Authors' Conclusions

- ECHELON-3 is the first randomized, placebo-controlled, phase 3 study to demonstrate overall survival benefit in a contemporary population of patients with R/R DLBCL who have received ≥2 prior lines of systemic therapy
- BV+Len+R met its primary objective, showing a statistically significant and clinically meaningful improvement in OS
  - Reduction in risk of death by 37% with median OS of 13.8 months
- Significant improvement was also observed for key secondary endpoints of PFS and ORR with BV+Len+R
  - Risk of progression or death was 47% lower with median PFS of 4.2 months
  - Significant benefit in ORR of 64% and a 40% CR rate
- Consistent benefit of BV+Len+R for OS, PFS, and ORR was observed regardless of CD30 expression
- BV+Len+R was well tolerated
  - Adverse events were manageable with dose modifications and consistent with the known safety profile of each individual drug[1-3]
- This triplet combination, with its promising OS benefit, has the potential to address the high unmet need in patients with R/R DLBCL, particularly those who are not able to receive CAR T-cell therapy or bispecific antibodies or have R/R disease following these treatments

Kim J, et al. Oral Presentation LBA7005. Presented at American Society of Clinical Oncology (ASCO) 2024, USA and Online, May 31-June 4, 2024.

BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, rituximab; R/R, relapsed or refractory.

1. Jacobsen ED, et al. *Blood*. 2015;125(9):1394-1402. 2. Witzig TE, et al. *Ann Oncol*. 2011;22(7):1622-1627. 3. Leonard JP, et al. *J Clin Oncol*. 2019;37(14):1188-1199.

Real-world outcomes of brentuximab vedotin as post-ASCT consolidation in RRHL: A systematic review and meta-analysis

Sureda A, et Al.
Abstract #P1101

A Sureda[1], A Pavlovsky[2,3,4], S Jha[5], D Haidar[5], F Kristo[6], V Stache[7], A Zomas[7]

[1]Institut Català d'Oncologia - Hospital Duran i Reynals, IDIBELL, Barcelona, Spain, [2]FUNDALEU Research Center, Buenos Aires, Argentina, [3]Centro de Hematologia Pavlovsky, Buenos Aires, Argentina, [4]Grupo Argentino de Tratamiento de la Leucemia Aguda (GATLA), [5]Takeda Pharmaceuticals International AG – Singapore Branch, Singapore, [6]Takeda Development Center Americas, Inc. (TDCA), Cambridge, United States of America, [7]Takeda Pharmaceuticals International AG, Zurich, SwitzerlandPresented at The European Hematology Association (EHA) 2024 Congress held from June 13-16, 2024 at Madrid, Spain

Introduction and Objective

- Based on the findings of the Phase 3 AETHERA trial, the FDA and EMA approved brentuximab vedotin (BV) as post-autologous stem cell transplantation (ASCT) consolidation in high-risk patients with relapsed/refractory Hodgkin lymphoma (RRHL) in 2015 and 2016, respectively.
- Recent real-world studies have reported outcomes of BV as post-ASCT consolidation, including HL cases evaluated for response by positron emission tomography-computed tomography (PET-CT) and cases with pre-ASCT BV exposure (salvage period).
- **Objective:** To enhance the strength of evidence on the effectiveness and safety of BV as post-ASCT consolidation or maintenance therapy in adult and pediatric patients with RRHL managed in contemporary clinical practice.

Real-world analyses are often nonrandomized, observational, retrospective studies that may have unobserved confounding and treatment selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution. Observational, retrospective or prospective analyses are not intended for direct comparison with clinical trials

ASCT: autologous stem cell transplantation; BV: brentuximab vedotin; EMA: European Medicines Agency; FDA: Food and Drug Administration; PET-CT: positron emission tomography-computed tomography; RRHL: relapsed/refractory Hodgkin lymphoma.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

Methods

- The systematic review was registered in PROSPERO (CRD42023471178) and conducted simultaneously across BIOSIS Previews®, Embase®, and MEDLINE via ProQuest-Dialog to obtain journal articles and conference abstracts (January 1998–October 2023).
- Abstracts not indexed in the above databases were obtained from pragmatic searches of conference proceedings (2014–2023).
- The DerSimonian and Laird random-effects method were used to pool data, regardless of the degree of heterogeneity between the study results.
- Heterogeneity between studies was evaluated by considering both the significance of the between-study heterogeneity and the magnitude of the I^2 value, with substantial heterogeneity assumed if I^2 was >50%.
- Heterogeneity was not calculated for outcomes provided by ≤2 studies.

Inclusion Criteria:

- **P**opulation: Adult and pediatric patients with RRHL.
- **I**ntervention: BV as consolidation or maintenance therapy after ASCT.
- **C**omparison: Any comparator.
- **O**utcome: Reporting at least one response/outcome.

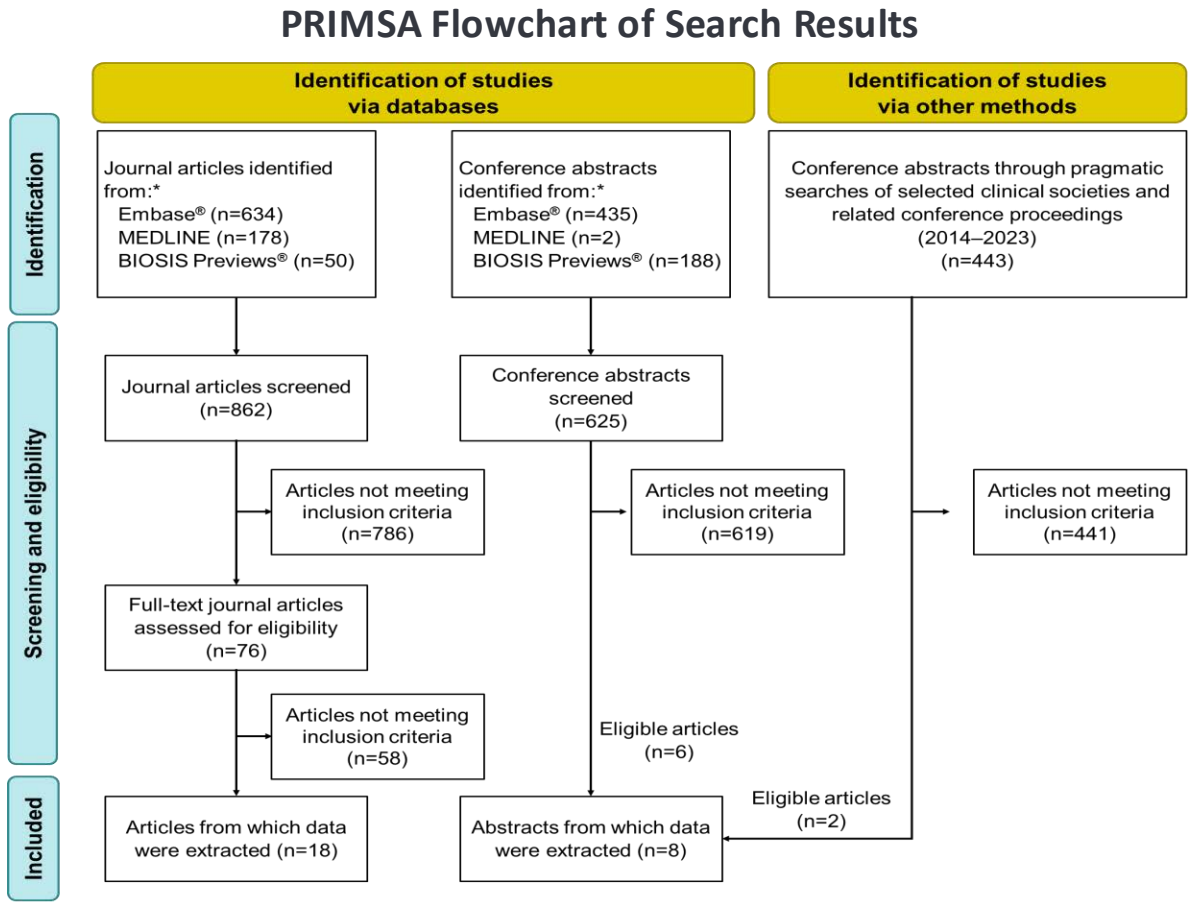
  Effectiveness outcomes: progression-free survival (PFS) and overall survival (OS).
  Safety outcomes: Adverse events (AEs).

AE: adverse event; ASCT: autologous stem cell transplantation; BV: brentuximab vedotin; OS: overall survival; PFS: progression-free survival; RRHL: relapsed/refractory Hodgkin lymphoma.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

Results – Study Characteristics

- Data were extracted from 1361 eligible patients in 18 journal articles and 8 conference abstracts2–27 as shown in PRISMA
- Most studies (n=16) reported scheduled administration of 16 BV cycles as post-ASCT consolidation, with a dosing regimen of 1.8mg/kg every 3 weeks, per the approved indication.
- 11 studies assessed pediatric patients.



*Duplicates removed; †Selected congresses: The American Society of Hematology (ASH) Annual Meeting and Exposition, European Hematology Association (EHA) Annual Congress, American Society of Clinical Oncology (ASCO) Annual Meeting, European Society for Medical Oncology (ESMO) Congress, International Symposium on Hodgkin Lymphoma (ISHL), International Conference on Malignant Lymphoma (ICML), British Society of Haematology (BSH) Annual Scientific Meeting, Society of Hematologic Oncology (SOHO) Annual Meeting, International Society for Pharmacoeconomics and Outcomes Research (ISPOR) European Congress.
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

ASCT: autologous stem cell transplantation; BV: brentuximab vedotin; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

Results – Patient Treatment Characteristics and Response

- Median age reported across the studies ranged from 14–37 years.
- Across studies, advanced-stage disease was reported in 44%–100% of patients, and 6%–57% of patients were PET negative pre-ASCT.
- Administration of BV prior to ASCT as a bridge to transplant was reported in 50% of all eligible patients.
- Across the included studies, single-agent BV was administered as post-ASCT consolidation in 53%–100% of patients.
- Across studies, the median number of BV cycles administered post-ASCT ranged from 4–16.
- Response rates prior to ASCT were reported in 13 studies: in these studies, complete response ranged from 18%–100% and partial response ranged from 10%–55% in all eligible patients.

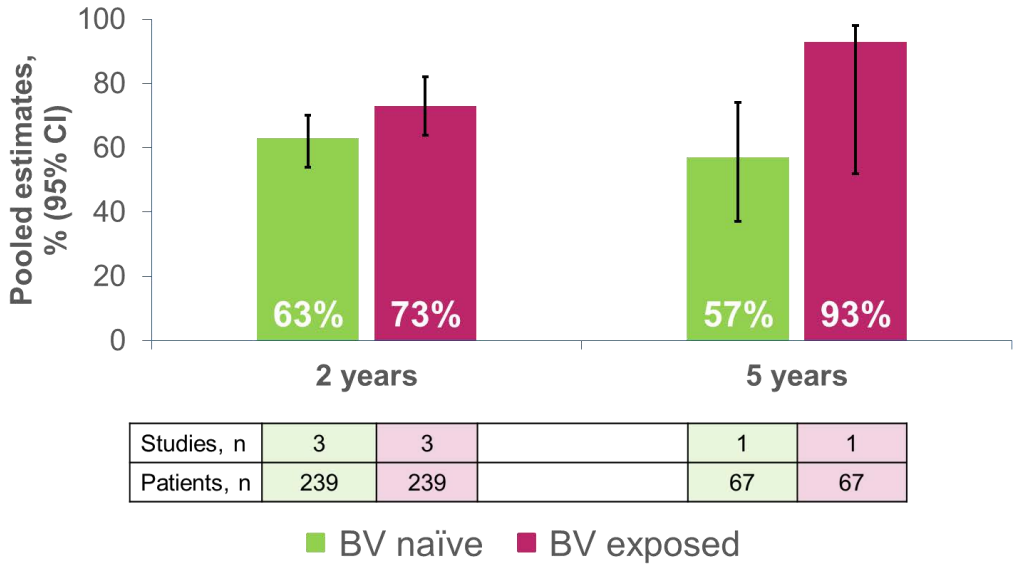
ASCT: autologous stem cell transplantation; BV: brentuximab vedotin; PET: positron emission tomography; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

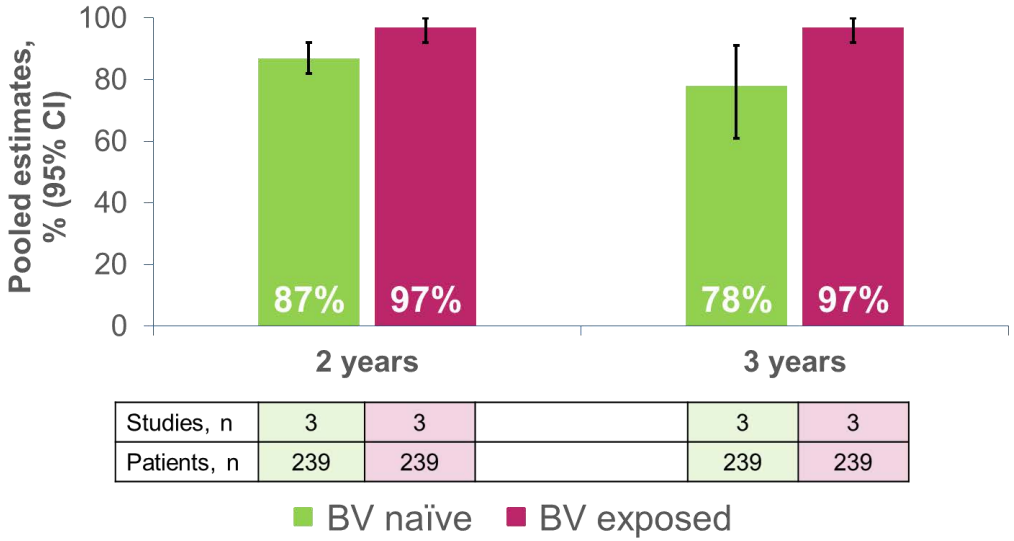
Results – PFS and OS estimates according to pre-ASCT BV exposure

- Patients who received BV as salvage therapy (BV exposed) had higher PFS and OS rates at 2, and 3 or 5 years compared with those who did not receive BV as salvage therapy (BV naïve)

PFS estimates at 2 and 5 years according to pre-ASCT BV exposure



OS estimates at 2 and 3 years according to pre-ASCT BV exposure

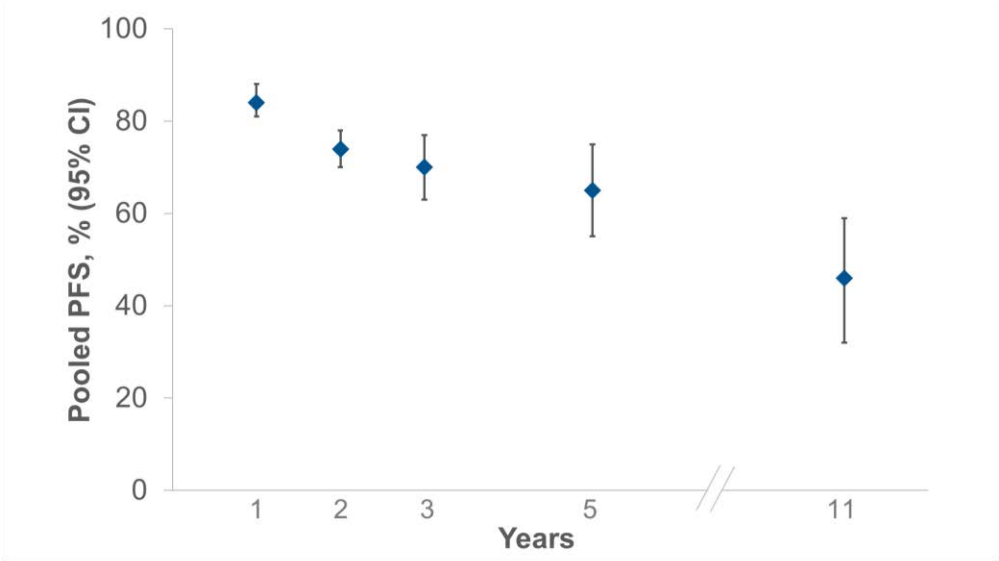


ASCT: autologous stem cell transplantation; BV: brentuximab vedotin; CI: confidence interval; OS: overall survival; PFS: progression-free survival.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

Results – Pooled PFS and OS estimates

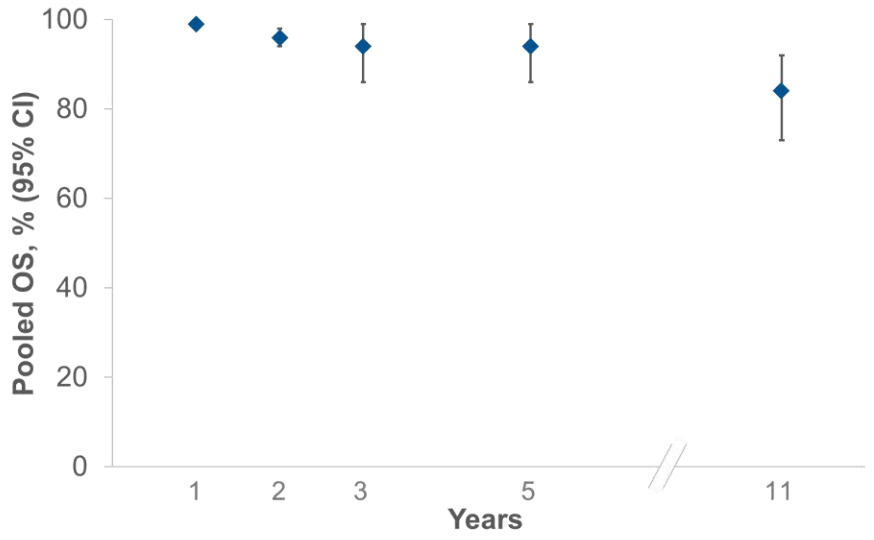
Pooled PFS Estimates



Studies, n	13	12	13	8	2
Patients, n	1048	981	1048	661	59

- Pooled estimated PFS rates (95% CI) at 2 and 5 years were 74% (70–78) and 65% (55–75), respectively

Pooled OS Estimates



Studies, n	9	10	8	4	1
Patients, n	466	747	460	504	53

- Pooled estimated OS rates (95% CI) suggested that 99% (98–100; reported/estimated OS rates: 95%–100%) of all patients were alive at 1 year of follow-up, 96% (94–98; reported/estimated OS rates: 83.3%–100%) at 2 years, and 94% (86–99; reported/estimated OS rates: 74.7%–100%) at 3 years

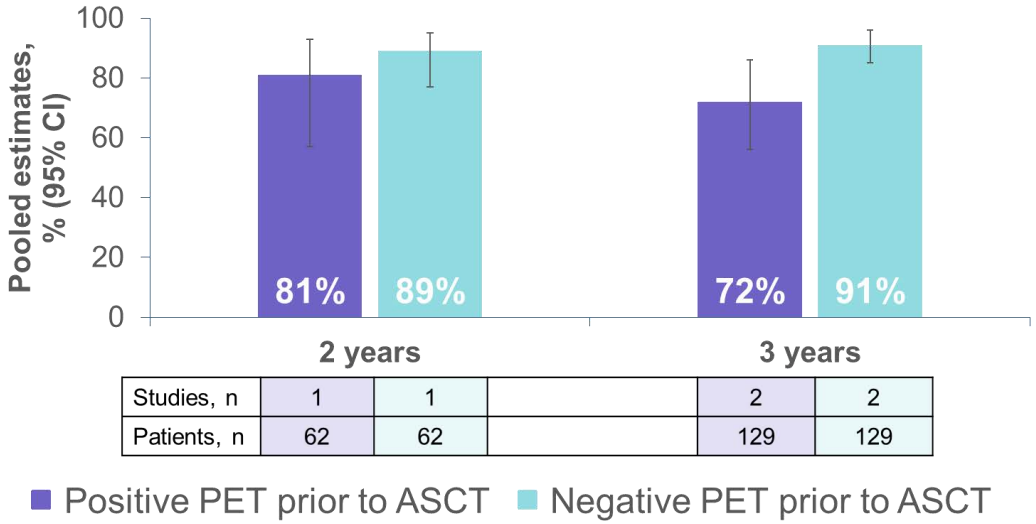
CI: confidence interval; OS, overall survival; PFS: progression-free survival.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

Results – PFS estimates according to pre-ASCT PET status

- Patients who had a negative PET scan before ASCT had improved PFS rates compared with those who had a positive PET scan before ASCT

PFS estimates at 2 and 5 years according to pre-ASCT PET status



Studies, n	1	1		2	2
Patients, n	62	62		129	129

ASCT: autologous stem cell transplantation; CI: confidence interval; PET: positron emission tomography; PFS: progression-free survival.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

Results – Adverse Events

- The most common AEs were any grade (95% CI) neuropathy (20% [6–37]) and neutropenia (17% [7–30])
  - The I^2 and P values indicate the variability and significance of heterogeneity between the included studies.

Outcome	Studies, n	Patients, n	Pooled estimates, % (95% CI)	Between-study heterogeneity	
				P value	I^2, %
Patients with any grade AE	4	154	49 (40–58)	0.33	13
Patients with Grade 3–4 AEs	2	30	2.4 (0–13)	NC	NC
Incidence of individual AEs*					
Neuropathy	10	515	20 (6–37)	<0.001	94
Motor neuropathy	6	325	0 (0–0.4)	0.14	38
Fatigue	7	331	0 (0–0.1)	0.51	0
Neutropenia	11	514	17 (7–30)	<0.001	89
Thrombocytopenia	7	331	0.5 (0–5)	0.004	69
Anemia	8	341	0.4 (0–4)	0.03	56
Pulmonary toxicity	7	331	0.2 (0–3)	0.03	56
Transaminitis	7	331	0.1 (0–3)	0.07	48
Infusion reaction	7	331	0.1 (0–1.5)	0.27	20
Nausea/vomiting	7	331	0 (0–0.4)	0.33	14
Infections	8	449	0.6 (0–5)	<0.001	79

*Incidence of AEs calculated.

AE: adverse events; CI: confidence interval; NC: not calculated.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

Author's Conclusions and Limitations

- This systematic review affirms the effectiveness and safety of BV as post-ASCT consolidation therapy in patients with RRHL. The pooled estimated PFS rates at 2 and 5 years of 74% (reported/estimated PFS rates: 33.3%–87.1%) and 65% (reported PFS rates: 0%–85%), respectively, align with the findings of AETHERA, which demonstrated improved PFS (2- and 5-year PFS rates of 63% and 59%, respectively) when compared with placebo.
- PFS and OS rates were estimated to be higher in patients with pre-ASCT BV exposure compared with those who were BV naïve before ASCT.
- Patients who had a negative PET scan before ASCT exhibited higher PFS rates compared with those who had a positive PET scan before ASCT, emphasizing the prognostic value of PET/CT assessment before ASCT.
- Neuropathy and neutropenia were frequently observed AEs, as reported in AETHERA; however, as is an inherent limitation in real-world studies, AEs may be under reported.
- Despite study and population heterogeneity, these results show the robustness of BV as post-ASCT consolidation across a diverse adult and pediatric population in the real world, extending beyond the treatment environment of AETHERA.

ASCT: autologous stem cell transplantation; BV: brentuximab vedotin; PET: positron emission tomography; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Sureda A, et al. Poster Presentation P1101. Presented at European Hematology Association (EHA) 2024, Spain and Online, June 13-16, 2024.

EHA EUROPEAN HEMATOLOGY ASSOCIATION

EHA2024
JUNE 13 - 16 | MADRID

Justin Ferdinandus, Horst Müller, Janina Jablonski, Andrea Kerkhoff, Sebastian Scholl, Yon-Dschun Ko, Max S. Topp, Hans-Joachim Beck, Vladan Vucinic, Wolfram Jung, Roland Schroers, Andreas Rank, Michael Fuchs, Gundolf Schneider, Volker Diehl, Peter Borchmann, Karolin Behringer

GHSG

Treatment Effects of BrECADD vs. BEACOPP on health-related Quality of Life: An Analysis of Patient Reported Outcomes in the randomized Phase III HD21 trial

INTRODUCTION

The randomized GHSG HD21 trial established PET-guided BrECADD as highly effective and tolerable first-line treatment for advanced-stage Hodgkin Lymphoma (AS-cHL).

AIM

To investigate the immediate and subsequent treatment effects of BrECADD compared to BEACOPP on health-related quality of life (HRQoL) in the HD21 trial.

METHOD

Patients with newly diagnosed AS-cHL treated within the GHSG HD21 (NCT02661503) trial in Germany received EORTC QLQ-C30, -CIPN20 and -FA12 questionnaires at baseline, interim, end-of-treatment, and during follow-up.

We used multiple regression analyses adjusted for age, sex and the respective baseline scores to investigate the effects of BrECADD vs. BEACOPP on patient reported outcomes.

We performed sensitivity analyses using the full information maximum likelihood method (FIML) to account for missing values (not shown in this poster).

RESULTS

In total, 917 patients consented to the HRQoL study and provided at least one valid HRQoL score.

After two cycles of chemotherapy, patients reported with BrECADD significantly less sensory peripheral neuropathy (β=-0.13, p<0.001), cognitive fatigue (β=-0.07, p=0.038) and dyspnea (β=-0.11, p=0.0016) as compared to eBEACOPP .

After four cycles, corresponding to the end of treatment for the majority of well-responding patients, we observed significant improvements with BrECADD in peripheral neuropathy, dyspnea, physical functioning and role functioning . These differences were not found in poor-responding patients treated with six cycles.

In the first and second year after treatment, patients in the BrECADD group reported significantly less symptoms and higher functioning compared to eBEACOPP, most notable a higher global health status (1st year: β=0.09,p=0.024; 2nd year: β=0.11,p=0.0089).

Sensitivity analyses with the FIML method confirmed the reported results.

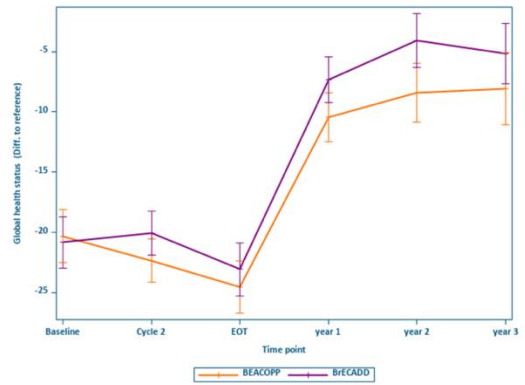
Figure 1: Heatmap summarizing treatment effects of BrECADD vs. BEACOPP on HRQoL in the GHSG HD21 trial

	c2	EOT-4	EOT-6	year 1	year 2
Global health status (positive numbers are favorable effects of BrECADD)					
Global health status (QLQ-C30)	0.05	0.04	0.02	0.09*	0.11**
Functioning (positive numbers are favorable effects of BrECADD)					
Cognitive functionig (QLQ-C30)	0.05	-0.01	0.08	0.03	0.1*
Emotional functioning (QLQ-C30)	0.06	0.04	0.01	0.04	0.16***
Physical functioning (QLQ-C30)	0.03	0.09*	-0.05	0.07	0.08
Role functioning (QLQ-C30)	0.03	0.11*	-0.04	0.03	0.04
Social functioning (QLQ-C30)	0.03	0.07	0.03	0.09*	0.11*
Symptoms (negative numbers are favorable effects of BrECADD)					
Sensory PNP (CIPN20)	-0.13***	-0.09*	-0.01	-0.04	-0.07
Motor PNP (CIPN20)	-0.06	-0.09*	-0.08	-0.05	-0.05
Physical Fatigue (FA12)	-0.03	-0.08	0.01	-0.02	-0.07
Emotional Fatigue (FA12)	-0.01	0	-0.05	-0.03	-0.11*
Cognitive Fatigue (FA12)	-0.07*	0.03	-0.01	0.03	0
Fatigue (QLQ-C30)	-0.03	-0.09	0.01	-0.03	-0.09*
Pain (QLQ-C30)	-0.06	-0.02	-0.06	-0.12**	-0.08
Dyspnoea (QLQ-C30)	-0.11**	-0.14**	-0.07	-0.05	-0.12**
Sleep (QLQ-C30)	-0.07	-0.02	-0.06	-0.12**	-0.15***

β: 0.15, 0.10, 0.05, 0.00, -0.05, -0.10

This heatmap summarizes treatment effects of BrECADD vs. BEACOPP on HRQoL in the GHSG HD21 trial; standardized regression coefficients β for 15 HRQoL variables at five time points. Regression analyses were adjusted for age, sex and respective baseline HRQoL scores. eBEACOPP = Bleomycin, etoposide, doxorubicine, cyclophosphamide vincristine, procarbazine and prednisone, BrECADD = brentuximab vedotin, etoposide, cyclophosphamide, doxorubicine, dacarbazine, dexamethasone, c2= after 2 cycles of chemotherapy, EOT-4= end of treatment after 4 cycles of chemotherapy, EOT-6= end of treatment after 6 cycles of chemotherapy, * = p < 0.05, ** = p < 0.01, *** = p < 0.001

Figure 2: Global Health status in the BrECADD and BEACOPP group: deviations from German reference values over time



This figure illustrates the mean deviations of global health status from German reference values over time including 95%-confidence intervals. eBEACOPP = Bleomycin, etoposide, doxorubicine, cyclophosphamide vincristine, procarbazine and prednisone, BrECADD = brentuximab vedotin, etoposide, cyclophosphamide, doxorubicine, dacarbazine, dexamethasone EndThera = End of treatment

AUTHORS' CONCLUSIONS

Individualized first-line treatment with BrECADD for AS-cHL significantly improves HRQoL compared to eBEACOPP.

Several stressful symptoms of chemotherapy were alleviated, and survivors reported higher functioning, which resulted in significantly improved and normalized global health status after treatment.

Combined with the high primary cure rate, BrECADD thus sets a new benchmark for the risk-benefit ratio of first-line treatment in patients with AS-cHL.

ACKNOWLEDGEMENT

We thank all colleagues from the German Hodgkin Study Group, as well as all patients and former patients for their great and continuous support, especially our patient representatives Lotte Kirch and Maximilian Büttner . The GHSG HD21 trial was funded by Takeda Oncology.

CONTACT INFORMATION

Dr. Justin Ferdinandus

German Hodgkin Study Group, Cologne, Germany

Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf, University of Cologne, Medical Faculty and University Hospital Cologne, Cologne, Germany

Mail: justin.Ferdinandus@uk-koeln.de

Twitter / X: @jusferdinandus

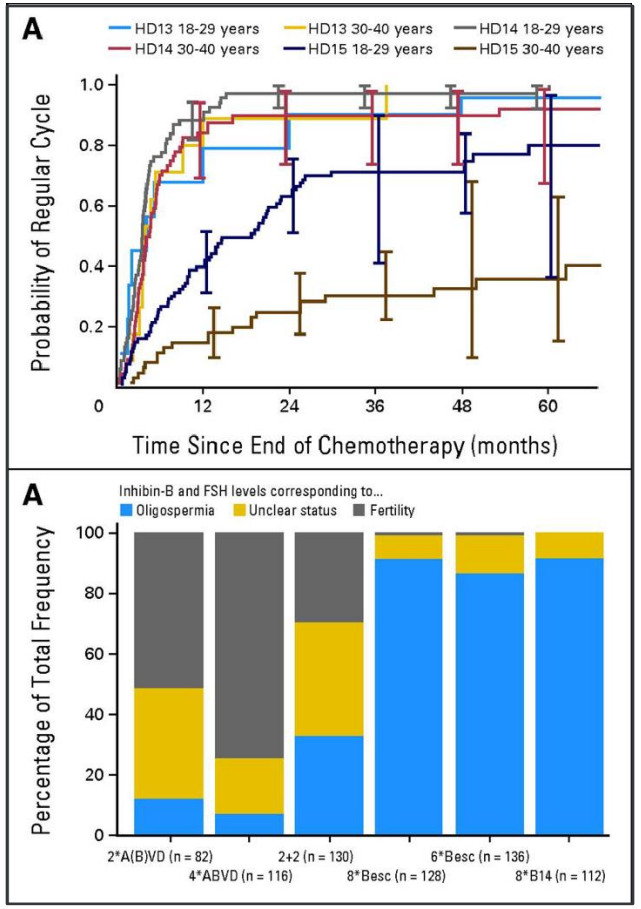
Gonadal function recovery and fertility in the phase III German Hodgkin Study Group HD21 trial

Justin Ferdinandus, Gundolf Schneider, Alden Moccia, Richard Greil, Mark Hertzberg, Valdete Schaub, Andreas Hüttmann, Felix Keil, Judith Dierlamm, Mathias Hänel, Urban Novak, Julia Meissner, Andreas Zimmermann, Stephan Mathas, Josée M Zijlstra, Alexander Fosså, Andreas Viardot, Bernd Hertenstein, Sonja Martin, Pratush Giri, Peter Kamper, Daniel Molin, Anne Sophie Robertz, Johannes Rosenbrock, Michael Fuchs, Peter Borchmann, Karolin Behringer

Gonadal function in HL patients

- Patients with HL are at risk for **prolonged or permanent gonadal function impairment**, especially when treated for advanced stage disease.
- Females at higher age and males in general are at particular risk.
- eBEACOPP is associated with increased gondal function impairment compared to ABVD, yet may be preferred given superior efficacy.

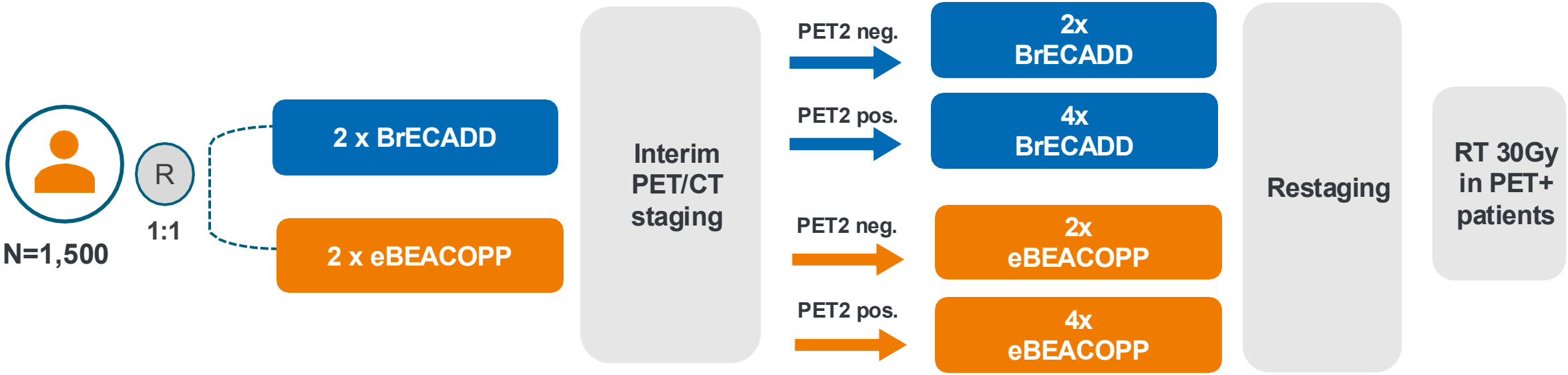
There is high unmet need for effective 1L treatments **without adverse effects on gonadal function** for this young patient cohort!



- Behringer K et al. JCO 2013
- Anderson et al., Lancet Oncol 2018
- Skoetz et al., Lancet Oncol 2013

GHSG HD21 study design and primary endpoints

HD21 is an ongoing, randomized, open-label, Phase 3 study of BrECADD versus eBEACOPP in patients with previously untreated, advanced cHL



Co-primary objectives:

- **Demonstrate reduced treatment-related morbidity (TRMB)** with BrECADD.
- **Demonstrate non-inferiority efficacy** of 4-6 x BrECADD compared with 4-6 x eBEACOPP in terms of PFS

Gonadal function: Definitions and methods

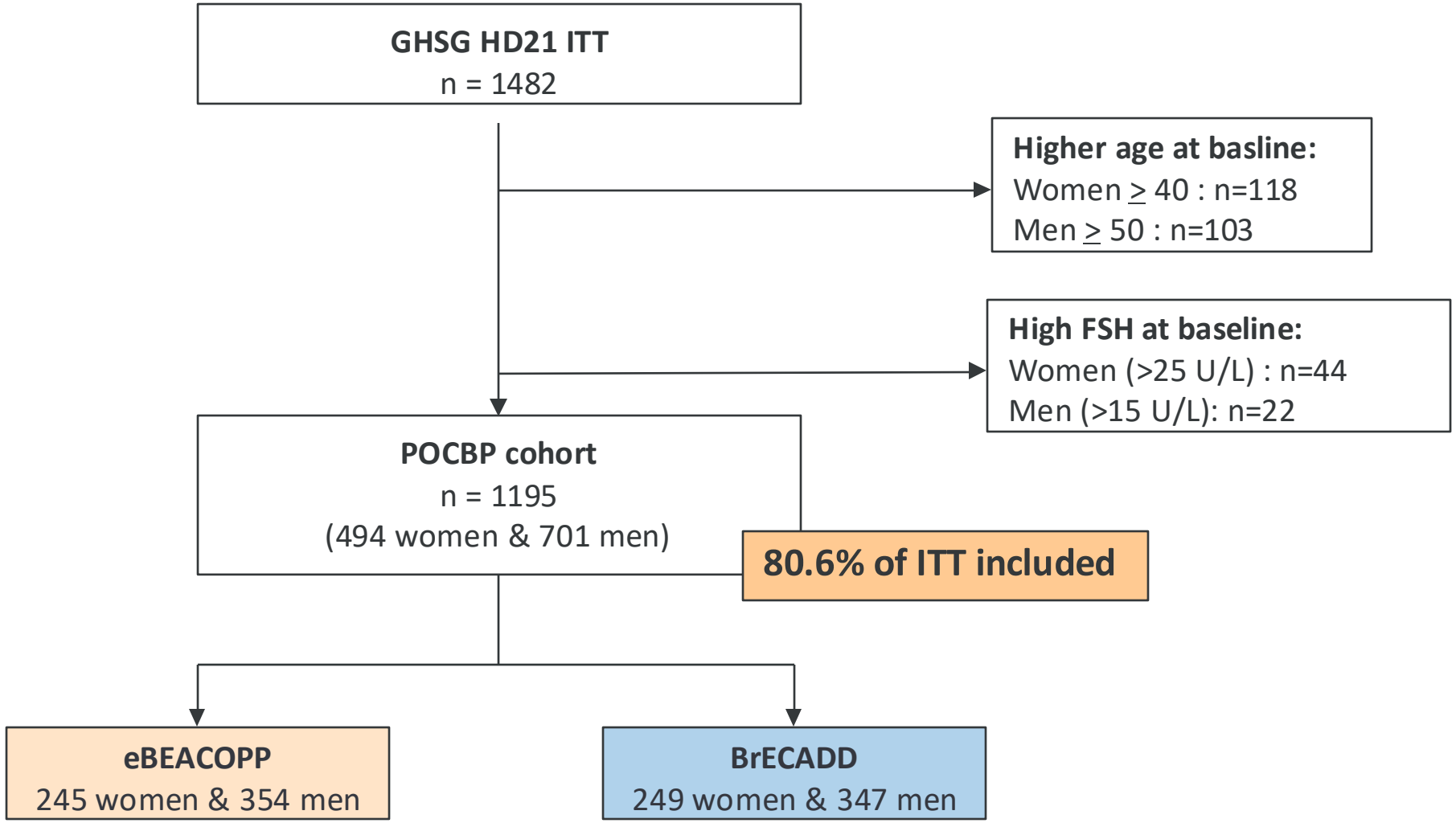
Definitions:

- **Patients of Childbearing Potential (POCBP) cohort:** Women up to 40 and men up to 50 years of age without baseline gonadal function impairment
- **Gonadal function impairment:** Follicle-stimulating hormone (FSH) serum levels >25 U/L for women and >15 U/L for men.
- **Time to gonadal function recovery**: end-of-treatment until the first measurement of FSH level below threshold or last FSH measurement (censor)

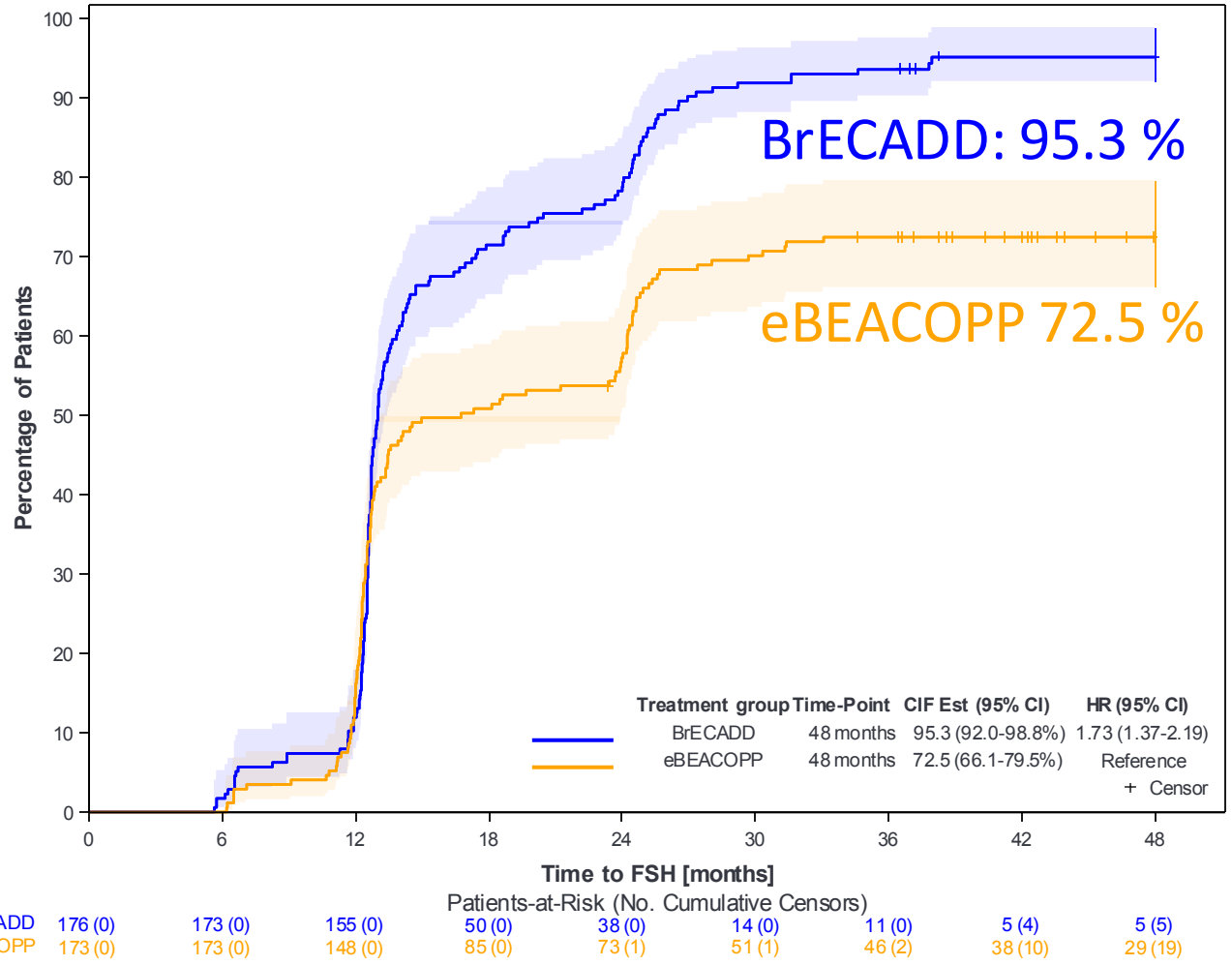
Statistical methods:

- Cox regressions to compare time-to-event outcomes

GHSG HD21 Patients of chidbearing potential (POCBP)



Women: Time to recovery of FSH (n=349)

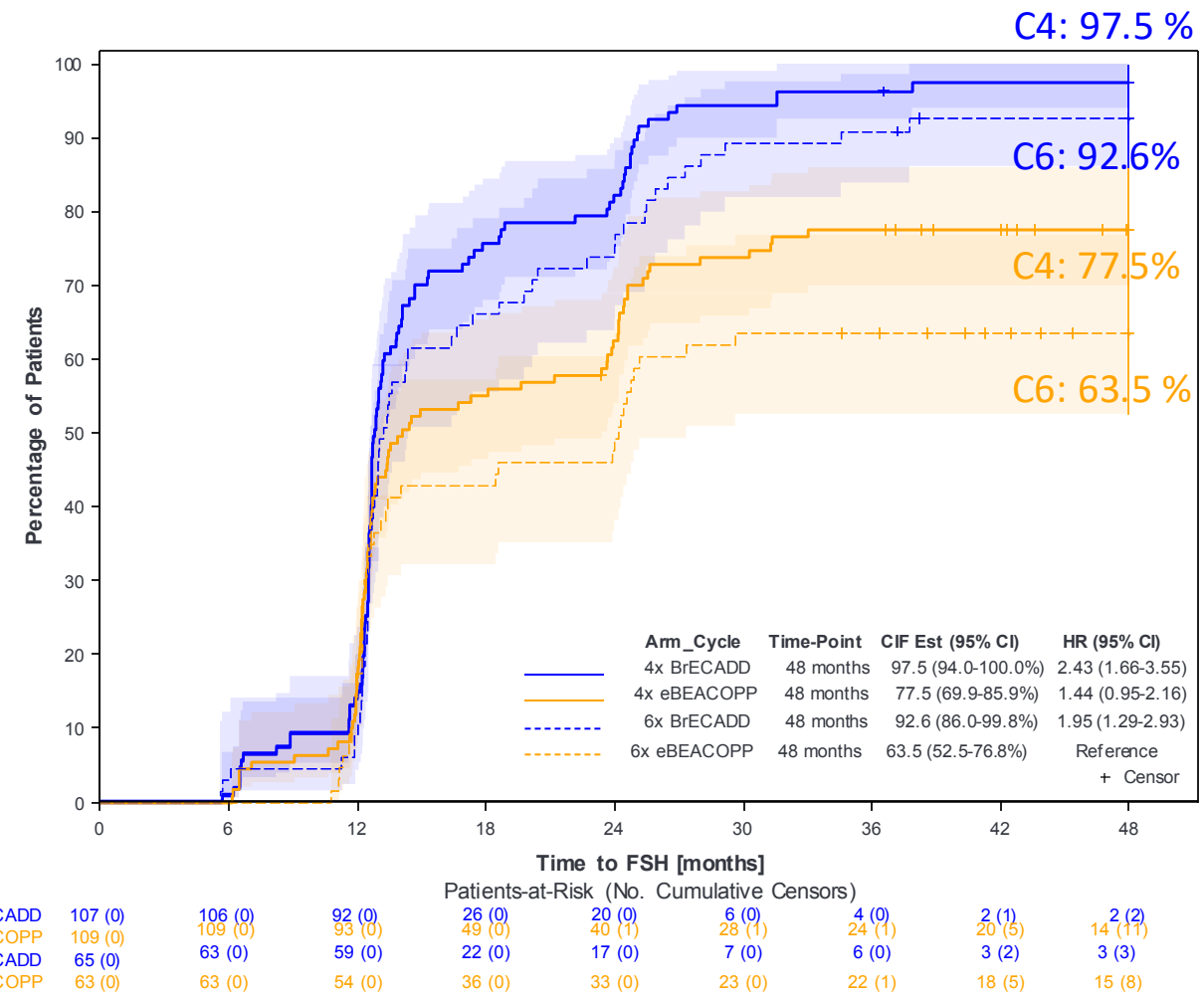


Significantly improved gonadal function recovery following BrECADD

- Overall: **HR 1.73**, CI95: 1.37-2.19
- A majority of women recover within the first 12 months

FSH < 25 U/L

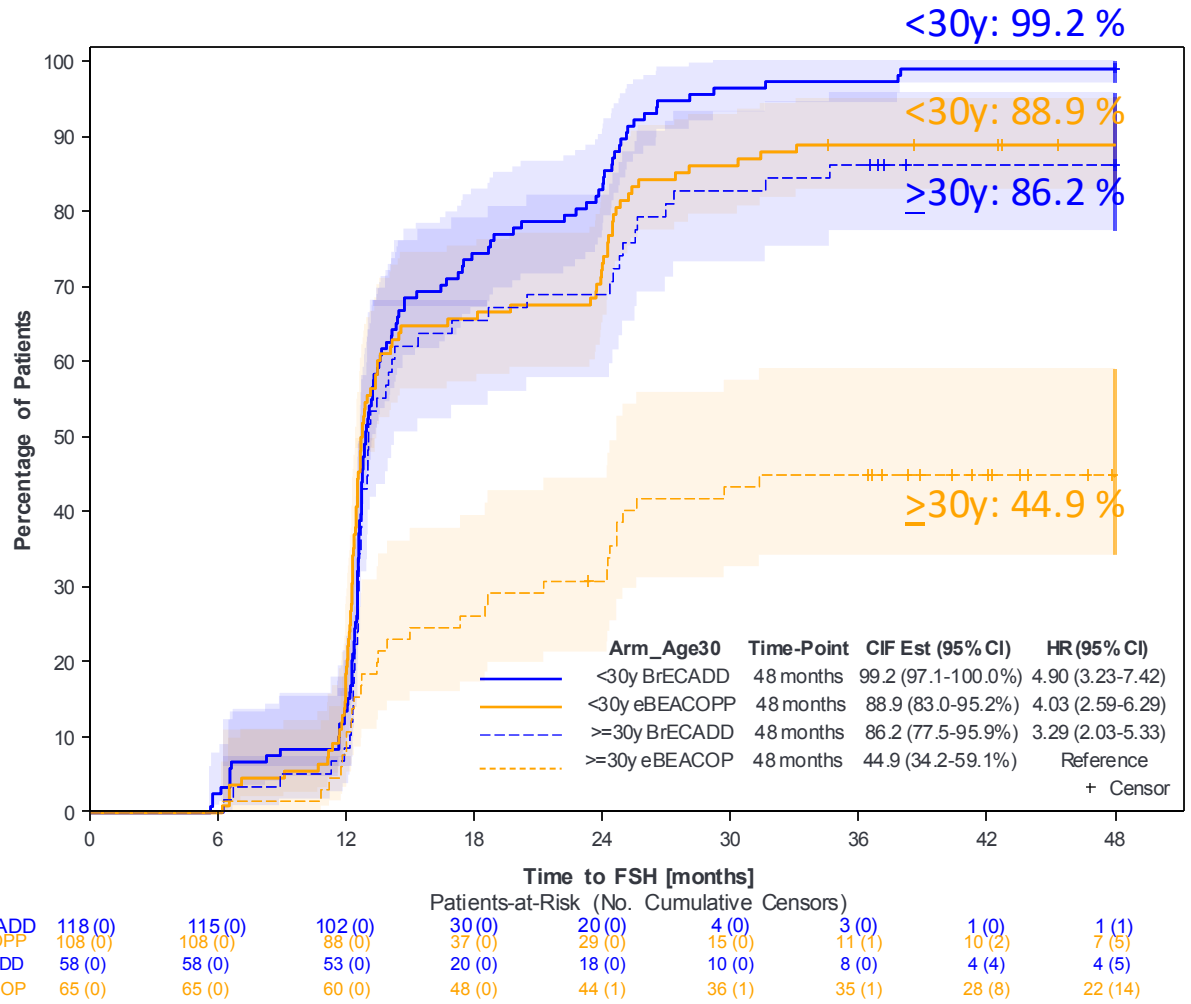
Women: Effect of **number of cycles**



- visible effect of treatment cycles, especially in eBEACOPP arm
- However, **main effect seems to be allocated treatment**

FSH < 25 U/L

Women: Effect of **age**



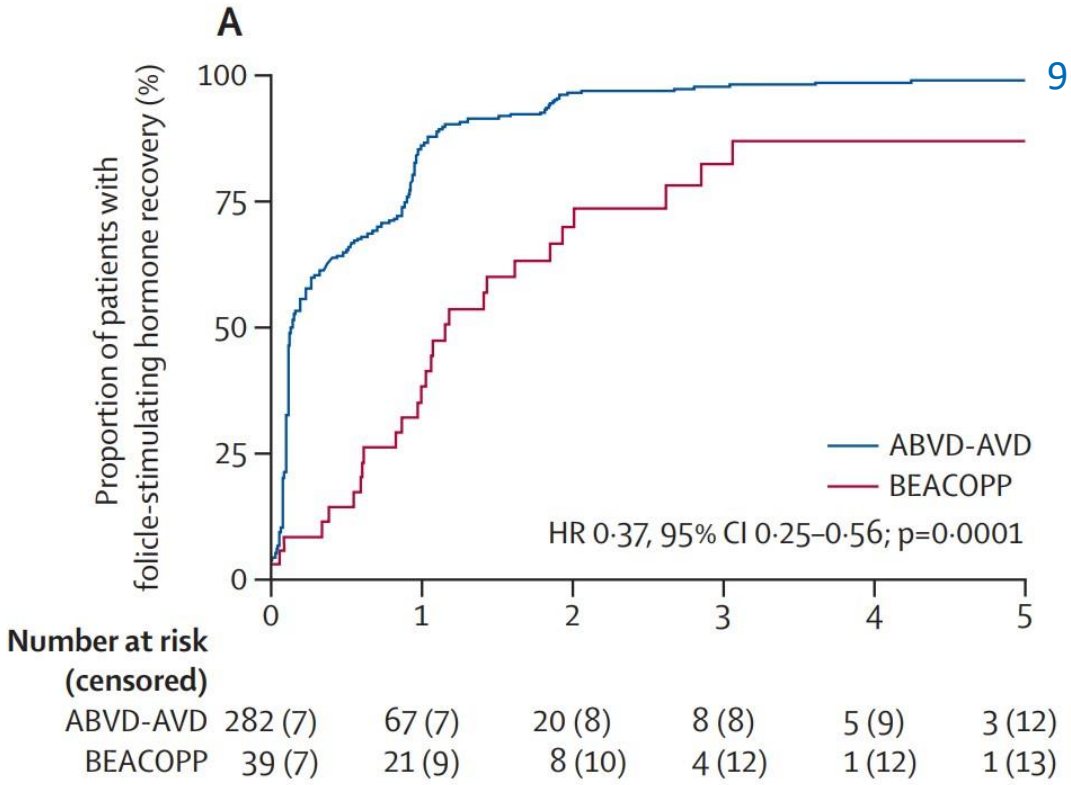
Effect on gonadal function recovery is age dependent:

- Gonadal function recovery occured in **every woman below 30y following BrECADD**.
- **Women > 30y derived the highest benefit from BrECADD** (HR 3.23, CI95: 2.03-5.33).

FSH < 25 U/L

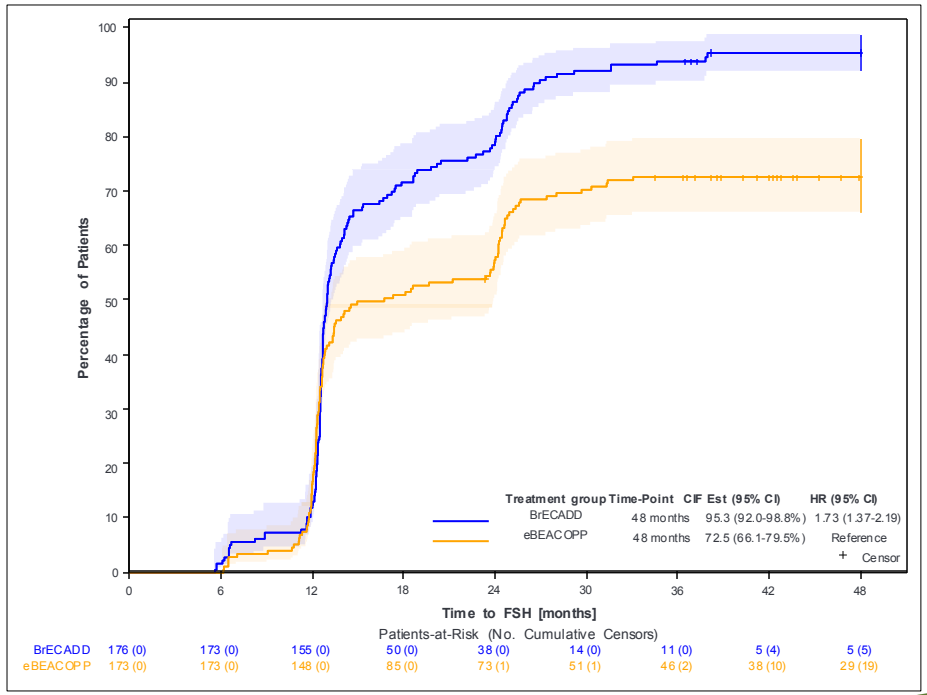
Women: Comparison to ABVD

RATHL



96 %

BrECADD



95.3 %

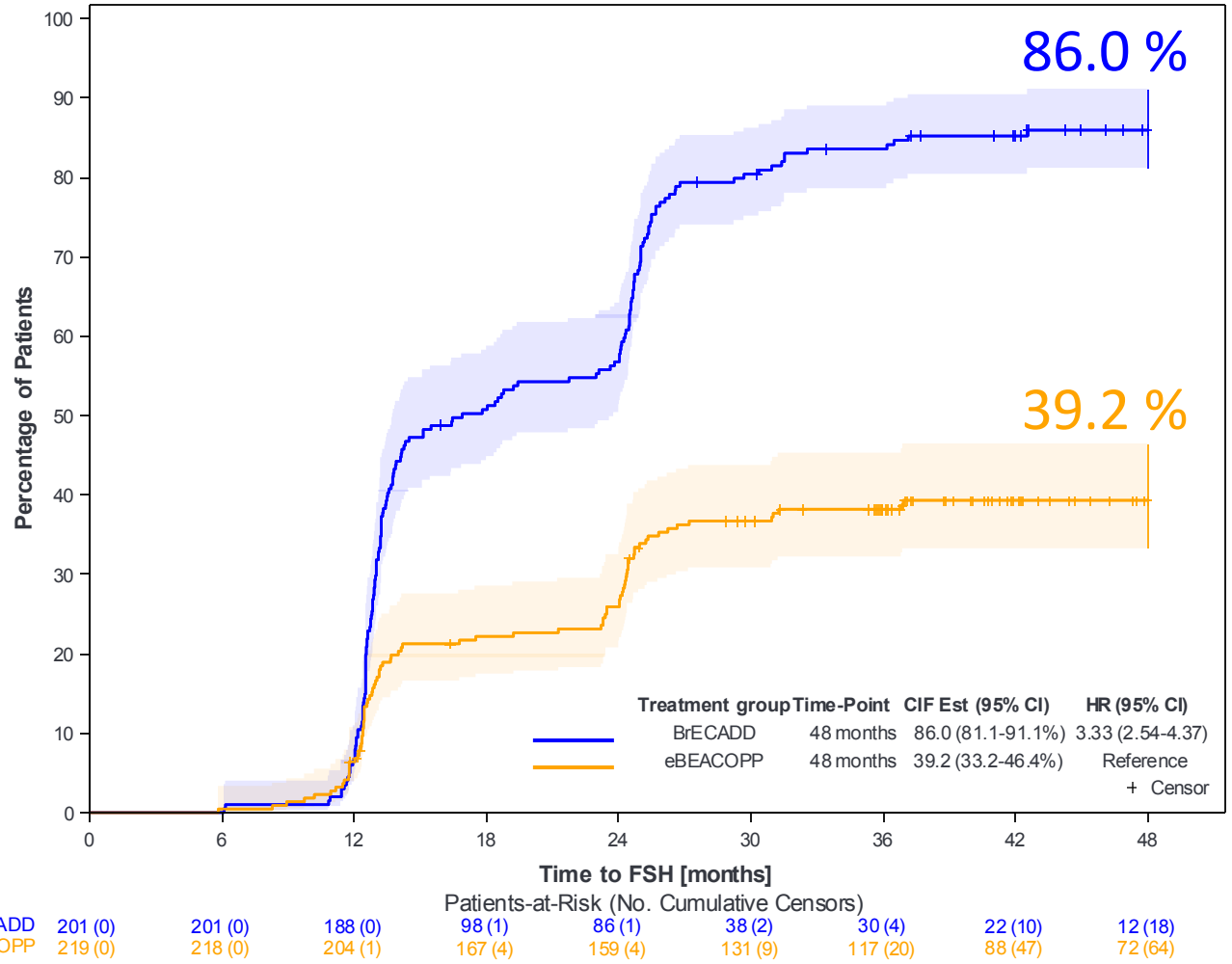
FSH < 25 U/L

Anderson et al., Lancet Oncol 2018

Gonadal function recovery of BrECADD in HD21 is comparable to ABVD-AVD cohort in RATHL

despite selection of PET-2 negative without relapse in RATHL

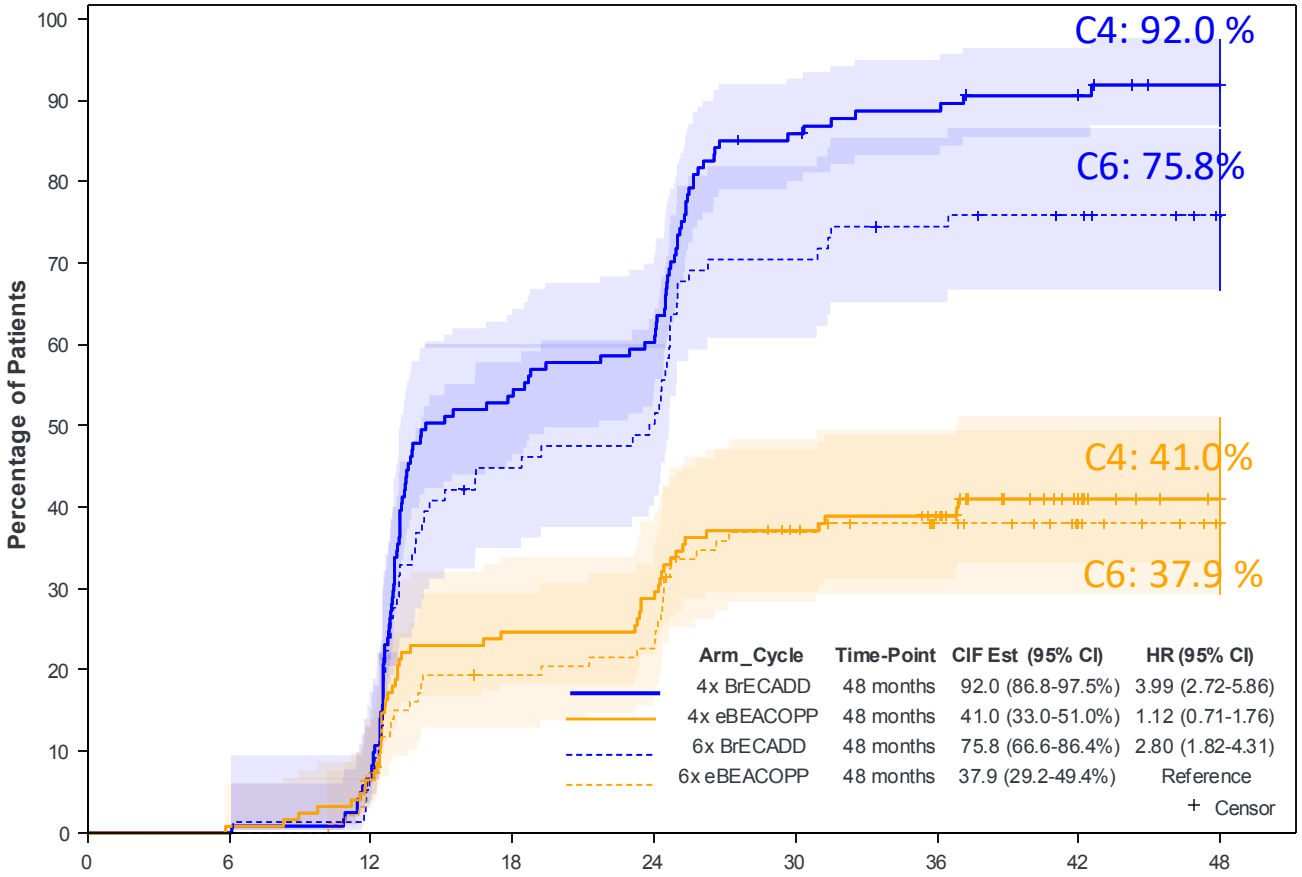
Men: Time to recovery of FSH (n=420)



- **Significantly improved gonadal function recovery following BrECADD** (HR 3.33, CI95: 2.54-4.37)
- Low rate of gonadal function recovery following eBEACOPP

FSH < 15 U/L

Men: Effect of **number of cycles**



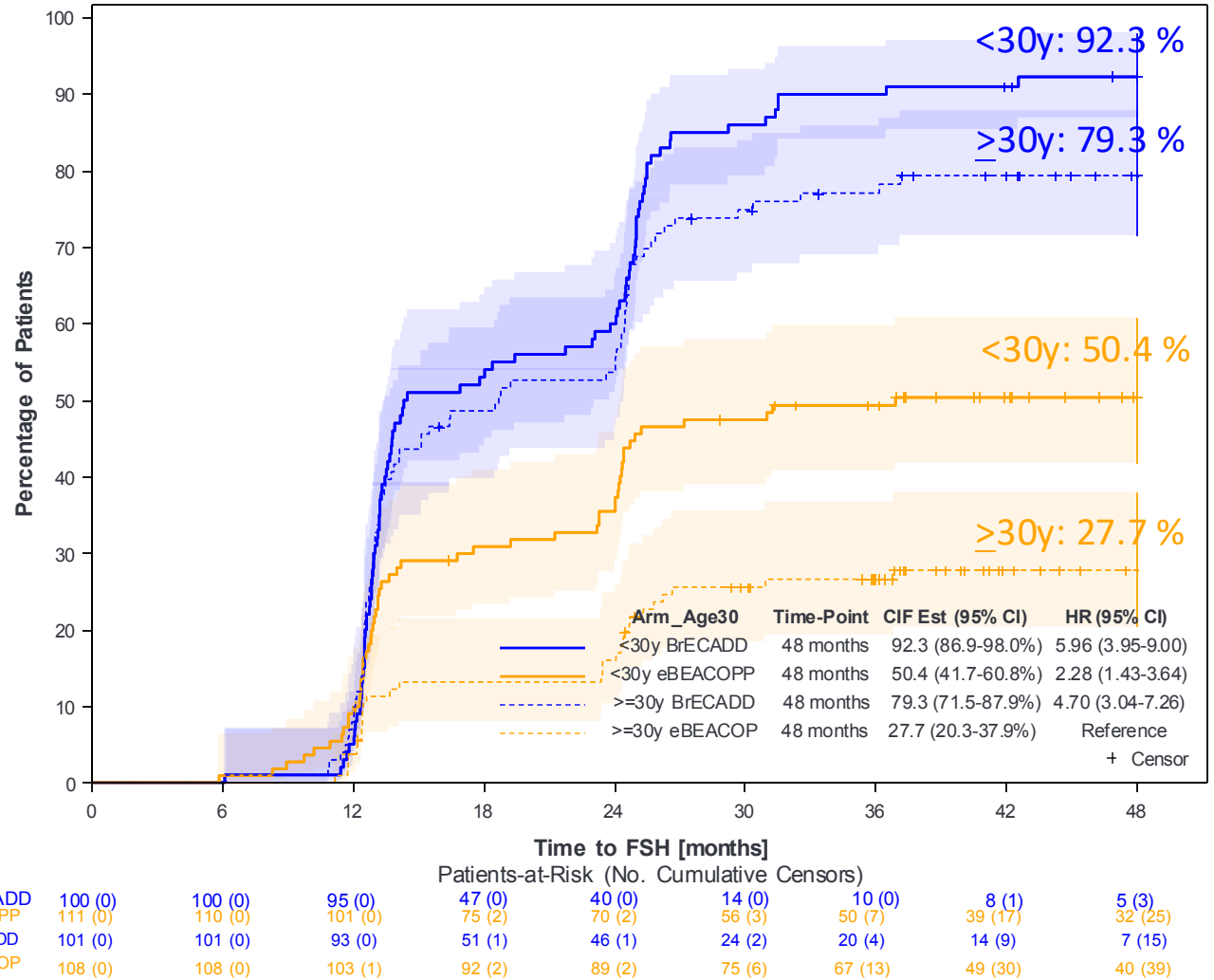
Patients-at-Risk (No. Cumulative Censors)

4x BrECADD	121 (0)	121 (0)	113 (0)	56 (0)	48 (0)	16 (1)	12 (2)	8 (5)	3 (8)
4x eBEACOPP	123 (0)	122 (0)	115 (0)	91 (2)	86 (2)	72 (6)	64 (12)	43 (31)	33 (41)
6x BrECADD	76 (0)	76 (0)	71 (0)	41 (1)	37 (1)	22 (1)	18 (2)	14 (5)	9 (10)
6x eBEACOPP	94 (0)	94 (0)	87 (1)	74 (2)	71 (2)	57 (3)	51 (8)	43 (16)	37 (23)

- No cycle effect in BEACOPP group: *„damage is done“*
- Slightly impaired recovery in 6x BrECADD group: cumulative effect of Cyclo + Eto?
- **Again, treatment allocation is the main effect.**

FSH < 15 U/L

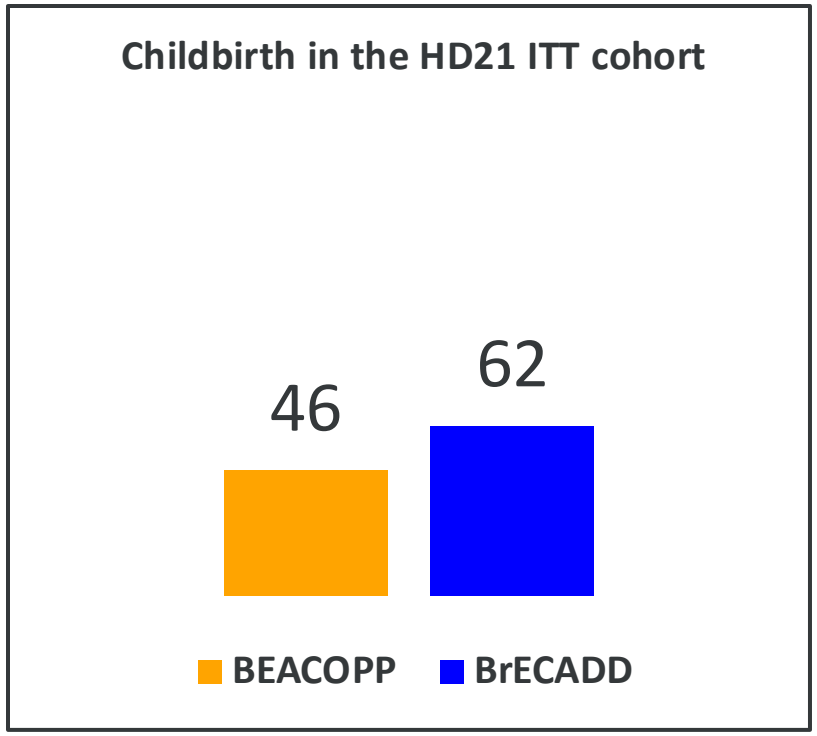
Men: Effect of **age**

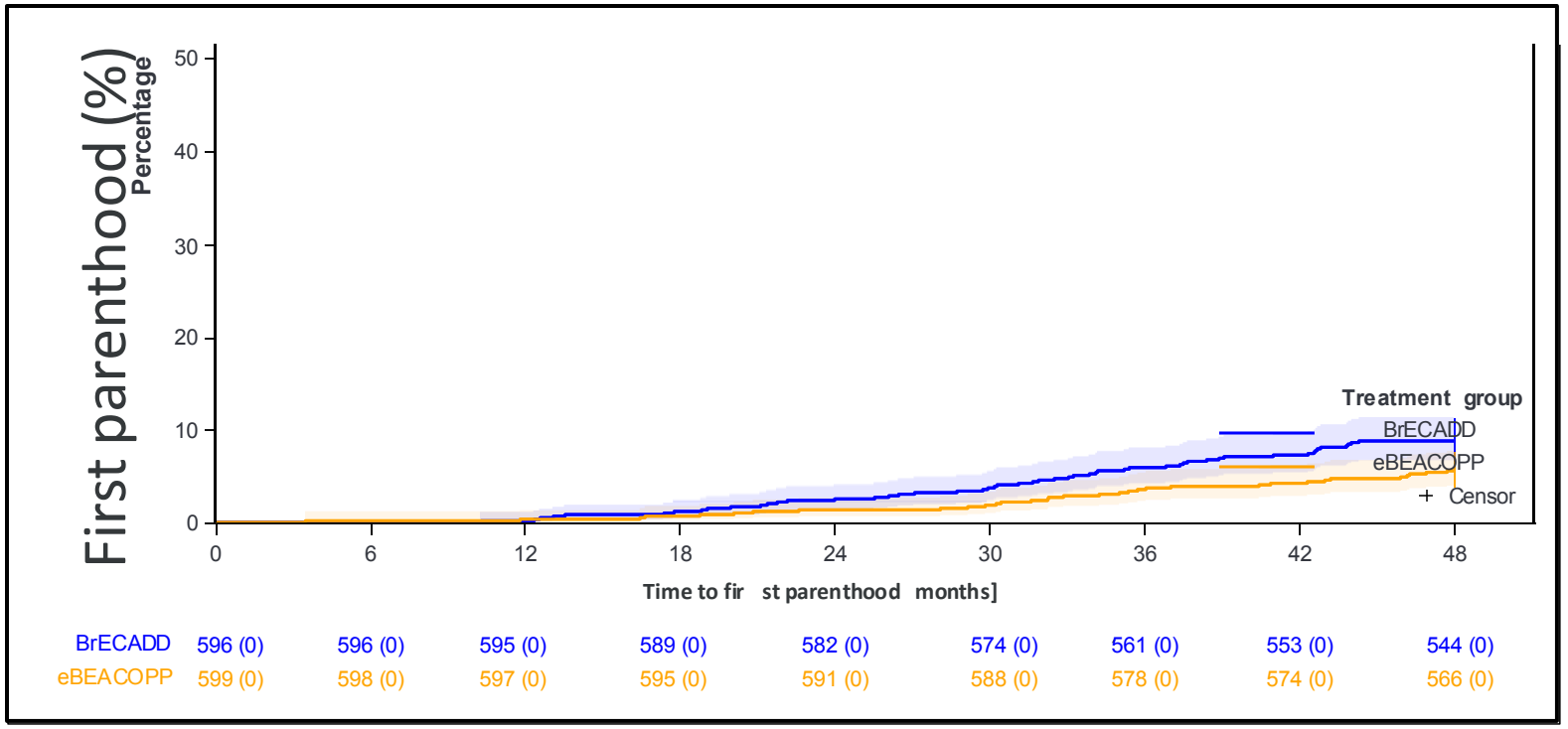


- Gonadal function recovery is age dependent.
- High treatment effects in all age groups

FSH < 15 U/L

GHSG HD21 Pregnancies and Childbirth



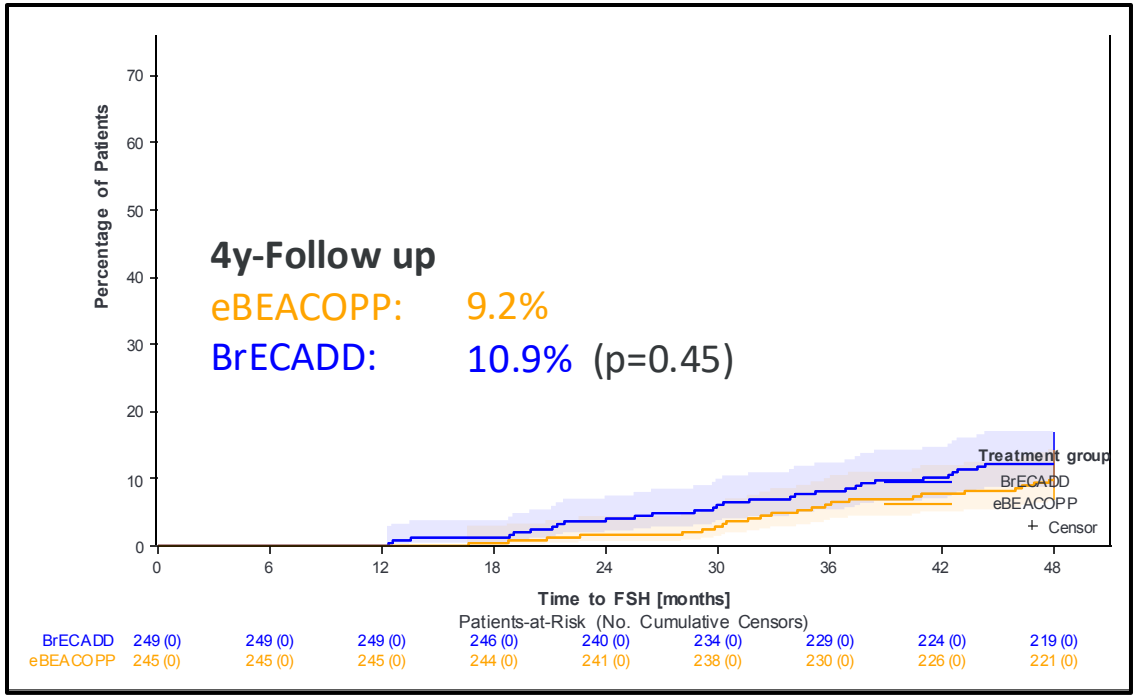


*

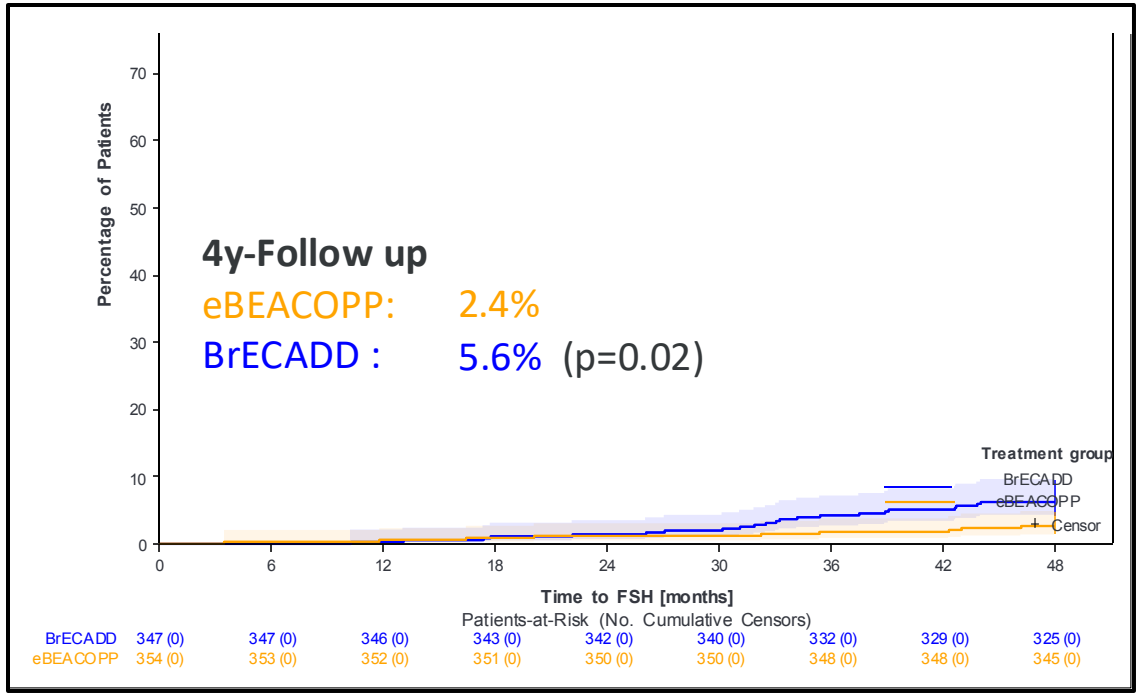
- Improved gonadal function recovery is accompanied by **higher rates of parenthood among patients treated with BrECADD**.
- Use of cryopreserved material per pregnancy: 4.5% (females) 14.7% (males)

GHSG HD21 Parenthood

Females (n=494)



Males (n=701)



- Improved gonadal function recovery is accompanied by **higher rates of parenthood among patients treated with BrECADD**.

HD21 Fertility Summary and Authors' Conclusions

- BrECADD features high gonadal function recovery:
  - Gonadal function recovery occurs in almost all women (95.3%) after receiving BrECADD.
  - Men of all age groups benefit from BrECADD (Overall: HR 3.3, CI95: 2.54-4.37).
  - Largest improvements in patients at risk for permanent gonadal damage when receiving eBEACOPP.

- Improved gonadal function recovery is accompanied by a higher rate parenthood in the BrECADD arm of HD21.

We strongly recommend BrECADD as standard treatment option for patients with AS-cHL <u>including</u> those with desire to have children.

Thank you very much for your attention!

- **Chairman:** P. Borchmann
- **Former-Chairman:** A. Engert
- **Honorary Chairman:** V. Diehl
- **Pathology:** A.C. Feller, F. Fend, M.L. Hansmann,
- W. Klapper, P. Möller, G. Ott, A. Rosenwald
- **Radiotherapy:** C. Baues, H. T. Eich **Nuclear**

Medicine: M. Dietlein, C. Kobe **Laboratory:** S. Borchmann

- **Physicians:** K. Behringer, B. Böll, P. Bröckelmann,
- D. Eichenauer, J. Ferdinandus, S. Gillessen, A.S. Roberts,
- B. v. Tresckow, J. Welters

TRIAL COORDINATION CENTER

Head: M. Fuchs

Trial physicians: H. Tharmaseelan

Data Management: B. Andrulevicius, B. Koch, S. Ladewig, B. van den Hoonaard

Project Management: S. Kreitz, N. Moroz, A. Müller, I. Oosterhaar, S. Sevimli-Abdis, M. Weber, L. Wolf

Quality Management: I. Oosterhaar

Database / IT: O.W. Abudu, L. Ganß, T. Schober

Statistics: I. Bühnen, J. Jablonski, H. Kaul, H. Müller, G. Schneider

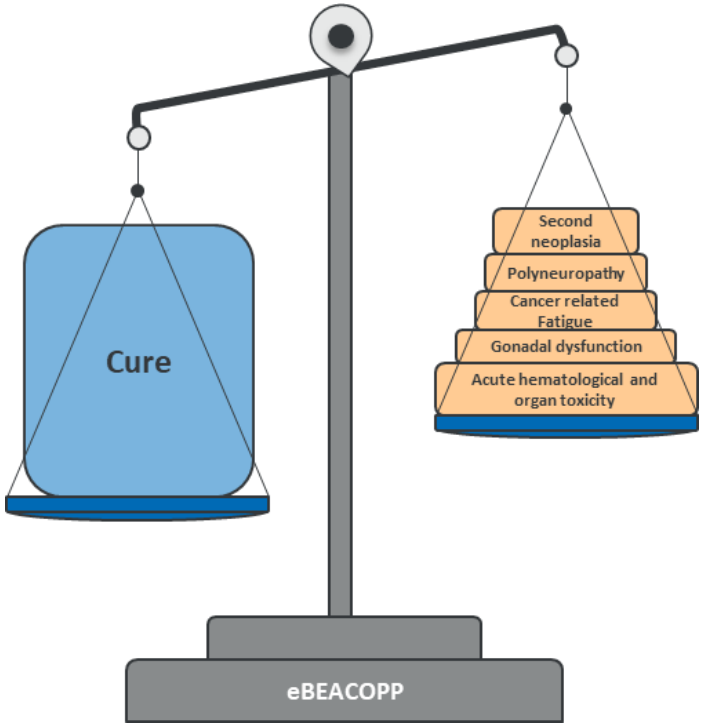
Assistant / Secretary: K. Rust, M. Schumacher, K. Tittmann

THE RANDOMIZED STUDY GHSG HD21 SHOWS SUPERIOR TOLERABILITY AND EFFICACY OF BRECADD VERSUS BEACOPP IN ADVANCED STAGE CLASSICAL HODGKIN LYMPHOMA

Peter Borchmann, Alden Moccia, Richard Greil, Gundolf Schneider, Mark Hertzberg, Valdete Schaub, Andreas Huettmann, Felix Keil, Judith Dierlamm, Mathias Hänel, Urban Novak, Julia Meissner, Andreas Zimmermann, Stephan Mathas, Josée M Zijlstra, Alexander Fossa, Andreas Viardot, Bernd Hertenstein, Sonja Martin, Pratyush Giri, Peter Kamper, Daniel Molin, Justin Ferdinandus, Michael Fuchs, Andreas Rosenwald, Wolfram Klapper, Hans T. Eich, Christian Baues, Michael Hallek, Markus Dietlein, Carsten Kobe, Volker Diehl on behalf of all GHSG HD21 study sites

GHSG HD21 rationale

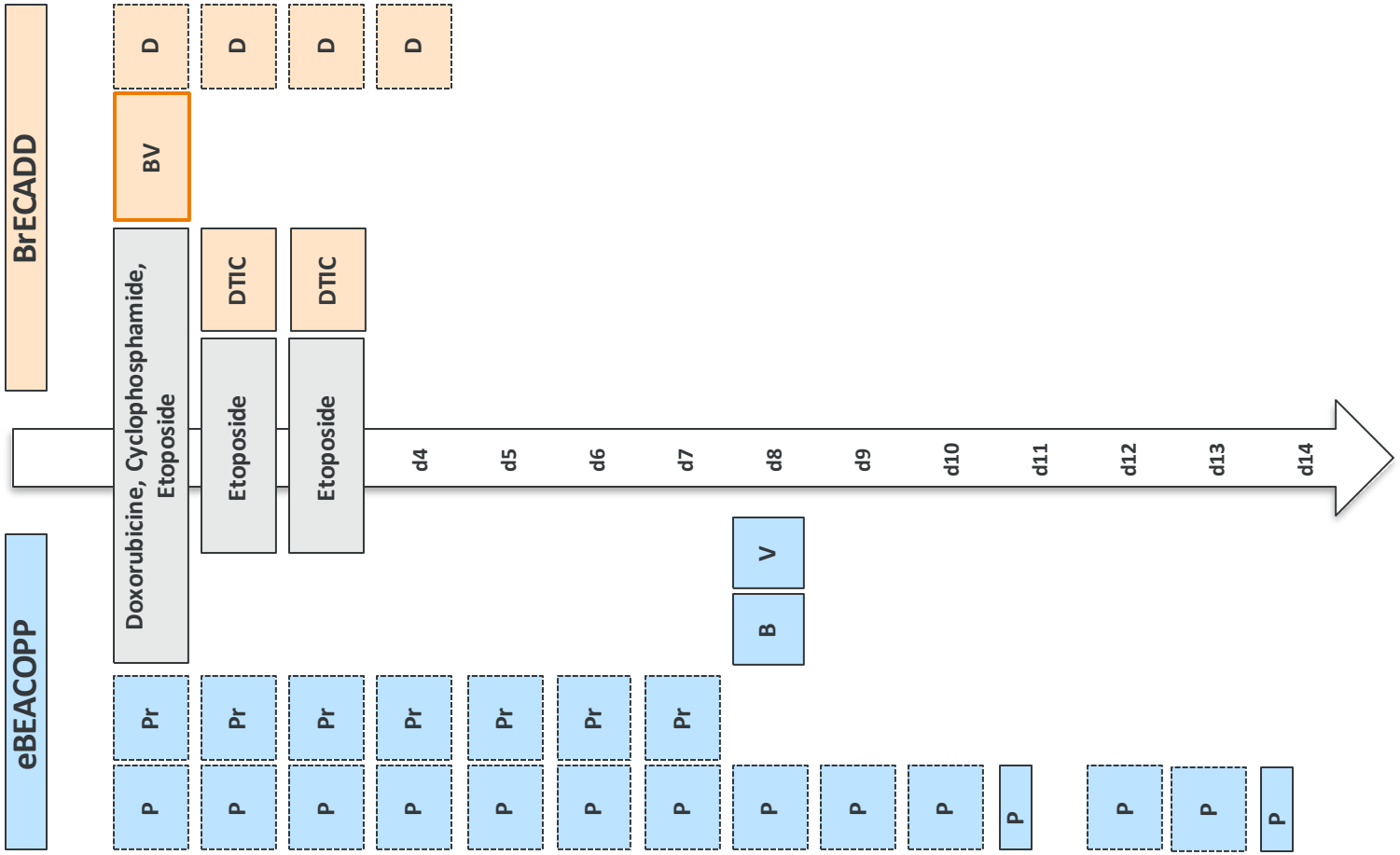
- Introduction of **eBEACOPP (HD9) improved progression-free survival (PFS) and subsequently overall survival (OS)**[1] by reduction of primarily progressive disease or early relapse (“Kairos-principle”).
- The benefit of this approach is most relevant for patients at higher risk for treatment failure. However, risk for acute and late or persisting toxicities is increased for all patients.
- High efficacy of eBEACOPP allowed to reduce treatment intensity to the **individual patients´ need** by early interim PET-guidance **from 8 to only 4 cycles** for most patients.[2]



➢ In HD21, we wanted to further improve this PET2-guided individualized approach by **modifying the eBEACOPP regimen with Brentuximab vedotin (BV),** a CD30-targeting antibody-drug conjugate.

[1]Diehl, V., et al., N Engl J Med, 2003. 348(24): p. 2386-95.
[2]Borchmann, P., et al., Lancet, 2018. 390(10114): p. 2790-2802.

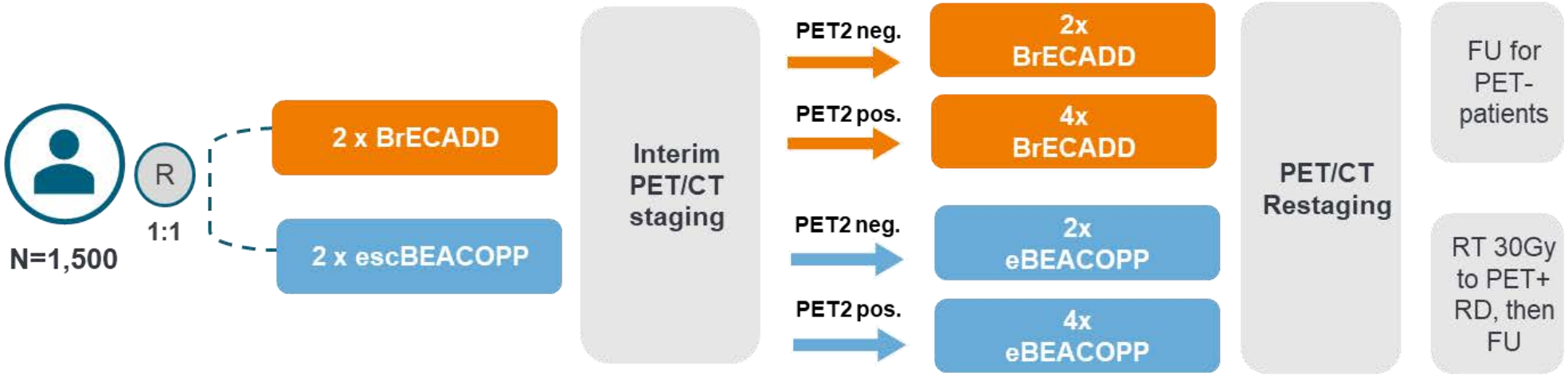
GHSG HD21 remodeling “eBEACOPP” to “BrECADD”



- The Kairos backbone **doxorubicin, cyclophosphamide, etoposide** was retained and *pre-defined dose de-escalation steps (DL 4, 3, 2, baseline) were identical in both groups*
- Introducing **Brentuximab Vedotin** (BV), **therefore omitting Bleomycin** (B, **pulmonary toxicity**) **and Vincristin** (V, **neuropathy**)
- Replacing **Procarbazine** (Pr) with the **less geno- and gonadotoxic Dacarbazine** (DTIC)
- Replacing 14 days of **Prednisone** (P) to 4 days of **Dexamethasone** (D)

GHSG HD21 study design and primary endpoints

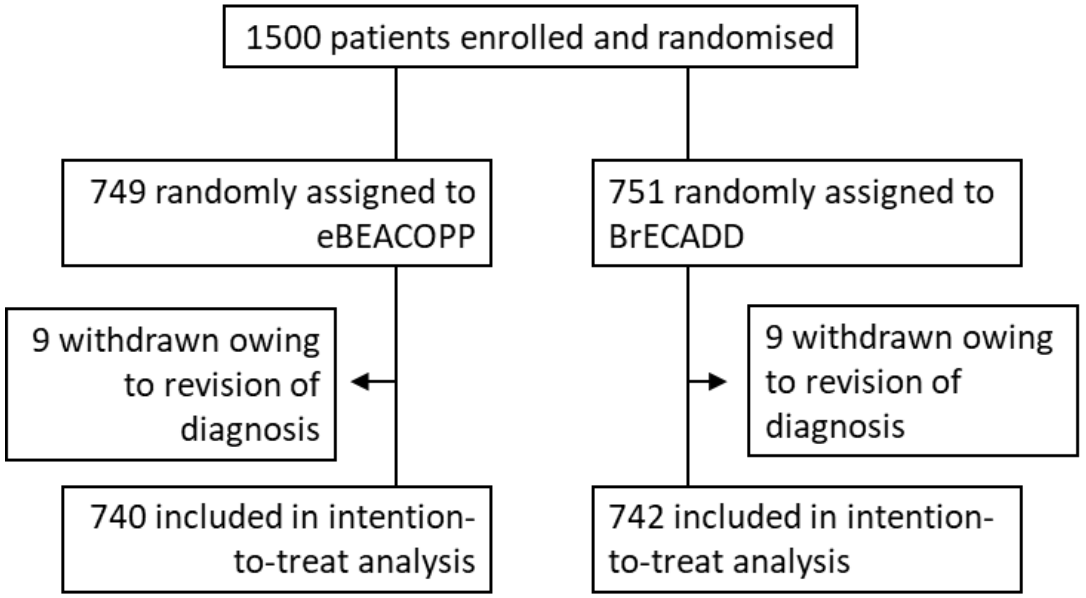
HD21 is an international randomized, open-label, phase 3 study of BrECADD versus eBEACOPP in adult patients < 60 yo with previously untreated, AS-cHL



Co-primary objectives:

- Demonstrate **superior tolerability** defined by treatment-related morbidity (TRMB) with BrECADD.
- Demonstrate **non-inferior efficacy** of 4-6 x BrECADD compared with 4-6 x BEACOPP determined by PFS (NI margin 6%, HR to be excluded 1.69)

GHSG HD21 trial profile and patient characteristics



- 1482/1500 patients recruited in nine countries and 233 study sites are available for PFS analysis
- TRMB was evaluated in patients with at least one cycle of therapy

eBEACOPP and BrECADD cohorts **were well balanced at baseline** for:

- stratification factors (sex, age, IPS, location of recruitment)
- median age: 31 y [18-61] vs 31 y [18-61]
- ECOG PS 0: 70% vs 69%
- B-Symptoms: 67% vs 68%
- Ann-Arbor stage: IIB 16% and III/IV 84% each
- histology: 55% vs 60% with subtype nodular sclerosis

and **for PET-based treatment guidance**

- PET2-negativity: 64% vs 64%
- PET-EOT positive RD: 17% vs 17%

GHSG HD21: TRMB endpoint summary

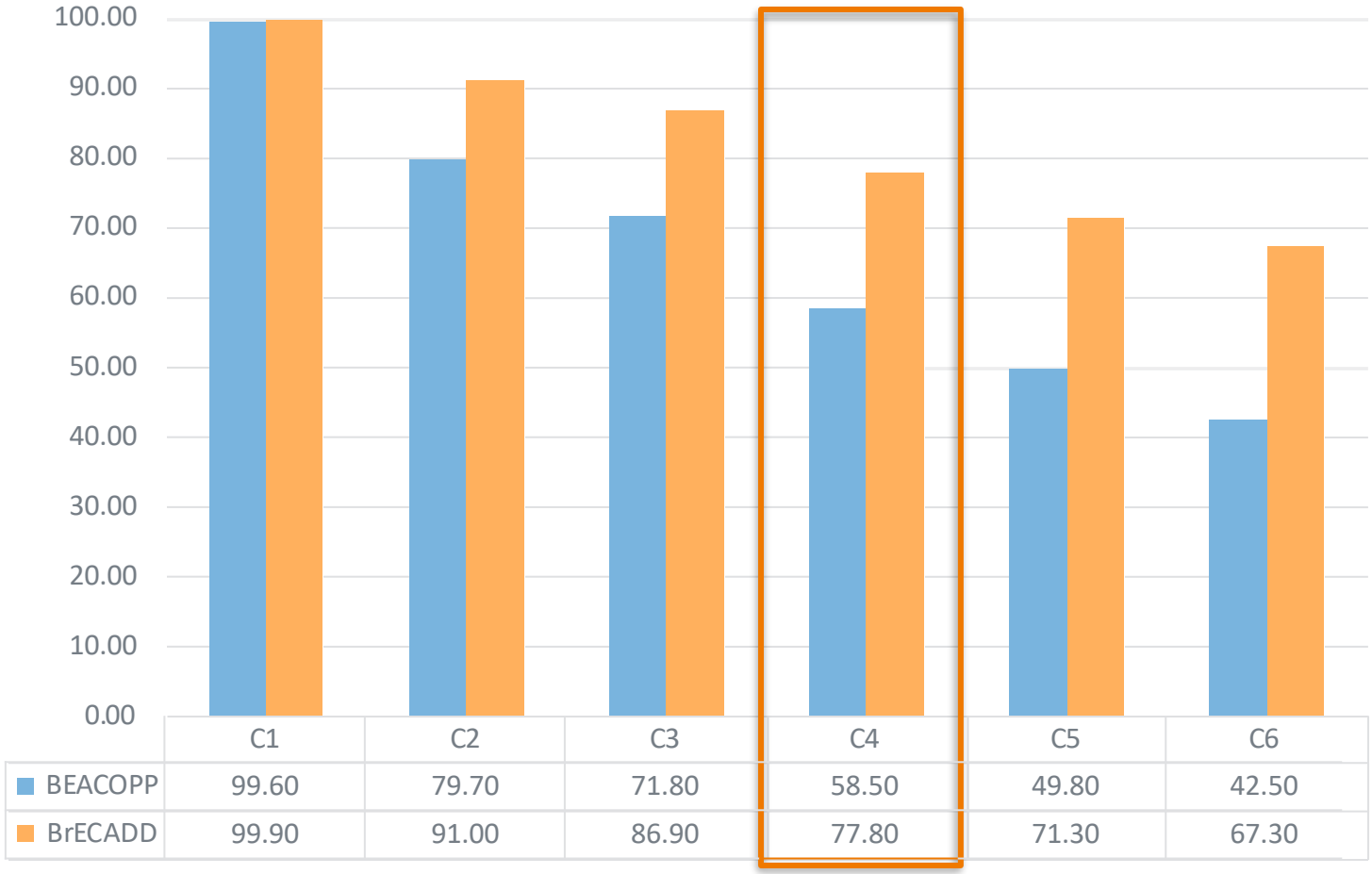
1. The first part of the combined primary endpoint showed a **significant reduction of *acute and severe treatment related adverse events* (TRMB) across all subgroups (IPS, sex, age) favouring**
   - **BrECADD** (312/738 patients [42%]) compared to the SOC
   - eBEACOPP (430/732 patients [59%]), relative risk 0·72; 95% CI 0·65–0·79, p<0·0001
2. The observed significant reduction in acute TRMB is **clinically meaningful** with reduction of
   - **transfusion frequency** for red blood cells (from 52% with eBEACOPP to 24% with BrECADD) and platelets (from 34% to 17%, respectively), and
   - **peripheral sensory neuropathy** grade 2 (3) from 14% (2%) to only 6% (1%)

4. Resolution of TRMB events in 675/677 patients (> 99%) treated with BrECADD

5. S228 GONADAL FUNCTION RECOVERY AND FERTILITY IN THE PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL

6. P1100 TREATMENT EFFECTS OF BRECADD ON HEALTH-RELATED QUALITY OF LIFE

HD21: Improved tolerability of BrECADD results in more patients treated with *full dose* (cyclo, etoposide, doxo) *per cycle* (%)



Early termination of the tubulin inhibitors VCR and BV

BV in BrECADD:
18/738 patients, 2·4%

VCR in eBEACOPP:
132/732 patients, 18·0%

Δ **15.6%**

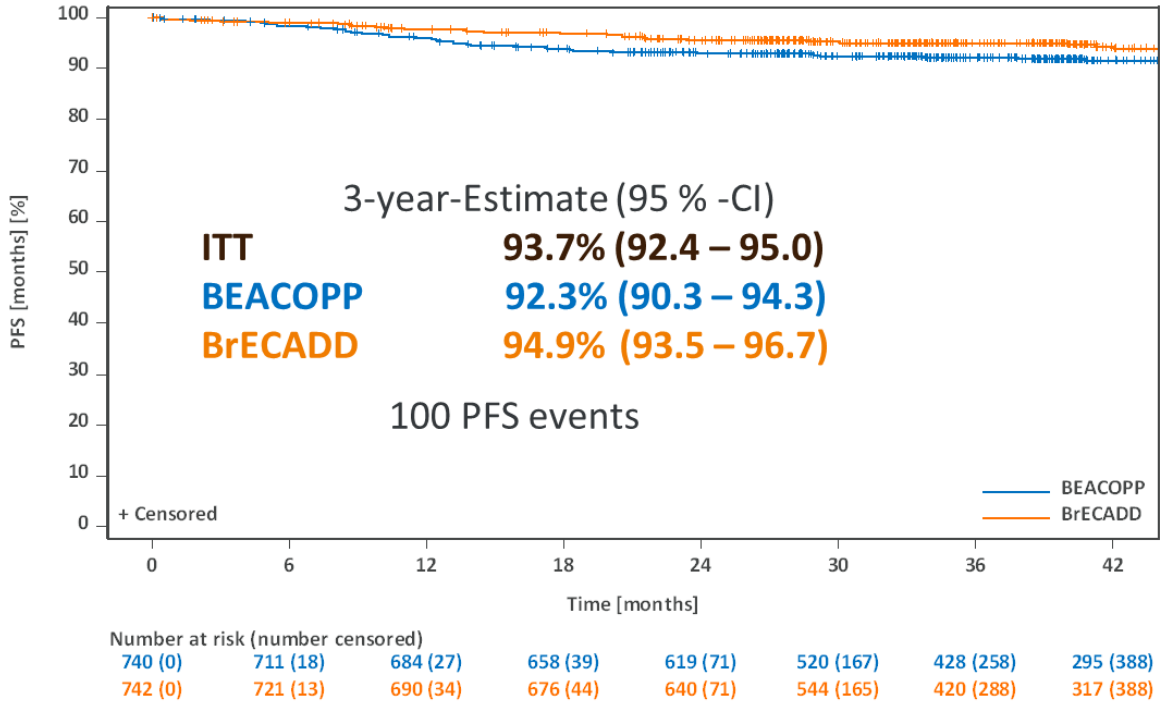
HD21 PFS endpoint at **interim analysis** (40 months mFU)

PFS events at interim analysis

	eBEACOPP N=740		BrECADD N=742	
	n	%	n	%
Progression/Relapse	55	7.4	32	4.3
Progression	**14**	**1.9**	**5**	**0.7**
Early Relapse, FU <= 1 year	**23**	**3.1**	**11**	**1.5**
Late Relapse, FU > 1 year	18	2.4	16	2.2
Death without PRO or REL	6	0.9	7	0.9
PFS events, total	61	8.4	39	5.3

Reduction of early PFS events with BrECADD

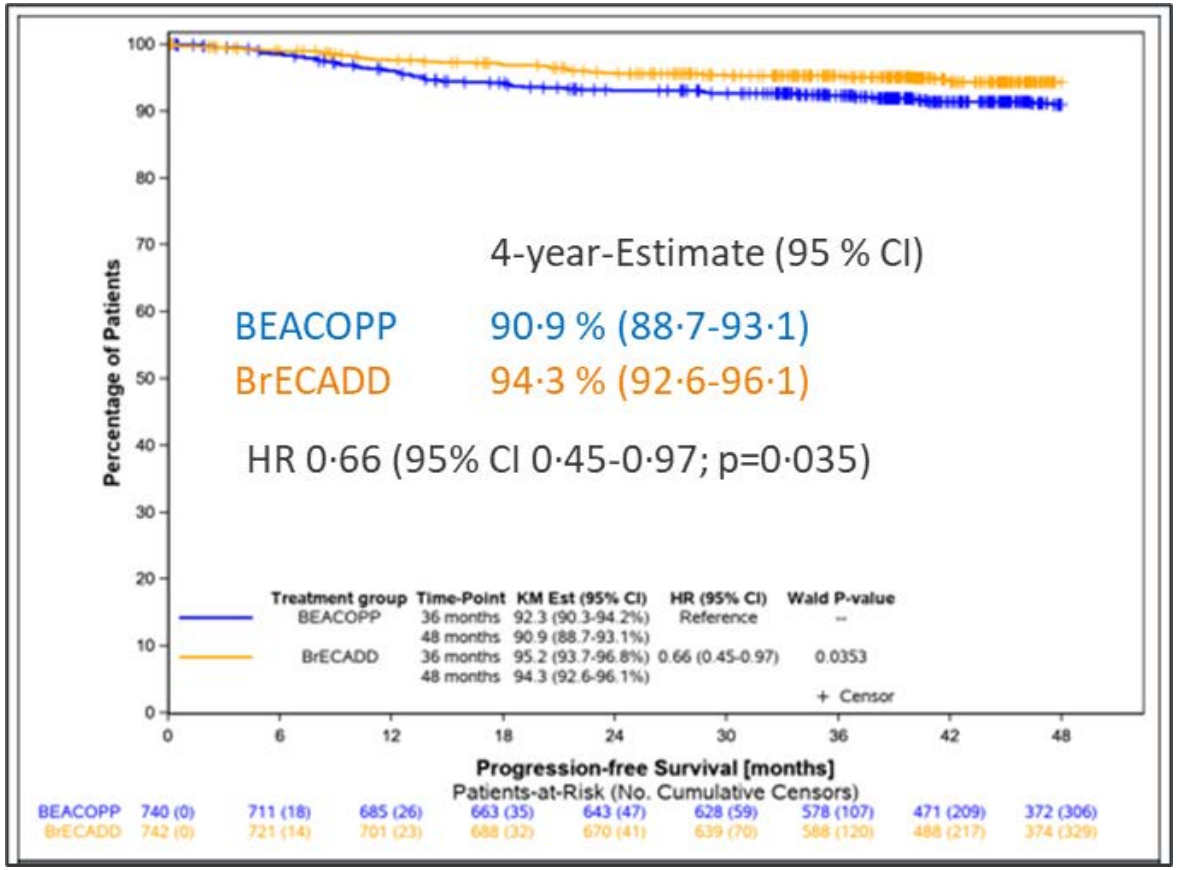
PFS at interim analysis



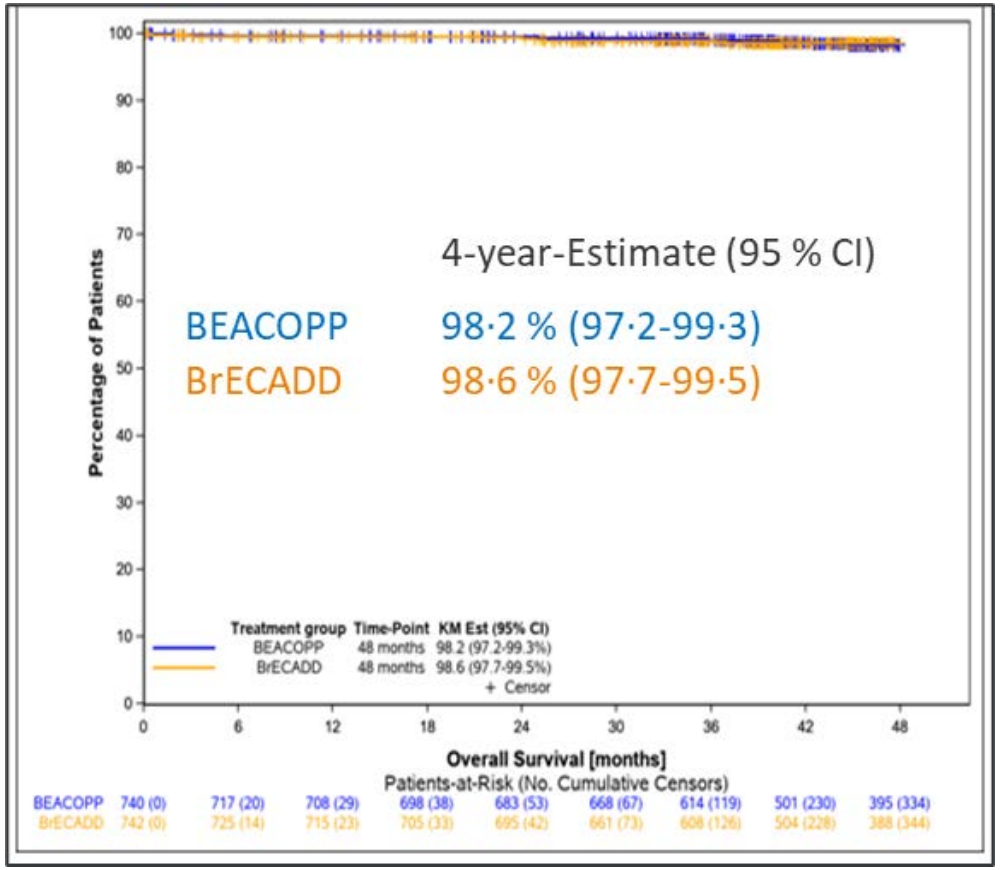
With a HR of 0.63 (99%-CI: 0.37 – 1.07) non-inferiority of BrECADD was fully established at interim analysis.

HD21 final analysis: BrECADD is superior to eBEACOPP (mFU 48 m)

Progression-free survival

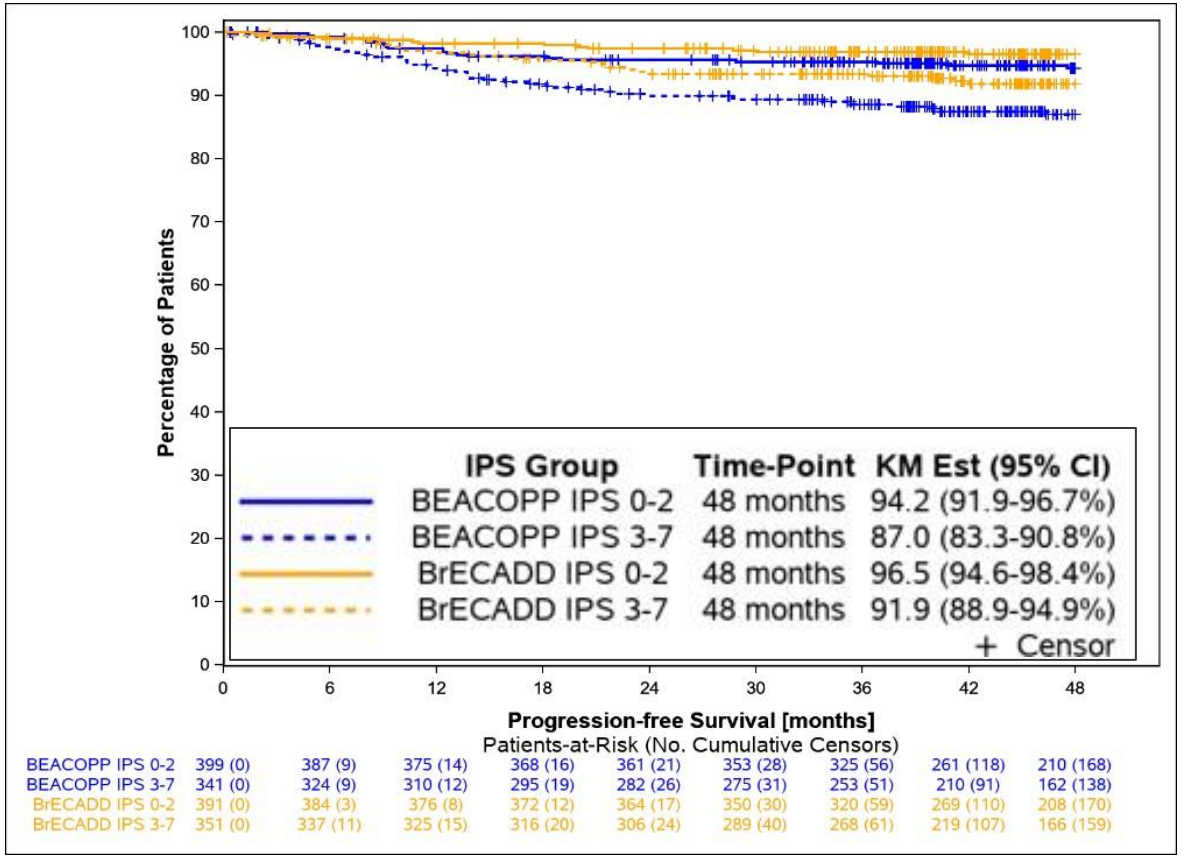


Overall survival

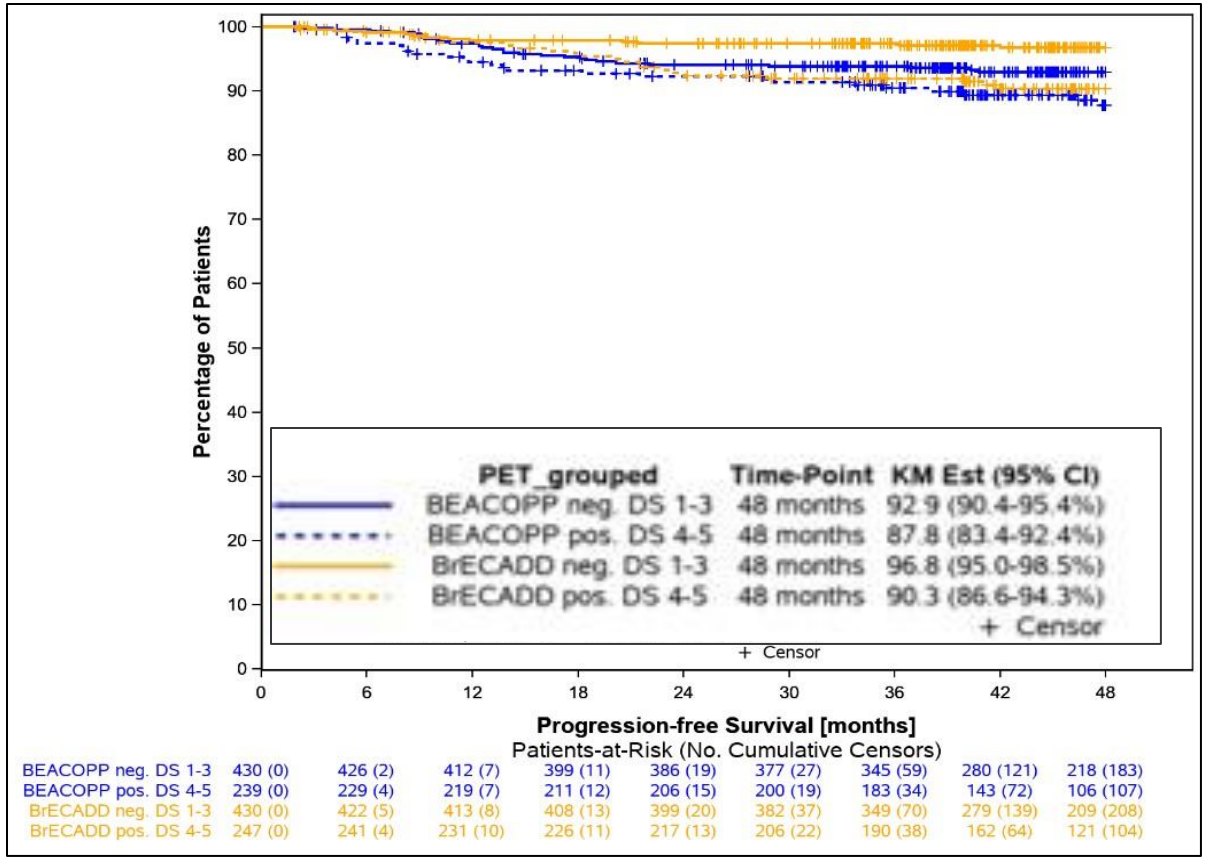


HD21 final analysis: PFS benefit of BrECADD is observed across relevant subgroups

PFS by baseline risk factor IPS (0-2 vs 3-7)



PFS by risk factor PET2-status



GHSG HD21 summary and Authors' conclusions

BrECADD is significantly better tolerated than eBEACOPP and

- recovery of TRMB after 12 months in > 99% of patients, and normalization of QoL
- improved feasibility (up to 25% higher rate of full dose Tx), and 16% less dose reductions of the tubulin inhibitor (MMAE/VCR)

- Efficacy of BrECADD is superior to eBEACOPP reaching
- an unprecedented PFS of 94.3% with mature FU of 4-years
  - most patients (64%) receive only 4 cycles (i.e. 12 weeks),
  - cumulative doses of cytotoxic drugs below critical thresholds (e.g. doxorubicin at 160 mg/m² for 2/3 of patients)

We recommend individualized PET2-guided BrECADD as a standard treatment option for AS-cHL.

1 Anderson et al, Lancet Oncol 2018; 19: 1328–37

Thank you very much for your attention!

- **Chairman:** P. Borchmann
- **Former-Chairman:** A. Engert
- **Honorary Chairman:** V. Diehl
- **Pathology:** A.C. Feller, F. Fend, M.L. Hansmann,
- W. Klapper, P. Möller, G. Ott, A. Rosenwald
- **Radiotherapy:** C. Baues, H. T. Eich
- **Nuclear Medicine:** M. Dietlein, C. Kobe
- **Laboratory:** S. Borchmann
- **Physicians:** K. Behringer, B. Böll, P. Bröckelmann,
- Eichenauer, J. Ferdinandus, S. Gillessen, A.S. Robertz,
- Volters

TRIAL COORDINATION CENTER

Head: M. Fuchs

Trial physicians: H. Tharmaseelan

Data Management: B. Andrulevicius, B. Koch, S. Ladewig, B. van den Hoonaard

Project Management: S. Kreitz, N. Moroz, A. Müller, I. Oosterhaar, S. Sevimli-Abdis, M. Weber, L. Wolf

Quality Management: I. Oosterhaar

Database / IT: O.W. Abudu, L. Ganß, T. Schober

Statistics: I. Bühnen, J. Jablonski, H. Kaul, H. Müller, G. Schneider

Assistant / Secretary: K. Rust, M. Schumacher, K. Tittmann

Real-world evidence study of brentuximab vedotin retreatment in patients with cutaneous T-cell lymphoma

Mitteldorf C, et Al.
Abstract #A-133

Christina Mitteldorf,[1] Adele de Masson,[2] Marie Beylot-Barry,[3] Marion Wobser,[4] Athanasios Zomas,[5] Vanessa Stache,[5] Chalid Assaf[6]

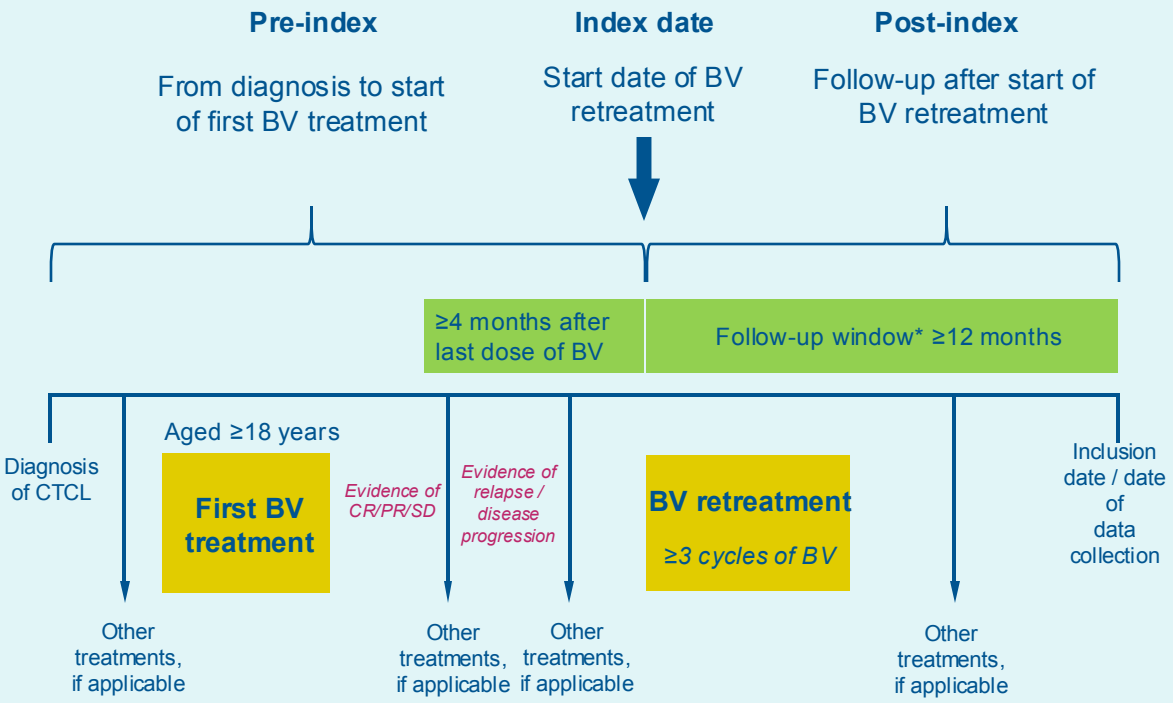
[1]University Medical Center, Göttingen, Germany; [2]Assistance Publique – Hôpitaux de Paris (AP-HP), Hôpital Saint Louis, Paris, France; [3]CHU de Bordeaux, Hôpital Saint Andre, Bordeaux, France; [4]University Hospital Wuerzburg, Wuerzburg, Germany; [5]Takeda Pharmaceuticals International AG, Zurich, Switzerland; [6]Helios Klinikum Krefeld, Krefeld, Germany

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Question

What is the efficacy and safety of brentuximab vedotin (BV) retreatment in patients with cutaneous T-cell lymphoma (CTCL) in a real-world setting?

Study design



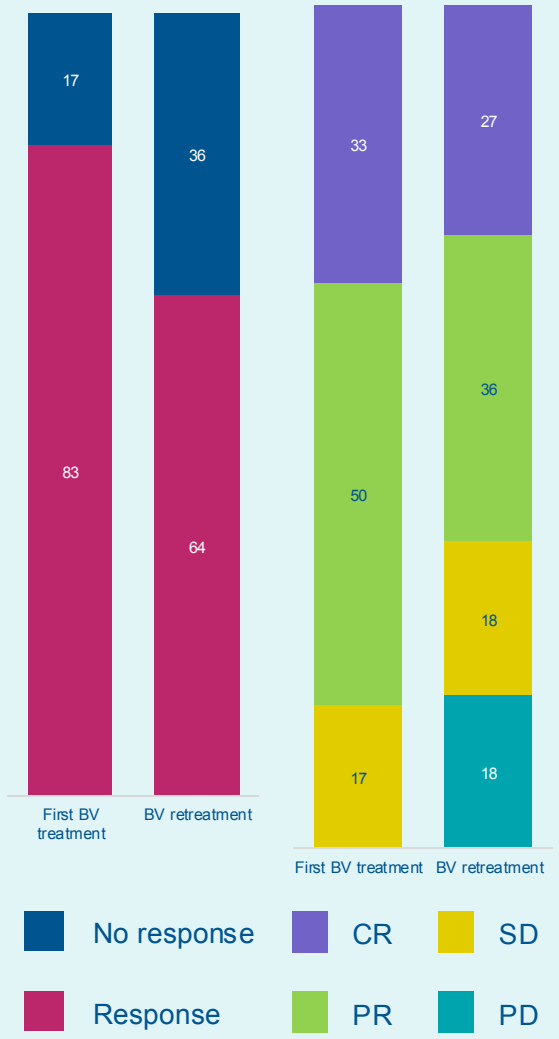
*Censored at discontinuation of BV retreatment, initiation of another CTCL treatment, death, loss to follow-up, or after 12 months of the post-index date.
CR, complete response; PR, partial response; SD, stable disease.

Key conclusions

This interim analysis of 12 patients in a retrospective chart review demonstrated a high objective response rate (ORR) and an acceptable safety profile with BV retreatment

Results

Figure 1: Response rates after first BV treatment and BV retreatment, %



AE, adverse event; AESI, AE of special interest; PD, progressive disease.

Table 1: Safety summary

	First BV treatment (N=12)	BV retreatment (N=12)
Median duration of treatment, months (range)	3.3 (0.7–7.6)	3.8 (0.9–13.3)
Median number of BV cycles (range)	5.5 (2–11)	6 (2–15)
Discontinued BV treatment, n (%)	9 (75)	8 (67)
Any AE, n (%)	9 (75)	5 (42)
Any AESI, n (%)*	5 (42)	1 (8)
Peripheral neuropathy†	4 (33)	1 (8)
Neutropenia	1 (8)	-

*AESIs includes peripheral sensory neuropathy, peripheral motor neuropathy, neutropenia, febrile neutropenia, and serious infection.
†Includes neuropathy peripheral, peripheral sensory neuropathy, and polyneuropathy.

A total of 25 AEs were reported in 9 patients (75%) after first BV treatment, and 7 AEs were reported in 5 patients (42%) after BV retreatment

Background

- Limited treatment options are available for relapsed/refractory CTCL[1]
- Allogeneic stem cell transplant is the only available curative therapy, and many patients may require retreatment with a drug that has been used previously[1,2]
- BV is approved for the treatment of adults with CD30+ CTCL who have received ≥1 prior systemic therapy[3]
- This approval was based on data from the phase III ALCANZA study, which showed a treatment benefit for BV compared to physicians' choice in patients with CTCL[4,5,6]
- While findings from real-world studies are consistent with the ALCANZA study,[4,5] currently there are no regional data available regarding the safety and effectiveness of BV retreatment in patients with CTCL
- We report an interim analysis of a retrospective chart review of patients with CTCL in Europe

1. Zinzani PL, et al. *Crit Rev Oncol Hematol*. 2016;99:228–240 2. Goyal A, Foss F. *Expert Rev Anticancer Ther.* 2024;24:41–58 3. European Medicines Agency. Brentuximab vedotin summary of product characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/adcetris-epar-product-information_en.pdf, last updated December 2023 4. Horwitz SM, et al. *Blood Adv.* 2021;5(23):5098–5160 5. Barta SK, et al. *Clin Lymphoma Myeloma Leuk* 2024;24:e21–e32.e4 6. Papadavid E, et al. *Br J Dermatol* 2021;185:1035–1044

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Methods

- This retrospective, multicenter chart review included eligible patients treated at 9 clinical sites in Germany, Spain, and France between January and June 2024
- The study design and eligibility criteria are shown in the **Summary Panel**
- The primary objectives were to describe the:
  - Effectiveness of BV re-exposure in patients with CTCL (ORR and progression-free survival [PFS])
  - Safety profile of BV re-exposure in patients with CTCL (including rates of peripheral neuropathy, neutropenia, and serious infections)

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Results

Patient demographics and clinical characteristics

- A total of 12 patients were included in this interim analysis
- Patient demographics and clinical characteristics are shown in **Table 2**
- Of 2 patients with primary cutaneous anaplastic large cell lymphoma (pcALCL), one had unknown TNM staging and the other had T2C, N0, M0, and B0A staging

Treatment patterns

- Patients received a median of 5.5 (range 2–11) cycles of BV at first treatment and 6 (range 2–15) cycles of BV at retreatment (**Table 3**)
- The median time between first BV treatment and BV retreatment was 1 year (range 0–3)
- Nine patients discontinued BV treatment before the planned number of cycles was reached during the first BV treatment and 8 patients discontinued during BV treatment (**Table 3**)
- Concomitant therapies received at first BV treatment, between BV treatments, and at BV retreatment are shown in **Figure 2**
  - Nine patients received therapies between first and BV retreatments
  - Systemic therapies received included chemotherapies (n=7), retinoids (n=1), histone deacetylase inhibitors (n=1), and other treatments (n=3)

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Table 2: Patient demographics and clinical characteristics

n (%)*	CTCL diagnosis (N=12)	First BV treatment (N=12)	BV retreatment (N=12)
Median age, years (range)	54 (12–73)	59 (29–80)	60 (30–83)
Male	7 (58)	–	–
Country			
France	7 (58)	–	–
Germany	5 (42)	–	–
Primary CTCL subtype			
Mycosis fungoides (MF)	8 (67)	–	–
Folliculotropic MF†	3 (38)	–	–
Classical type†	5 (63)	–	–
Sézary syndrome (SS)	2 (17)	–	–
pcALCL	2 (17)	–	–
CD30 expression tested	8 (67)	10 (83)	8 (67)
CD30 expressed‡	6 (75)	10 (100)	8 (100)
<10%	2 (33)	2 (20)	2 (25)
10–50%	2 (33)	6 (60)	4 (50)
>50%	1 (17)	1 (10)	–
Unknown	1 (17)	1 (10)	2 (25)
Comorbidities			
Yes	3 (25)	3 (25)	3 (25)
No	6 (50)	9 (75)	9 (75)
Unknown	3 (25)	–	–
Type of comorbidity§,**			
Cardiovascular disease	1 (33)	2 (67)	2 (67)
Autoimmune disease	–	1 (33)	1 (33)
Hypothyroidism	1 (33)	–	–
Solid tumor	–	1 (33)	1 (33)
Other	1 (33)	3 (100)	2 (67)

*Unless stated otherwise; †Denominator is total number of patients with MF subtype of primary CTCL; ‡Denominator is total number of patients with CD30 expression at CTCL diagnosis; §Denominator is total number of patients with any comorbidity at CTCL diagnosis; ¶Denominator is total number of patients with any skin symptoms at the time of BV treatment; **Categories are not mutually exclusive; ††Denominator is total number of patients with MF or SS as the primary CTCL subtype.

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Table 2: Patient demographics and clinical characteristics (ctd)

n (%)*	CTCL diagnosis (N=12)	First BV treatment (N=12)	BV retreatment (N=12)
Skin symptoms at time of BV treatment¶,**		7 (58)	6 (50)
Rash	–	3 (43)	2 (33)
Dry skin	–	3 (43)	3 (50)
Pruritus/itching	–	4 (57)	3 (50)
Redness, irritation, burning	–	5 (71)	4 (67)
Scabbing, flaking	–	1 (14)	1 (17)
Erosions	–	1 (14)	1 (17)
Skin induration and oozing	–	1 (14)	1 (17)
Other	–	1 (14)	1 (17)
TNMB staging††			
T (skin)			
T2A	–	–	1 (1)
T2B	1 (10)	1 (10)	2 (20)
T3	4 (40)	7 (70)	7 (70)
T3A	–	1 (10)	–
T4	2 (20)	1 (10)	–
Unknown	3 (30)	–	–
N (lymph node)			
N0	4 (40)	9 (90)	7 (70)
N1	–	–	1 (10)
N1A	1 (10)	–	–
N3	–	–	2 (20)
N3A	1 (10)	1 (10)	–
Nx	1 (10)	–	–
Unknown	3 (30)	–	–
M (viscera)			
M0	7 (70)	10 (100)	10 (100)
Unknown	3 (30)	–	–
B (blood)			
B0A	4 (40)	5 (50)	8 (80)
B1A	–	1 (10)	–
B2A	2 (20)	1 (10)	–
Unknown	4 (40)	3 (30)	2 (20)

*Unless stated otherwise; †Denominator is total number of patients with MF subtype of primary CTCL; ‡Denominator is total number of patients with CD30 expression at CTCL diagnosis; §Denominator is total number of patients with any comorbidity at CTCL diagnosis; ¶Denominator is total number of patients with any skin symptoms at the time of BV treatment; **Categories are not mutually exclusive; ††Denominator is total number of patients with MF or SS as the primary CTCL subtype.

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

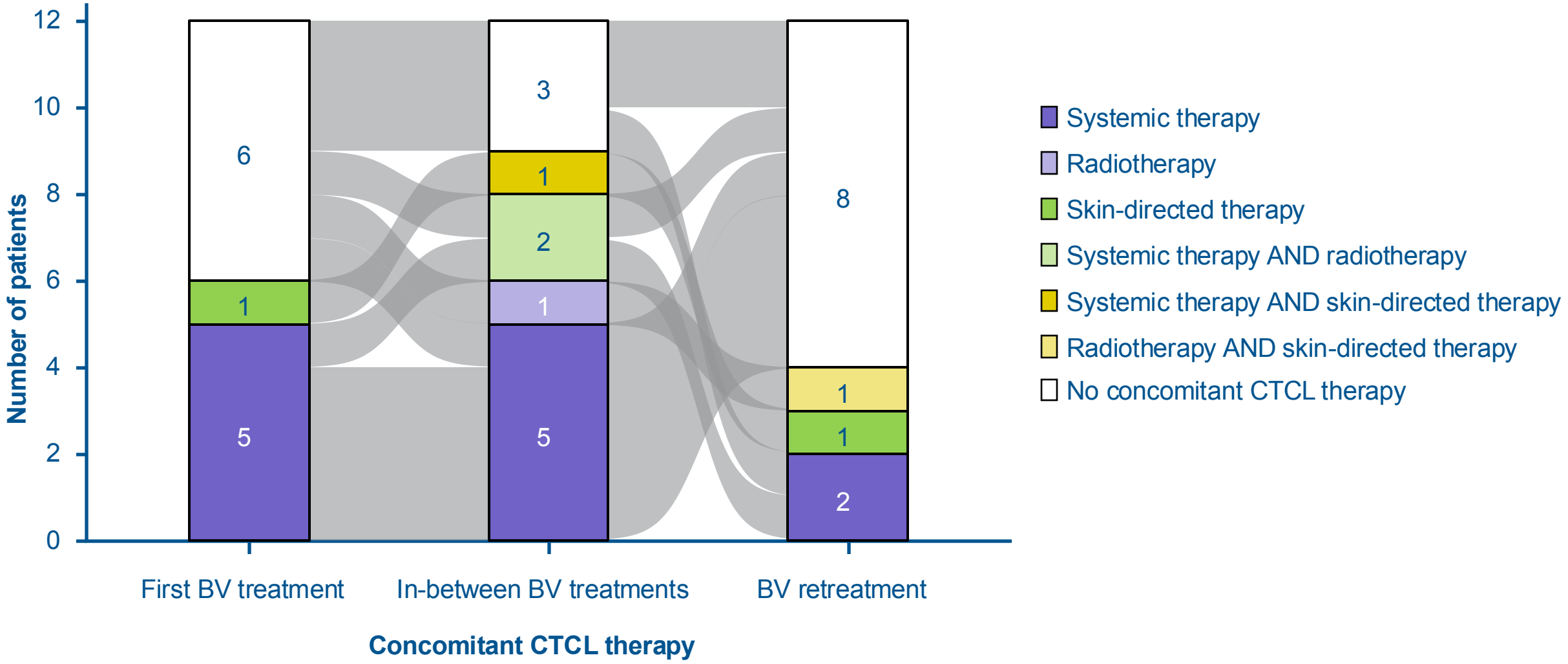
Table 3: Summary of treatment duration and reasons for discontinuation of BV treatment

n (%)*	First BV treatment (N=12)	BV retreatment (N=12)
Median duration of treatment, months (range)	3.3 (0.7–7.6)	3.8 (0.9–13.3)
Median number of BV cycles (range)	5.5 (2–11)	6 (2–15)
Discontinued BV treatment†‡	9 (75)	8 (67)
Toxicity	2 (22)	2 (25)
Disease progression	2 (22)	4 (50)
Patient decision	1 (11)	-
Physician decision	1 (11)	1 (13)
Reached sufficient level of response§	1 (100)	-
Other§	-	1 (100)
Other reason for discontinuation	5 (56)‖	2 (25)¶

*Unless stated otherwise; †Categories are not mutually exclusive; ‡Denominator is total number of patients who discontinued BV treatment; §Denominator is total number of patients with 'physician decision' given as the reason for discontinuation of BV treatment; ‖Includes complete response before allograft (n=2), complete remission before allograft, almost complete remission before allograft, suspected drug side effect (all n=1); ¶Response almost complete (n=1) and complete remission (n=1).

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Figure 2: Change in concomitant therapies over time from first BV treatment



Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

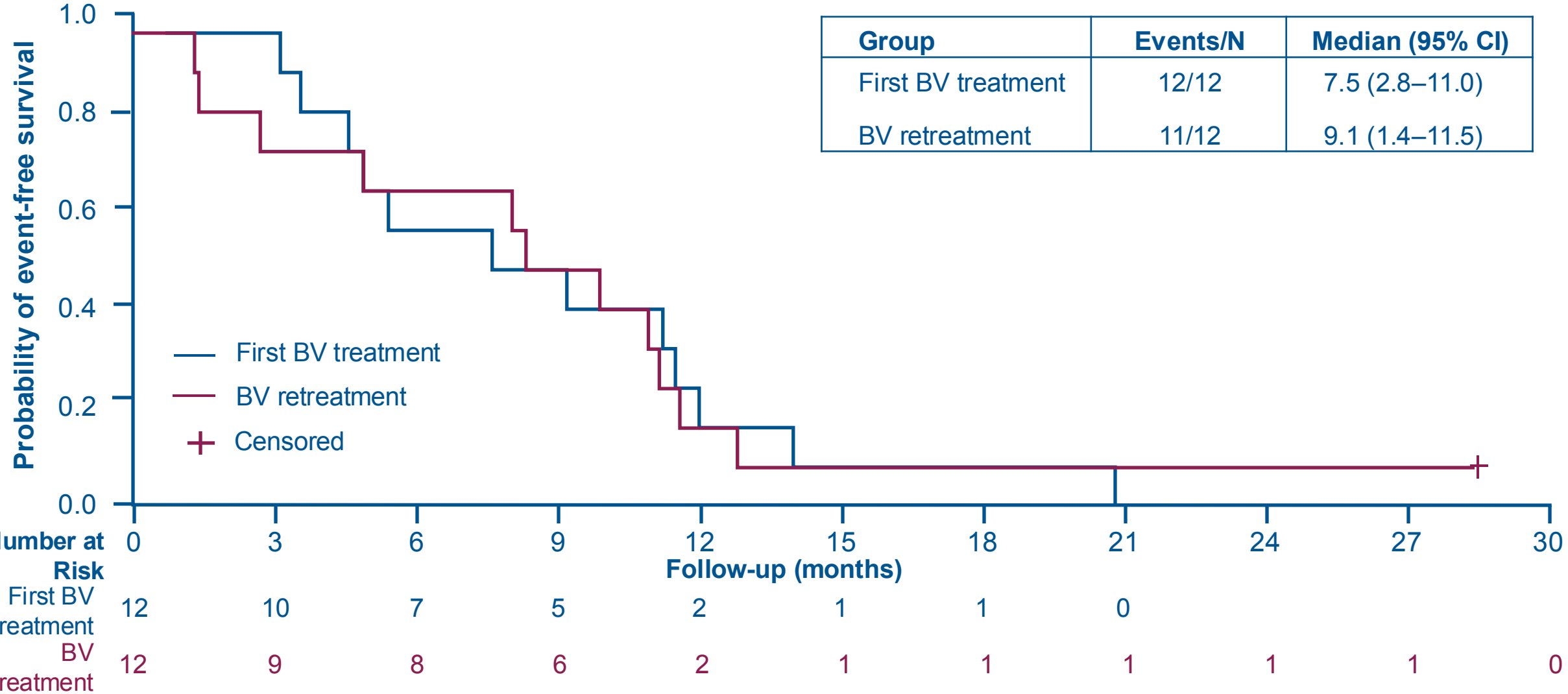
Results (ctd)

Efficacy

- A summary of responses (n=12 evaluable at first BV treatment, n=11 evaluable at BV retreatment) is shown in **Figure 1 in the Summary Panel**
  - The ORR was 83% after first BV treatment and 64% with BV retreatment
  - After the first BV treatment, there were 4 CR, 6 PR, 2 SD
  - At BV retreatment, there were 3 CR, 4 PR, 2 SD, and 2 PD
  - Of 8 patients with MF, 6 responded to first BV treatment and 4 responded at retreatment
  - Both patients with SS responded to first BV treatment and 1 responded on retreatment
  - Both patients with pcALCL responded to first BV treatment and retreatment
  - Of the 10 patients who responded to first BV treatment, 8 were CD30-positive and of the 7 patients who responded at BV retreatment, 5 were CD30-positive; the remainder did not have CD30 data available (there were no CD30-negative responses)
- Median PFS was shorter with the first BV treatment (7.5 months, 95% confidence interval [CI]: 2.8–11.0) compared to BV retreatment (9.1 months, 95% CI: 1.4–11.5) (**Figure 3**)

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Figure 3: Progression-free survival after first BV treatment and at BV retreatment



Group	Events/N	Median (95% CI)
First BV treatment	12/12	7.5 (2.8–11.0)
BV retreatment	11/12	9.1 (1.4–11.5)

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Results (ctd)

Safety

- A safety summary is shown in **Table 1 in the Summary Panel**
- A total of 25 AEs were reported in 9 patients (75%) after first BV treatment, and 7 AEs were reported in 5 patients (42%) after BV retreatment
- Incidence rates of individual AEs are shown in **Table 4**
- One patient experienced grade 2 peripheral sensory neuropathy after the first BV treatment, which was considered by the investigator as definitely related to BV treatment, with improvement reported after 46 days but with resolution unknown or not recorded
- One patient experienced grade 1 neutropenia after the first BV treatment, which was considered by the investigator as possibly related to BV treatment, and resolved after 28 days
- AEs reported between BV treatments were: graft-versus-host disease in gastrointestinal tract (n=2), in liver (n=1), and in skin (n=3); leukopenia (n=1); and skin reaction (n=1)
- At the last follow-up, 5 patients had died due to disease progression (n=3), sepsis (n=1), and pneumonia (n=1)

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Table 4: Summary of AEs

Any grade* AEs, n (%)	First BV treatment (N=12)	BV retreatment (N=12)
Peripheral neuropathy†	6 (50)	2 (17)
Nausea	3 (25)	–
Toxic skin eruption	3 (25)	–
Abdominal pain	2 (17)	–
Pyrexia	2 (17)	1 (8)
Alopecia	1 (8)	–
Constipation	1 (8)	–
Diarrhea	1 (8)	–
Myalgia	1 (8)	–
Neutropenia	1 (8)	–
Rash erythematous	1 (8)	–
Tachyarrhythmia	1 (8)	–
Vasoplegia syndrome	1 (8)	–
Paresthesia	–	1 (8)
Rhinorrhea	–	1 (8)
Thrombocytopenia	–	1 (8)
Vomiting	–	1 (8)

*Any grade AEs were grade ≤3; no grade 4 or 5 AEs were reported; †Includes neuropathy peripheral, peripheral sensory neuropathy, and polyneuropathy.

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Author's Conclusions

- Despite small patient numbers, results from this interim analysis of a retrospective, multicenter chart review demonstrated that retreatment with BV is feasible, with responses observed in patients who achieved CR, PR, or SD on prior BV treatment and had disease progression/relapse
- BV retreatment was generally well-tolerated with few patients discontinuing due to AEs; AEs were generally low grade and consistent with the known safety profile of BV
- Study enrollment is ongoing; when available, further results will add to the real-world evidence on BV retreatment and help inform treatment decisions for patients with CTCL who have limited options available

Mitteldorf C, et al. Poster Presentation A-133. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Sub-analysis of the BELIEVE STUDY: Effectiveness and safety for re-treatment with Brentuximab-vedotin in relapsed/refractory (R/R) Cutaneous T Cell Lymphoma (CTCL): a retrospective medical chart review study in Spain. NCT:04998331

Sureda A, et Al.
Abstract #A-111

Anna Sureda-Balari[1], Ramón García-Sanz [2] (co-authors), Eva Domingo-Domenech[1], Francisco J. Capote[3], Antonio Gutierrez[4], Antonia Rodriguez[5], Pablo Ortiz-Romero[6,7], Marta Grande[8,9], and Lourdes Baeza-Montañez[8].

1. Institut Catala D'oncologia, Hospital Duran i Reynals. IDIBELL. L'Hospitalet de Llobregat, Barcelona, Spain; 2. Hospital Universitario Gregorio Marañon, Madrid, Spain; 3. Hospital Universitario Puerta del Mar, Cádiz, Spain; 4. Hospital Son Espases IdISBa, Palma de Mallorca, Spain; 5. Hematology Department, Hospital Universitario 12 de Octubre, Madrid, Spain; 6. Dermatology Department, Hospital Universitario 12 de Octubre, Madrid, Spain; 7. Institute i+12, Medical school, Universidad Complutense de Madrid, Spain; 8. Medical Department, Takeda Farmacéutica España S.A, Madrid, Spain; 9. Universidad de Alcalá, Alcalá de Henares, Madrid, Spain.

Sureda A, et al. Poster Presentation A-111. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Introduction and Methods

Introduction

- Brentuximab vedotin (BV) is a CD30-directed antibody-drug conjugate.
- Its efficacy in patients with CD30+ R/R malignancies has been shown in pivotal studies.
- The aim of this study was: **to describe effectiveness and safety of BV retreatment in R/R CD30+ cutaneous T cell lymphoma (CTCL) patients in a real-world setting in Spain.**

Methods

- The BELIEVE study is a noninterventional, retrospective chart review conducted in 30 Spanish sites (2014-2022).
- Adult patients with CD30+ malignancies including classical Hodgkin lymphoma, systemic anaplastic large cell lymphoma and CTCL, including primary cutaneous anaplastic large cell lymphoma (pcALCL) and mycosis fungoides (MF) treated with BV (evidence of objective response, OR) and having received ≥2 doses of BV as retreatment were included.
- Patients were followed up to ≥6 months or treatment discontinuation due to death or toxicity

BV, brentuximab vedotin; CD30, cluster differentiation 30; CTCL, cutaneous T cell lymphoma; R/R, relapsed/refractory

Sureda A, et al. Poster Presentation A-111. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Results – Baseline Characteristics

- Of 43 patients included, 14 were CTCL: 12 MF and 2 pcALCL.
- At BV retreatment 50% of patients had advanced disease

CTCL Patient Characteristics	CTCL patients n=14
Mean age, years (SD)	52.9 (13.5)
Male, %	57.1%
Disease stage at BV retreatment, n	
Stage IB	1
Stage IIB	3
Stage III	0
Stage IVA	4
Stage IVB	3
Missing	3
ECOG PS grade 0-1, %	91.7%
Treatments between the first course of BV and BV retreatment, n (SD) Median number of lines, n (range)	8.8 (6.9) 6.5 (2-30)
Transplants after first BV treatment, n	
1 autologous transplant	0
2 autologous transplants in tandem	0
2 allogenic transplant	1
Allogenic transplants after BV retreatment, n	2

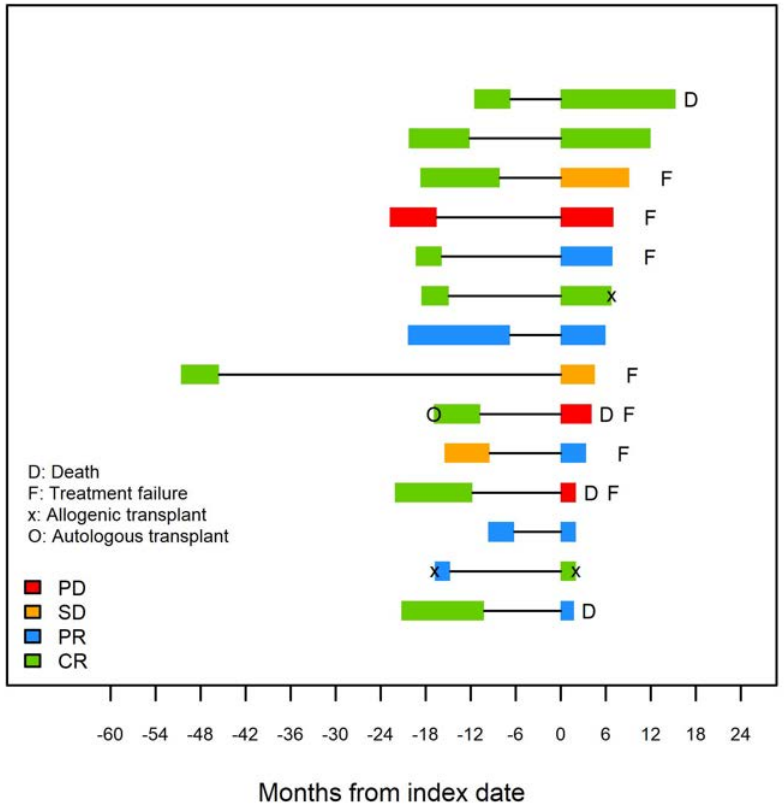
BV, brentuximab vedotin; CTCL, cutaneous T cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Score; MF, mycosis fungoides; pcALCL, primary cutaneous anaplastic large cell lymphoma

Sureda A, et al. Poster Presentation A-111. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Results – Efficacy

- The median time from first BV treatment to retreatment initiation was 11 (6–45) months
- ORR was 64.3%, 28.6% of patients achieved CR (n=4), 5 (35.7%) achieved PR and progression was observed in 21.4% of patients (n=3)
- After 24 months, 4/14 patients died due to progression

Duration of first course of BV and BV retreatment for CTCL patients



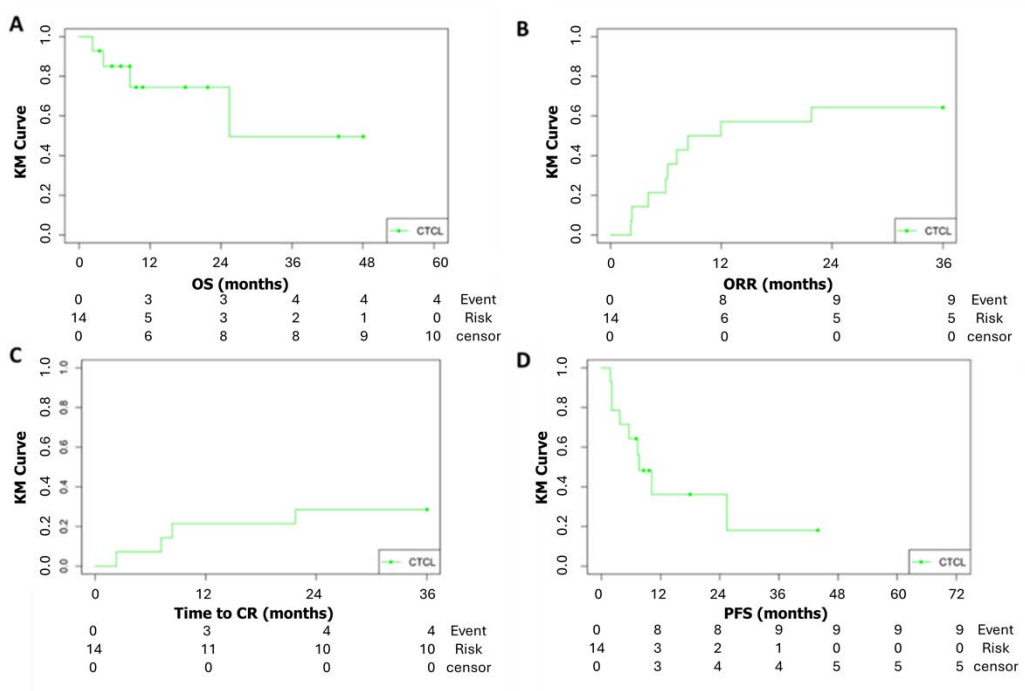
BV, brentuximab vedotin; CR, complete response, CTCL, cutaneous T cell lymphoma; ORR, overall response rate; PR, partial response; PD, progressive disease; SD, stable disease

Sureda A, et al. Poster Presentation A-111. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Results – Efficacy

- The median number of cycles during the first treatment with BV was 8 (3-16) and 7 (3-14) during retreatment, respectively. The median (SD) initial dose was 1.8 (0.2) mg/kg for first BV treatment and BV retreatment.
- Median OS was 25.4 (2.3-25.4) months, with four patients died due to progression
- Median PFS was 5.6 months (1.8-25.4)
- Median time to achieve CR was 8 months (2.3-21.7)

Kaplan -Meier estimates of Overall Survival, time to OR, CR and PFS in CTCL patients at retreatment with BV



BV, brentuximab vedotin; CR, complete response, CTCL, cutaneous T cell lymphoma; OS, overall survival; PFS, progression free survival

Sureda A, et al. Poster Presentation A-111. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Results – Safety Profile

- 4 patients experienced AEs related to BV retreatment, mainly peripheral sensory neuropathy (PSN).
- SAEs were reported in 3 patients (21.4%) corresponding to PSN, neutropenia and bacteraemia.
- No Grade 5 events were reported during retreatment.

AE, adverse event; BV, brentuximab vedotin; PSN, peripheral sensory neuropathy; SAE, serious adverse event

Sureda A, et al. Poster Presentation A-111. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

Author’s Conclusion

- The BELIEVE study is the first real word evidence study in Spain that assesses the role of BV as retreatment.
- BV retreatment seems to be a promising and tolerable treatment alternative for CTCL patients.

BV, brentuximab vedotin; CTCL, cutaneous T cell lymphoma

Sureda A, et al. Poster Presentation A-111. Presented at EORTC Cutaneous Lymphoma Tumour Group (EORTC-CLTG) 2024, Switzerland, October 9-11, 2024.

THE BELIEVE STUDY: Effectiveness and safety for re-treatment with brentuximab-vedotin in relapsed/refractory (r/r) Hodgkin lymphoma: A retrospective medical chart review in Spain. NCT:04998331

Sureda A, et al.
Abstract #P134

Anna Sureda-Balari[1], Ramón García-Sanz [2] (co-authors), Eva Domingo-Domenech[1], Francisco J. Capote[3], Antonio Gutierrez[4], Antonia Rodriguez[5], Marta Grande[6,7], and Lourdes Baeza-Montañez[6].

1. Institut Catala D'oncologia, Hospital Duran i Reynals. IDIBELL. L'Hospitalet de Llobregat, Barcelona, Spain; 2. Hospital Universitario Gregorio Marañon, Madrid, Spain; 3. Hospital Universitario Puerta del Mar, Cádiz, Spain; 4. Hospital Son Espases IdISBa, Palma de Mallorca, Spain; 5. Hospital Universitario 12 de Octubre, Madrid, Spain; 6. Medical Department, Takeda Farmacéutica España S.A, Madrid, Spain; 7. Universidad de Alcalá, Alcalá de Henares, Madrid, Spain.

Sureda A, et al. Poster Presentation P134. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Introduction and Methods

Introduction

- Brentuximab vedotin (BV) is a CD30-directed antibody-drug conjugate.
- Its efficacy in patients with CD30+ R/R malignancies has been shown in pivotal studies but limited data on R/R patients receiving BV retreatment showed promising clinical outcomes but no standard salvage treatment is in place2-4.
- The aim of this study was: **to describe effectiveness and safety of BV retreatment in R/R CD30+ classical Hodgkin lymphoma (cHL) patients in Spain.**

Methods

- The **BELIEVE study** is a noninterventional, retrospective chart review conducted in 30 Spanish sites (2014-2022).
- Adult patients with CD30+ malignancies including cHL, systemic anaplastic large cell lymphoma and cutaneous T cell lymphoma (primary cutaneous anaplastic large cell lymphoma and mycosis fungoides) treated with BV (evidence of objective response, OR) and having received ≥2 doses of BV as retreatment were included.
- Follow up was up to ≥6 months, treatment discontinuation due to death, or toxicity.

BV, brentuximab vedotin; CD30, cluster differentiation 30; cHL, classical Hodgkin Lymphoma; OR, objective response R/R, relapsed/refractory

Sureda A, et al. Poster Presentation P134. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results – Baseline Characteristics

- Of 43 patients included, 16 had cHL.

	cHL patients n=16
Mean age, years (SD)	36.2 (13.3)
Male, %	56.2%
Disease stage at BV retreatment, n	
Stage I	1
Stage II	5
Stage III	2
Stage IV	5
Missing	3
ECOG PS grade 0-1, %	90%
Treatments between the first course of BV and BV retreatment, n(%) Median number of lines, n (range)	13 (81.2%) 1 (1-5)
Transplants after first BV treatment, n 1 autologous transplant 2 autologous transplants in tandem 1 allogenic transplant	 4 1 5
Allogenic transplants after BV retreatment, n	4

BV, brentuximab vedotin; cHL, classical Hodgkin lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Score

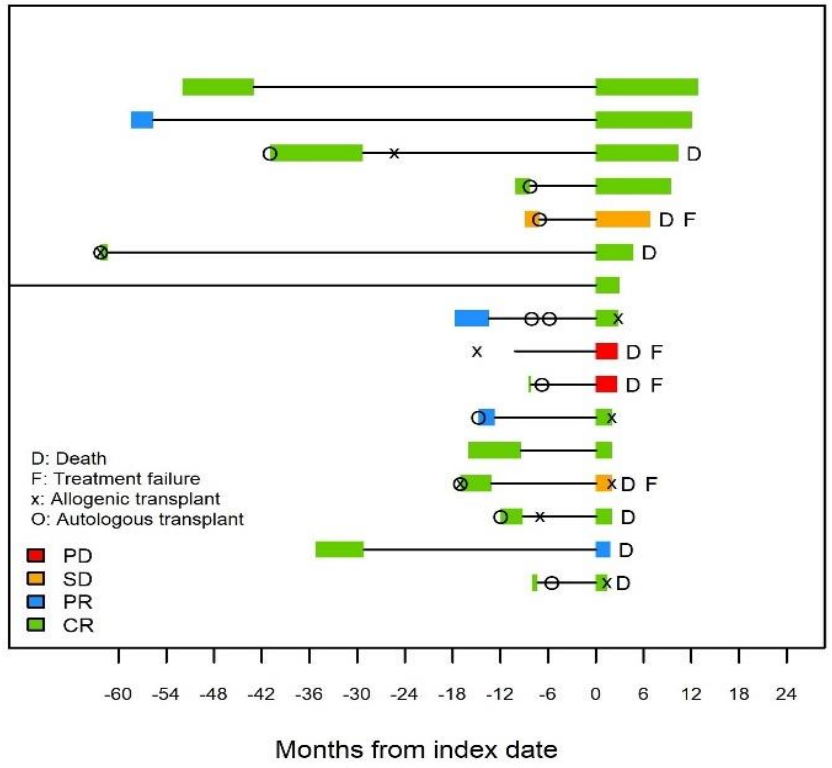
Sureda A, et al. Poster Presentation P134. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results – Efficacy

- The median number of cycles during the first treatment with BV was 4 (2-16) and 4.5 (2-18) during retreatment, respectively. The median (SD) initial dose was 1.8 (0.2) mg/kg for first BV treatment and BV retreatment.

- OS was reported for 56.2% patients.
- After 24 months, 56.0% of patients died due to progression.
- ORR was 75.0%, 68.8% of patients achieved CR (n=11), 1 (6.2%) achieved PR and progression was observed in 2 patients (12.5%).

Duration of first course of BV and BV retreatment for cHL patients



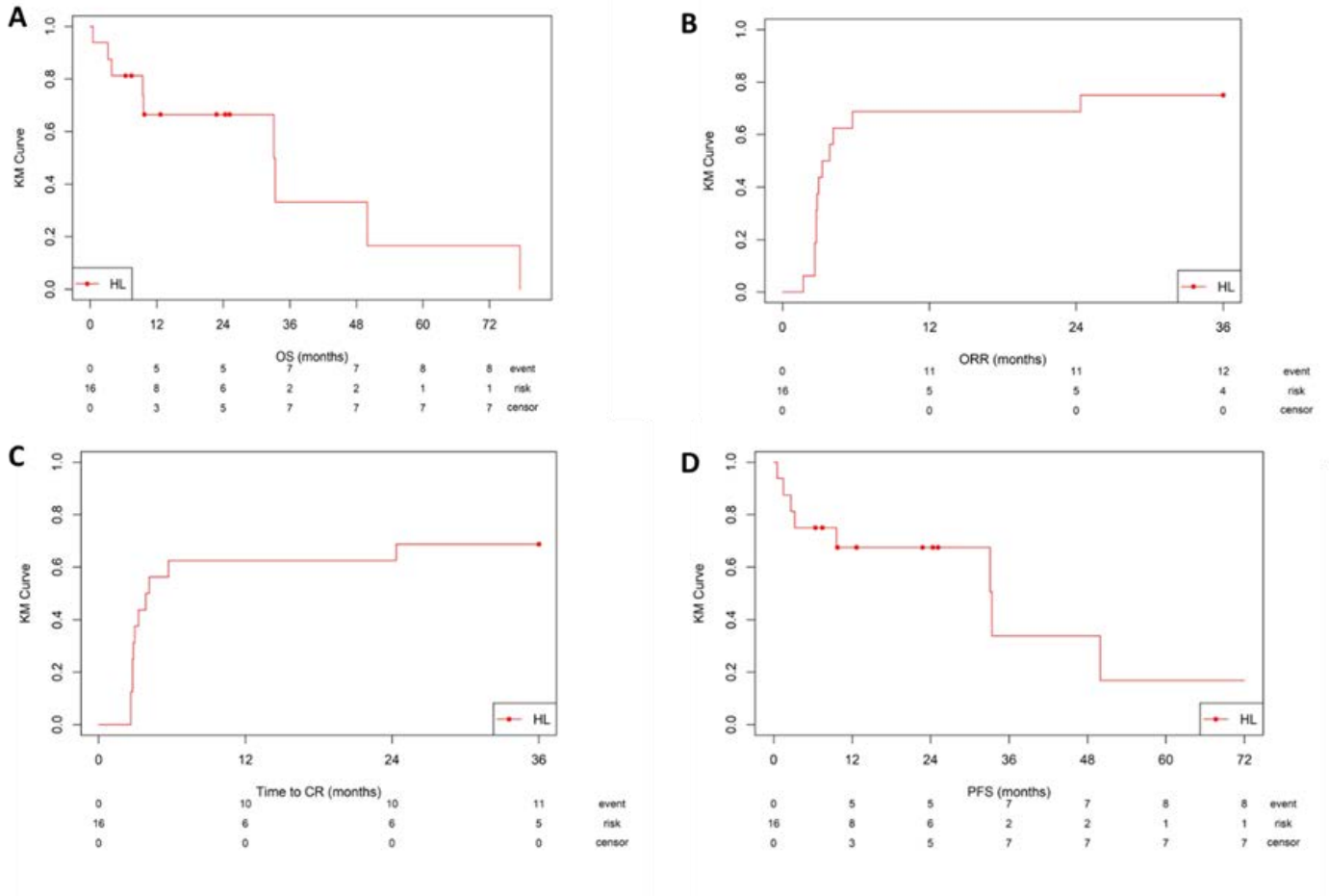
BV, brentuximab vedotin; CR, complete response; cHL, classical Hodgkin lymphoma; ORR, overall response rate; OS, overall survival; PR, partial response; PD, progressive disease; SD, stable disease

Sureda A, et al. Poster Presentation P134. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results – Efficacy

- Median OS was 33.1 months (0.5-77.5 months) with a median PFS of 9.6 months (0.5-77.5).
- Median time to achieve CR was 3 months.

Kaplan -Meier estimates of Overall Survival, time to OR, CR and PFS in cHL patients at retreatment with BV



BV, brentuximab vedotin; CR, complete response; OR, objective response; OS, overall survival; PFS, progression free survival

Sureda A, et al. Poster Presentation P134. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results – Safety Profile

- Regarding safety, 53.8% of patients presents AEs related to BV retreatment, mainly peripheral sensory neuropathy. 2 patients experienced SAEs (12.5%): peripheral motor and sensory neuropathy. No grade 5 events were reported during BV retreatment.

AE, adverse event; BV, brentuximab vedotin; SAE, serious adverse event

Sureda A, et al. Poster Presentation P134. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Authors' Conclusion

- The **BELIEVE study** is the first real word evidence study in Spain that assesses the role of BV as retreatment.
- BV retreatment seems to be a promising and tolerable treatment alternative for cHL patients.
- Safety results were manageable with dose modification or interruption.

BV, brentuximab vedotin; cHL, classical Hodgkin Lymphoma

Sureda A, et al. Poster Presentation P134. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Brentuximab Vedotin Exposure and Long-Term Efficacy Analysis in Patients With Classical Hodgkin Lymphoma: Analysis of the Phase 3 ECHELON-1 Study

Zhang Z, et al.
Abstract #P008

Zufei Zhang,[1]* Daping Zhang,[1] * Fei Jie,[1] Keenan Fenton,[1] Evelyn Rustia,[1] Consuelo Glenn,[1] Michelle Fanale,[1] Tatyana Feldman,[2] Stephen Ansell,[3] Yen Lin Chia [1]

[1] Pfizer, Bothell, WA, USA; [2] John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ, USA; [3]Mayo Clinic, Rochester, MN, USA

*Both authors contributed equally.

Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Background

- BV is a CD30-directed antibody-drug conjugate approved for multiple cancer types, including previously untreated advanced or metastatic cHL
- In the phase 3 ECHELON-1 (NCT01712490) study, BV combination vs ABVD (A+AVD vs ABVD) showed superior OS (hazard ratio), 0.59; 95% CI, 0.40-0.88;P=0.009) in patients with previously untreated stage III or IV cHL
  - BV dose adjustments, including dose modifications (eg, reduction, delay) and discontinuations, were recommended for managing AEs, including PN
- Here, we evaluated the impact of dose adjustments on efficacy and safety outcomes from the ECHELON-1 study

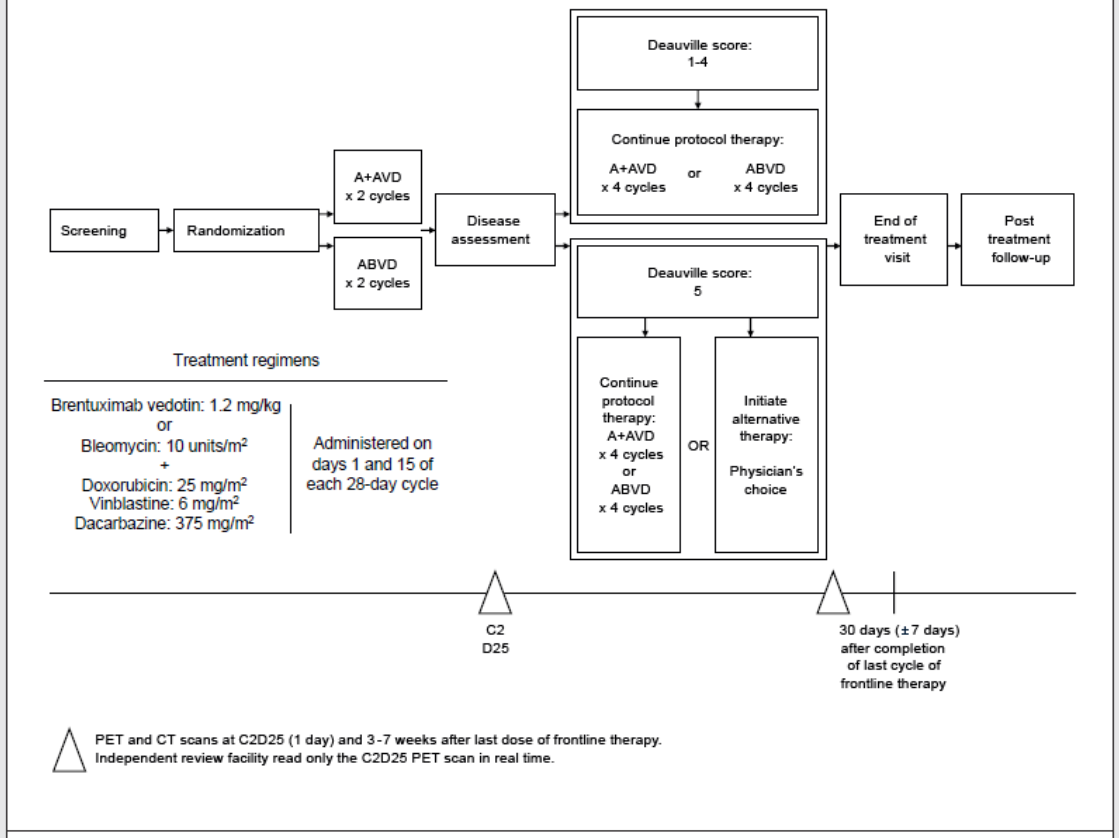
A+AVD, brentuximab vedotin, doxorubicin, vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; AE, adverse event; BV, brentuximab vedotin; CD30, cluster differentiation 30; cHL, classical Hodgkin Lymphoma; OS, overall survival; PN, peripheral neuropathy; R/R, relapsed/refractory

Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Methods

- The study design of ECHELON-1, which was used for this analysis, is presented in Figure 1
- This analysis included patients who received ≥1 dose of BV and had evaluable BV pharmacokinetic (PK) data (n=661)
  - Exposure-response (ER) analyses were developed to characterize the relationship between exposure and efficacy or safety endpoints
  - Time-averaged BV exposures up to an event of interest (C_{avg}) were estimated via a validated population PK model and used for ER analyses
  - Survival benefits (OS, PFS) were stratified by BV C_{avg} using Kaplan-Meier curves to identify any underlying relationships; a univariate Cox proportional hazards model was used to assess the significance of relationships between OS or PFS and C_{avg}
  - A logistic regression model was used to assess the relationship between percentage of subjects with PN and BV exposure. The effects of clinically relevant covariates (body weight and BMI) on PN incidence were explored

Figure 1. Study Schema



A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine; ABVD, bleomycin in combination with doxorubicin, vinblastine, and dacarbazine; BV, brentuximab vedotin; C2D25, cycle 2 day 25; CT, computed tomography; PET, positron emission tomography.

BV, brentuximab vedotin; BMI, body mass index; ER, exposure-response; OS, overall survival; PFS, progression free survival; PK, pharmacokinetic; PN, peripheral neuropathy;

Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results

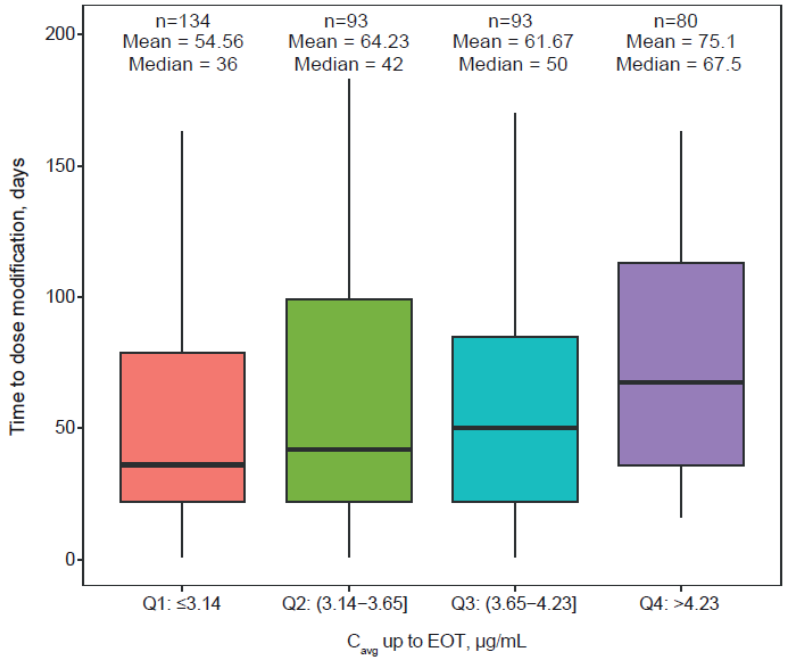
- Of 661 patients, 60.5% had BV dose modifications, and 11.0% discontinued BV (Table 1)
- Patients in the A+AVD group with lower BV C_{avg} had higher dose modification rates and shorter time to dose modification (Figure 2), with similar treatment duration across exposure quartiles, suggesting that patients continued to benefit from BV despite protocol-defined dose adjustments for AE management

Table 1: Summary of BV Dose Intensity, Dose Adjustments, and Survival Outcomes by BV C_{avg} Quartiles

	A+AVD BV C_{avg} quartiles				A+AVD (n=661)	ABVD (n=659)
	Q1	Q2	Q3	Q4		
BV relative dose intensity, median (range), %[a]	97.8 (39.3-107.5)	99.7 (16.7-110.2)	99.7 (45.4-114.3)	99.0 (41.7-108.5)	99.5 (16.7-114.3)	NA
Treatment duration, median (range), weeks[a,b]	25.0 (2.0-35.0)	24.6 (2.0-34.1)	24.1 (2.0-32.3)	24.0 (2.0-31.9)	24.1 (2.0-35.0)	NA
BV dose modifications, % (events/n)[a]	81.2 (134/165)	57.1 (93/163)	55.7 (93/167)	48.2 (80/166)	60.5 (400/661)	NA
BV dose discontinuation, % (events/n)[a]	13.9 (23/165)	11.7 (19/163)	6.6 (11/167)	12 (20/166)	11.0 (73/661)	NA
6-year OS rate (95% CI), %	92.2 (86.7-95.5)	92.0 (86.2-95.4)	96.3 (91.1-98.5)	94.9 (90.1-97.4)	93.9 (91.6-95.5)	89.4 (86.6-91.7)
6-year PFS rate (95% CI), %	82.8 (75.9-87.9)	78.1 (70.1-83.9)	85.4 (78.9-90.1)	82.5 (75.7-87.6)	82.3 (79.0-85.0)	74.5 (70.8-77.8)

A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine; ABVD, bleomycin in combination with doxorubicin, vinblastine, and dacarbazine; BV, brentuximab vedotin; C_{avg}, time-averaged brentuximab vedotin exposures up to an event of interest; NA, not applicable; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; PN, peripheral neuropathy; Q, quartile.
[a]Included all patients randomized to the A+AVD arm who received ≥1 BV dose and had evaluable PK data (n=661). BV exposure quartiles were based on on-treatment C_{avg} of the BV active analyte: Q1, ≤3.14 µg/mL (n=165); Q2, >3.14 to ≤3.65 µg/mL (n=163); Q3, >3.65 to ≤4.23 µg/mL (n=167); and Q4, >4.23 µg/mL (n=166).
[b]Intended treatment duration was 24 weeks, consisting of six 28-day cycles.

Figure 2: Time to Dose Modifications Stratified by C_{avg} Quartiles



C_{avg}, time-averaged brentuximab vedotin exposures up to an event of interest; EOT, end of treatment.

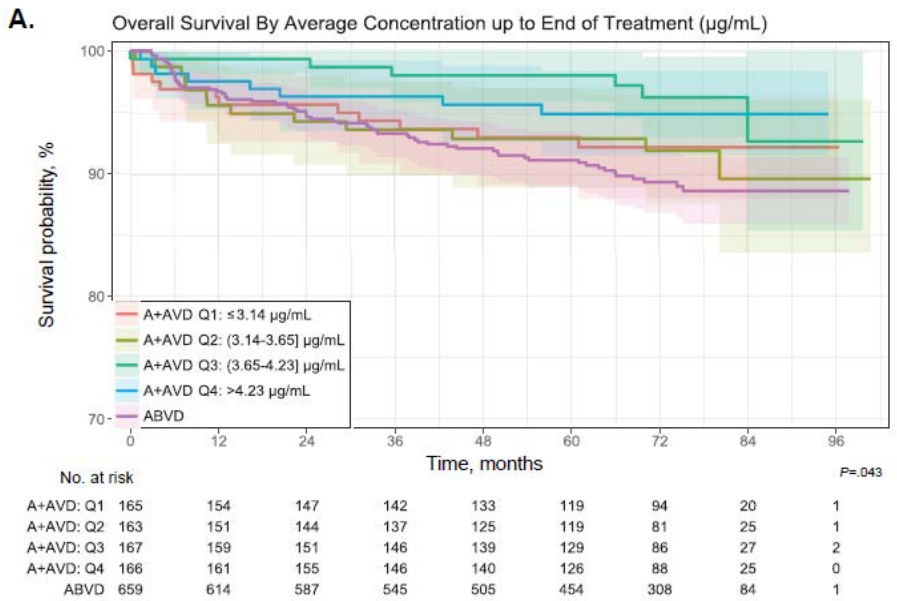
A+AVD, brentuximab vedotin, doxorubicin, vinblastine and dacarbazine; AE, adverse event; BV, brentuximab vedotin

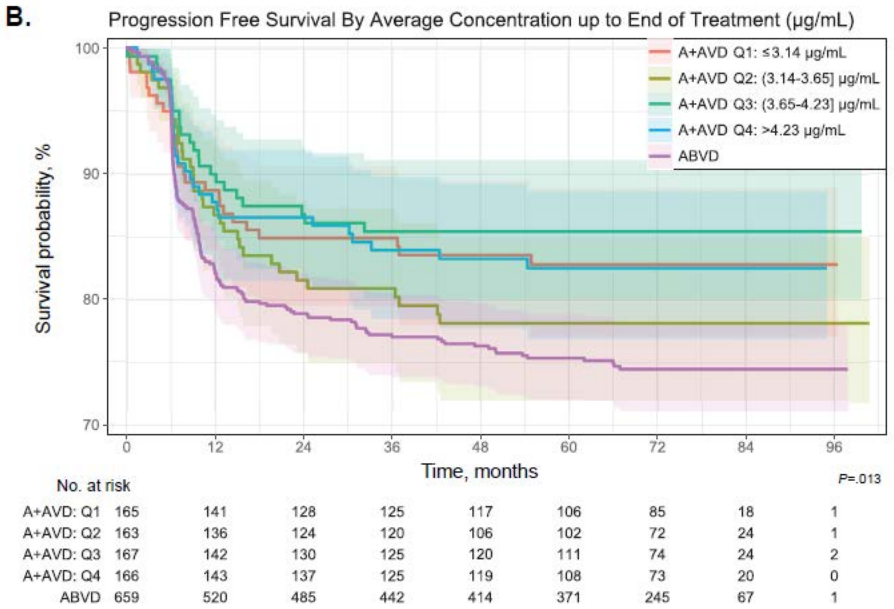
Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results

- Long-term OS (Figure 3A) and PFS (Figure 3B) benefits were observed with A+AVD in all BV C_{avg} exposure quartiles vs ABVD despite dose adjustments

Figure 3: Kaplan-Meier Curves of (A) OS and (B) PFS Stratified by C_{avg} Quartiles





A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine; ABVD, bleomycin in combination with doxorubicin, vinblastine, and dacarbazine; C_{avg}, time-averaged brentuximab vedotin exposures up to an event of interest; EOT, end of treatment; Q, quartile.

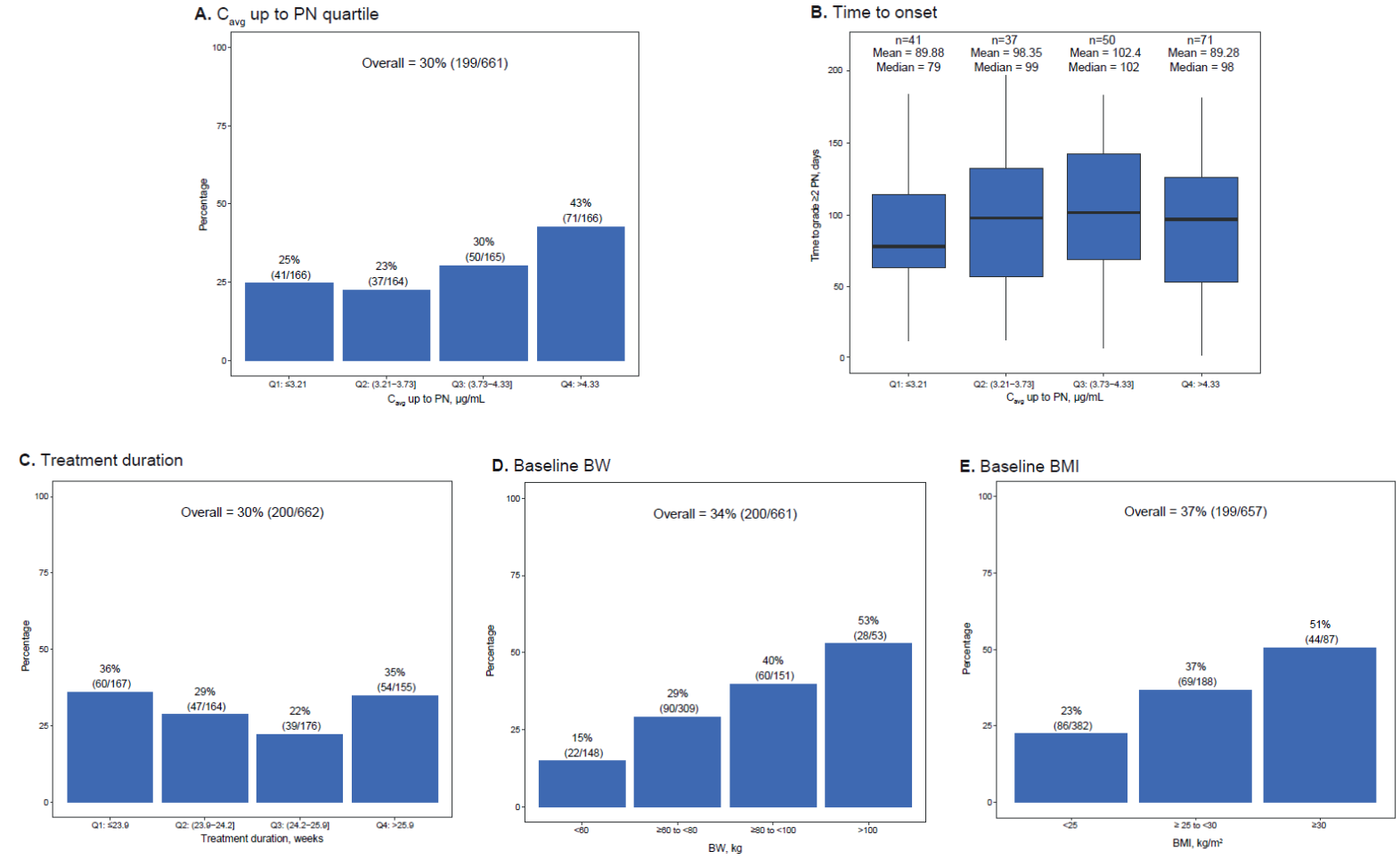
A+AVD, brentuximab vedotin-doxorubicin, vinblastine and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; BV, brentuximab vedotin; OS, overall survival

Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results

- In patients with higher C_{avg} up to PN, higher incidences of grade ≥2 PN were observed with similar times to onset in the highest 3 C_{avg} quartiles and shortest time to onset in the lowest quartile (Figure 4A, 4B)
- The observed incidence rate of grade ≥2 PN was similar across BV treatment duration quartiles (Figure 4C)
- The incidence of grade ≥2 PN incidences was higher in patients with higher body weight (Figure 4D) and body mass index (Figure 4E)
    - Prior analyses showed that BV exposure increased with body weight

Figure 4: Incidence and Time to Onset of Grade ≥ PN Subgroup Analysis



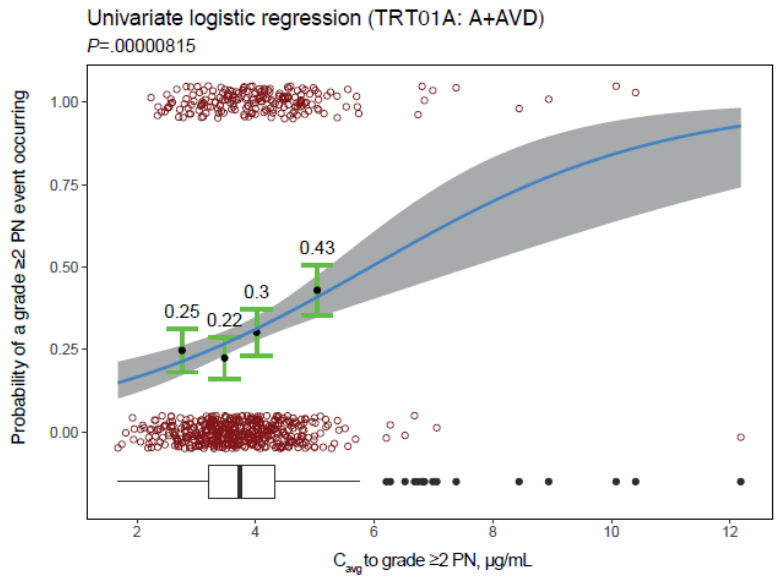
BMI, body mass index; BV, brentuximab vedotin; BW, body weight; C_{avg}, time-average BV exposures up to an event of interest; PN, peripheral neuropathy

Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Results

- Univariate logistic regression analysis showed that the probability of experiencing grade ≥2 PN increased with higher C_{avg} (Figure 5)

Figure 5: Exposure-Response Univariate Logistic Model between C_{avg} and Probability of Grade ≥2 PN[a]



A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine; C_{avg}, time-averaged brentuximab vedotin exposures up to an event of interest; PN, peripheral neuropathy.
*The observed values (0=no event, 1=event) are represented as maroon open circles on the plot. The observed probabilities and associated 90% CI are overlaid as filled circles and error bars, binned by exposure quartiles. Gray band represents the 5th–95th percentile CI of the fit.

- The consistent OS benefit observed in patients with and without grade ≥2 PN, along with data on PN resolution or improvement at end of treatment and last follow up (Table 2), indicates that dose modifications in ECHELON-1 were able to manage PN events while retaining efficacy

Table 2: Resolution or Improvement of PN

	A+AVD (n=442)[a]	ABVD (n=286)[a]
At end of treatment, n (%)		
Resolution of or improvement in PN events	226 (51)	174 (61)
Resolution of all PN events	122 (28)	139 (49)
Ongoing grade ≥2 PN events	133 (30)	42 (15)
At last follow up, n (%)		
Resolution of or improvement in PN events	295 (67)	214 (75)
Resolution of all PN events	191 (43)	174 (61)
Ongoing grade ≥2 PN events	91 (21)	32 (11)

A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine; ABVD, bleomycin in combination with doxorubicin, vinblastine, and dacarbazine; PN, peripheral neuropathy.
*Patients with ≥1 treatment-emergent PN event.

OS, overall survival; PN, peripheral neuropathy

Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

Authors' Conclusions

- At 6 years of follow-up, brentuximab vedotin (BV) in combination with doxorubicin, vinblastine, and dacarbazine (A+AVD) showed a survival benefit and manageable safety profile compared with bleomycin in combination with doxorubicin, vinblastine, and dacarbazine (ABVD) in patients with previously untreated stage III or IV classical Hodgkin Lymphoma (cHL)
- Dose modifications were commonly used to manage adverse events (AEs)
  - Treatment completion was reported in 89% of patients with A+AVD and 91% of patients with ABVD
- A+AVD showed a long-term progression-free survival (PFS) and overall survival (OS) benefit compared with chemotherapy across BV exposure quartiles
  - Patients continued to have greater benefit from BV vs chemotherapy despite protocol-specified dose adjustments for AE management
- Higher incidences of grade ≥2 peripheral neuropathy (PN) were observed in higher BV exposure quartiles, but recommended dose adjustments were effective for AE management

Zhang Z, et al. Poster Presentation P008. Presented at Internation Symposium on Hodgkin Lymphoma (ISHL) 2024, Germany, October 26-28, 2024.

PET-Guided BrECADD in Older Patients with Advanced-Stage Classic Hodgkin Lymphoma:

Results from a Phase 2 Part of the GHSG HD21 Trial

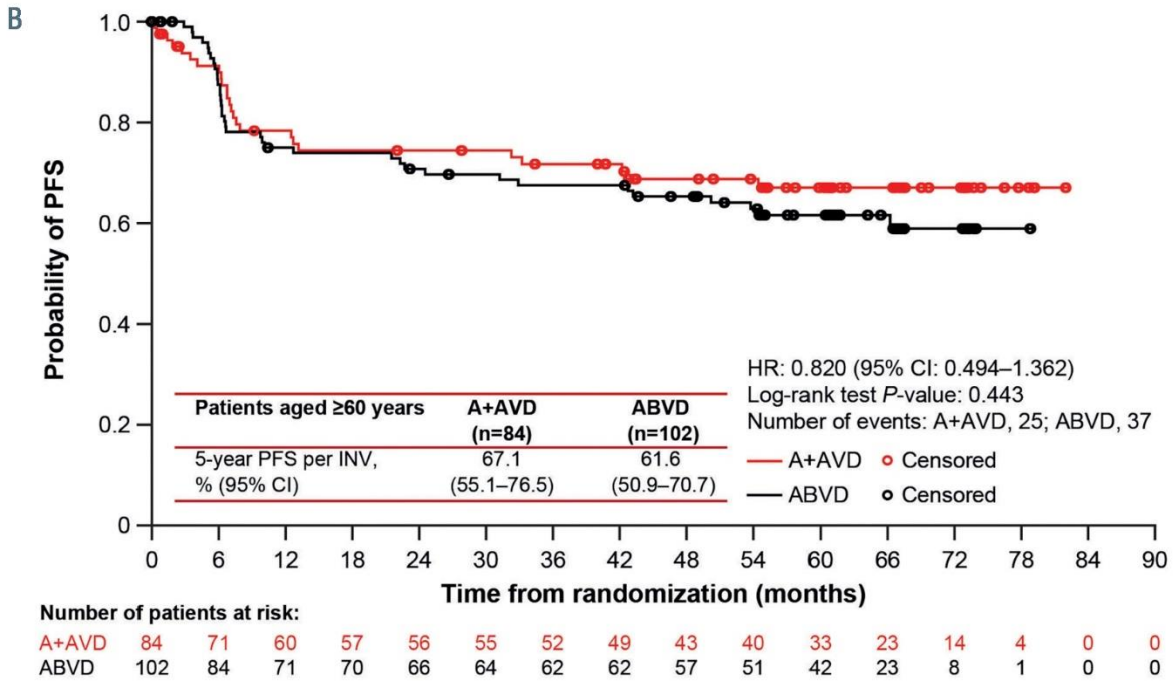
Justin Ferdinandus, Helen Kaul, Alexander Fosså, Andreas Hüttmann, Felix Keil, Yon-Dschun Ko, Felicitas Hitz, Michaela Schwarz, Corinna Trenker, Andrea Kerkhoff, Peter Staib, Kai Wille, Irmgard Dresel, Dennis Hahn, Bernd Hertenstein, Peter Moosmann, Ulrich Mey, Stefan Balabanov, Tasman Armytage, Fernando Roncolato, Johannes C. Hellmuth, Stefanie Kreissl, Michael Fuchs, Gundolf Schneider, Hishan Tharmaseelan, Dennis A. Eichenauer, Bastian von Tresckow, Peter Borchmann, Paul J. Bröckelmann on behalf of GHSG HD21 Investigators

Background

Treatment of advanced-stage Hodgkin Lymphoma (AS-cHL) evolved with novel agents like Brentuximab Vedotin (BV).

Older patients did not benefit significantly from recent improvements.[1] BEACOPP not feasible with a treatment-related mortality of approx. 15% in this group.[2]

PET-guided BrECADD is more tolerable compared to eBEACOPP[3], raising the question of its feasibility for older patients.



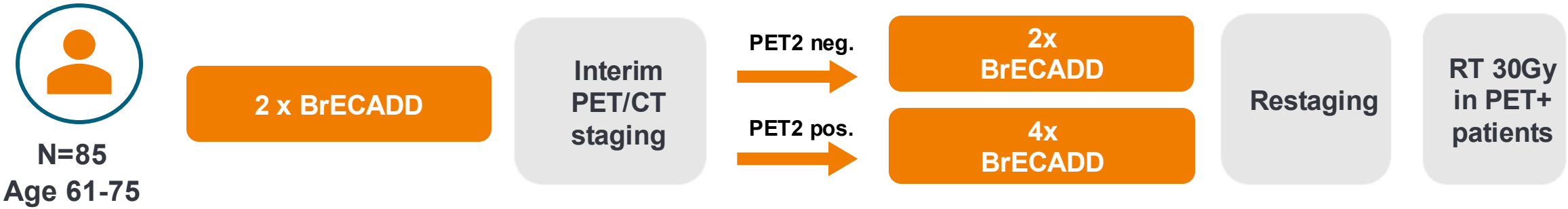
➢ **High unmet need for effective treatment options in patients with AS-cHL older than 60 years.**

GHSG

1 Evens, AM et al., Hemasphere 2022
2 Wongso, D et al., JCO 2013
3 Borchmann, P et al., Lancet, 2024

Study Design: GHSG HD21 Older Cohort

Prospective, international, multicenter, single-arm add-on cohort to the HD21 trial



Trial objectives

- Primary: Estimate efficacy of PET-guided BrECADD defined as CR rate after chemotherapy (primary endpoint).
- Secondary: Further explore efficacy, safety and feasibility of PET-guided BrECADD in older patients.

GHSG

Baseline Characteristics

ITT population (n=83)

Characteristic		No. (%)
Age	Median (IQR, range)	67 (63 – 70, 61 – 75)
Sex	Female	32 (39)
	Male	51 (61)
CIRS-G Sum Score	Mean (SD)	3.7 (2.7)
	Median (range)	3 (0 – 10)
Comorbidities	Absent	11 (13)
	Present	72 (87)
ECOG	0	39 (47)
	1	29 (35)
	2	15 (18)
Ann Arbor Stage	II	3 (4)
	III	35 (42)
	IV	45 (54)
IPS	0-2	22 (27)
	3-7	61 (73)
Histologic subtype	Nodular sclerosis	20/66 (30)
	Mixed cellularity	17/66 (26)
	Lymphocyte depleted	1/66 (3)
	Lymphocyte-rich	1/66 (2)
	other cHL	1/66 (3)
	cHL unspecified	25/66 (38)

Summary

83 patients with a median age of 67 years (range: 61-75) were included in the ITT cohort.

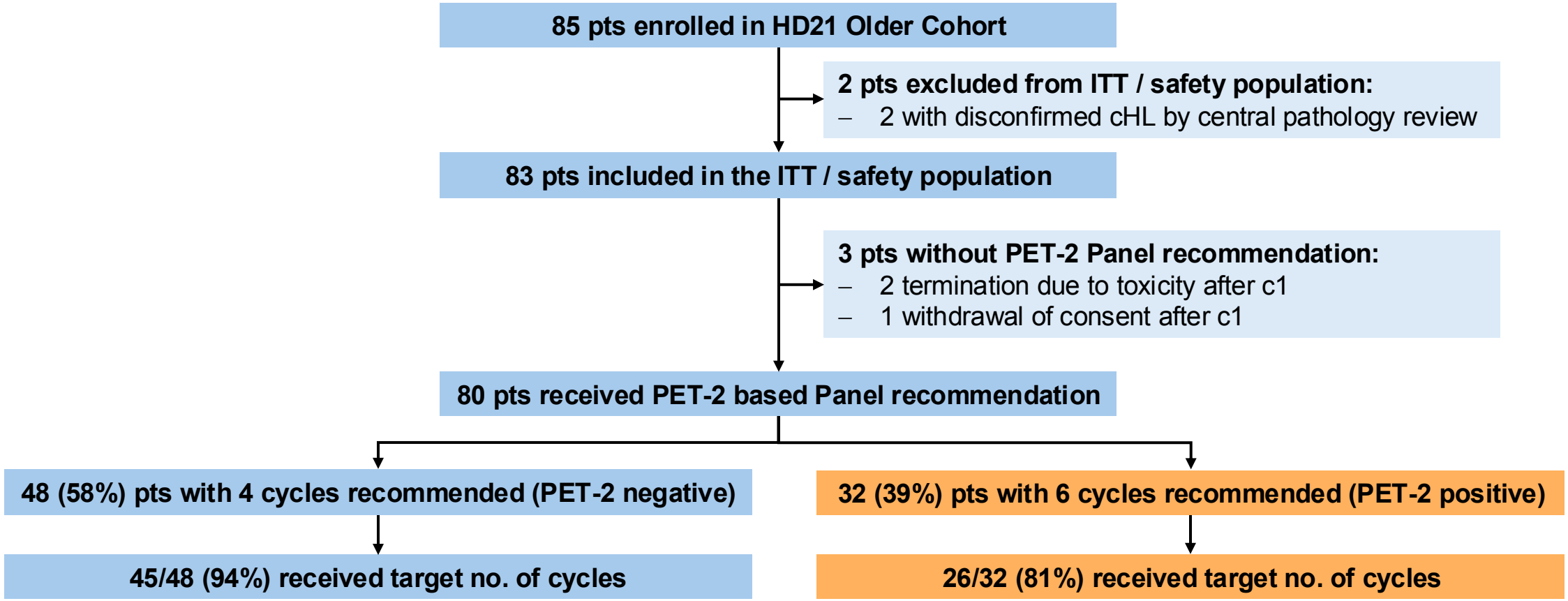
A majority had stage IV (54%), B-symptoms (76%) and an IPS ≥3 (73%) and presented with comorbidities (87%).

Mean Cumulative Illness Rating Scale-Geriatric (CIRS-G) score of 3.7 (SD 2.6).

- **Older patients with comorbidities were enrolled.**
- **CIRS-G suggests relatively good fitness compared to literature.[1-2]**

1 Evens, AM et al., JCO 2018
2 Wilson, MR et al., Br J Hem 2023

Trial flowchart



- High treatment completion rate, especially in PET-2 negative patients.
- A majority of patients achieved CR in PET2 and was scheduled for 4 cycles of BrECADD.

GHSG

Adverse Events

ITT population (n=83)

Most common toxicities were hematologic, incl. anemia (69%) and thrombocytopenia (86%).

Neutropenic fever occurred in 46 (55%) patients.

Sensory peripheral neuropathy (PN) was observed in 33 (40%) of patients, with 10 (12%) patients experiencing grade ≥ 2 neuropathy.

Any Treatment-related morbidity (TRMB) event[1] was reported in 66 (80%) patients (95% CI: 69-88).

- **More AEs compared to younger patients.**
- **PN rate comparable to ABVD.[2]**

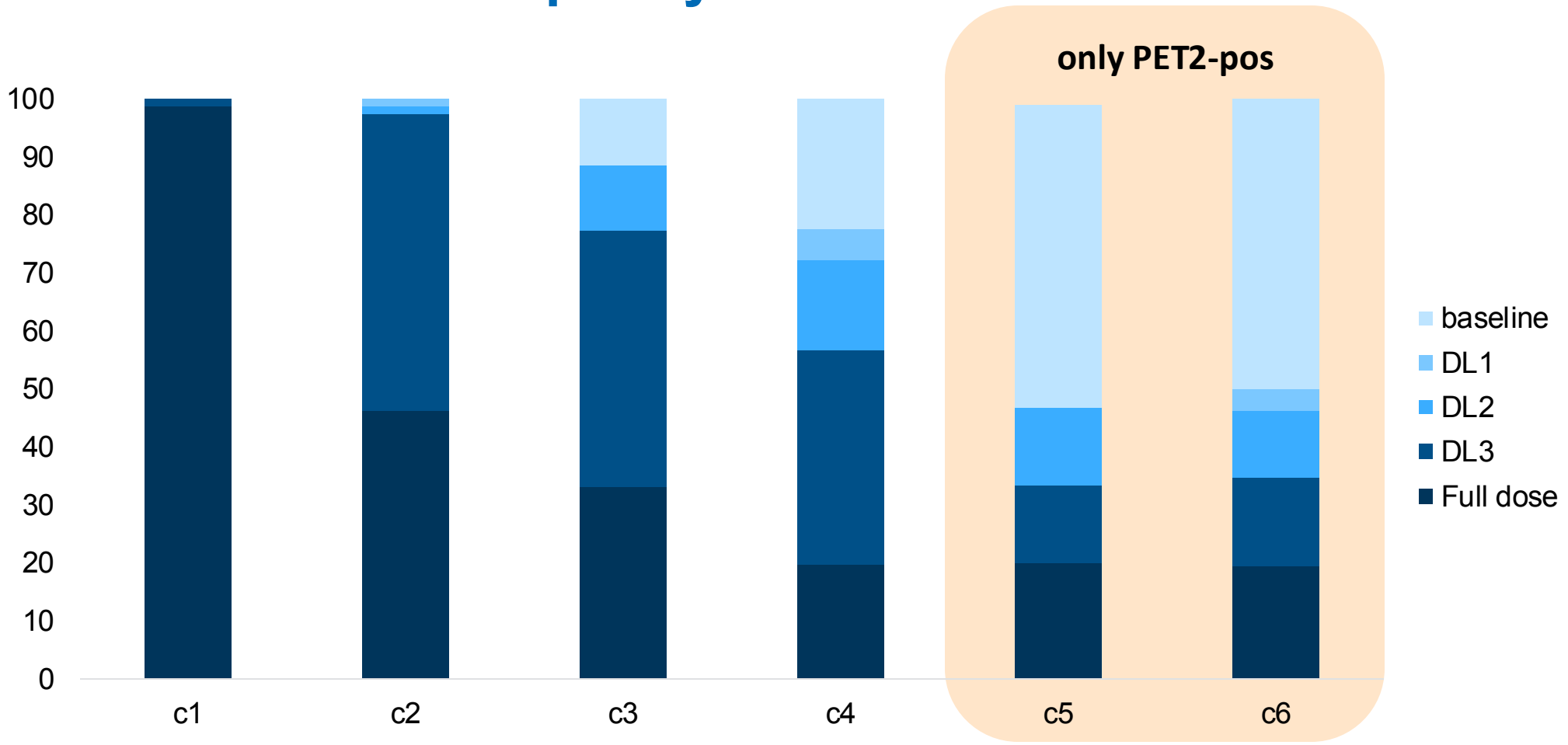
Adverse event*	Any Grade (%)	Grade ≥ 3 (%)
Anemia	81 (98)	57 (69)
Thrombocytopenia	78 (94)	71 (86)
Leukopenia	81 (98)	80 (96)
Neutropenic fever	46 (55)	46 (55)
Infection	55 (65)	39 (47)
Cardiac disorders	23 (28)	2 (2)
Gastrointestinal disorders	60 (72)	19 (23)
Nausea	30 (36)	4 (5)
Mucositis	47 (57)	14 (17)
Peripheral sensory neuropathy**	33 (40)	1 (1)
Nervous system disorder (other than neuropathy)	24 (29)	3 (4)
Renal and urinary disorders	12 (15)	3 (4)
Respiratory, thoracic and mediastinal disorders	37 (45)	5 (6)
Skin and subcutaneous tissue disorders	35 (42)	1 (1)
Hematological TRMB event (%)	60 (72)	
Organ TRMB event (%)	28 (34)	
Any TRMB event (%)	66 (80)	

* Frequency ≥10%, ** PNP G2 or higher in 11 (12%) pts, TRMB = Treatment-related morbidity

GHSG

1 Borchmann, P et al., Lancet, 2024
2 Evens, AM et al., Hemasphere 2022

Dose Levels of BrECADD per cycle



- Higher rate of per-protocol dose reductions compared to younger patients.
- However, most patients (87%) completed the target number of cycles

GHSG

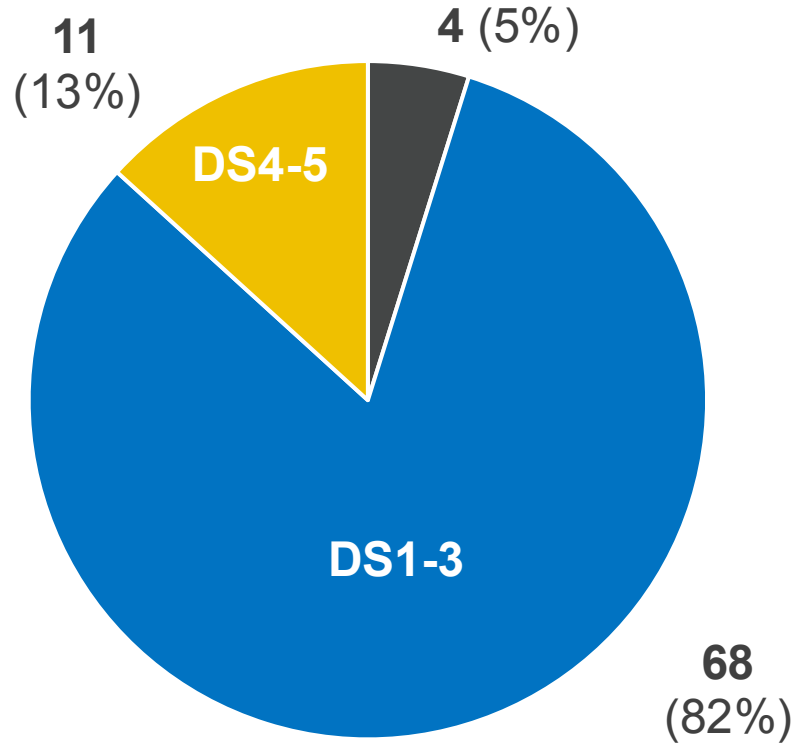
Primary Endpoint: Centrally Reviewed CR Rate after Chemotherapy

CR rate after Chemotherapy 68/83 (82%; 95%CI 72 – 90)

- 4 cycles: 45/48 (94%; 95%CI 83 – 99)
- 6 cycles: 23/32 (72%; 95%CI 53 - 86)

Non-CR due to:

- Non-CR (DS4-5) in RE-4/6 by central review (N=11)
- RE-4/6 not done & no interim response by central review (N=4)

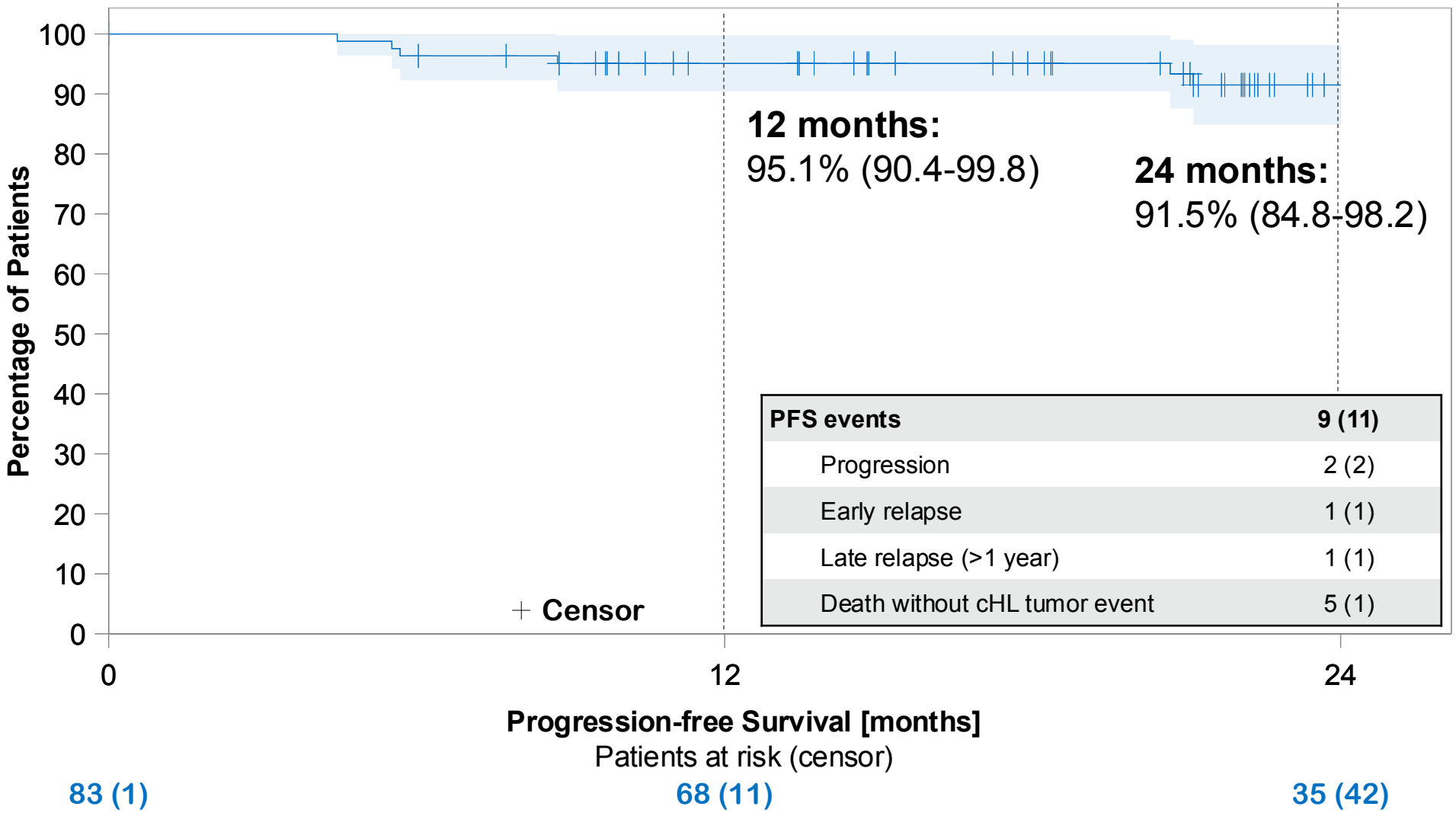


Most patients (82%) were in CR after receiving PET-guided BrECADD.

GHSG

Progression-free survival

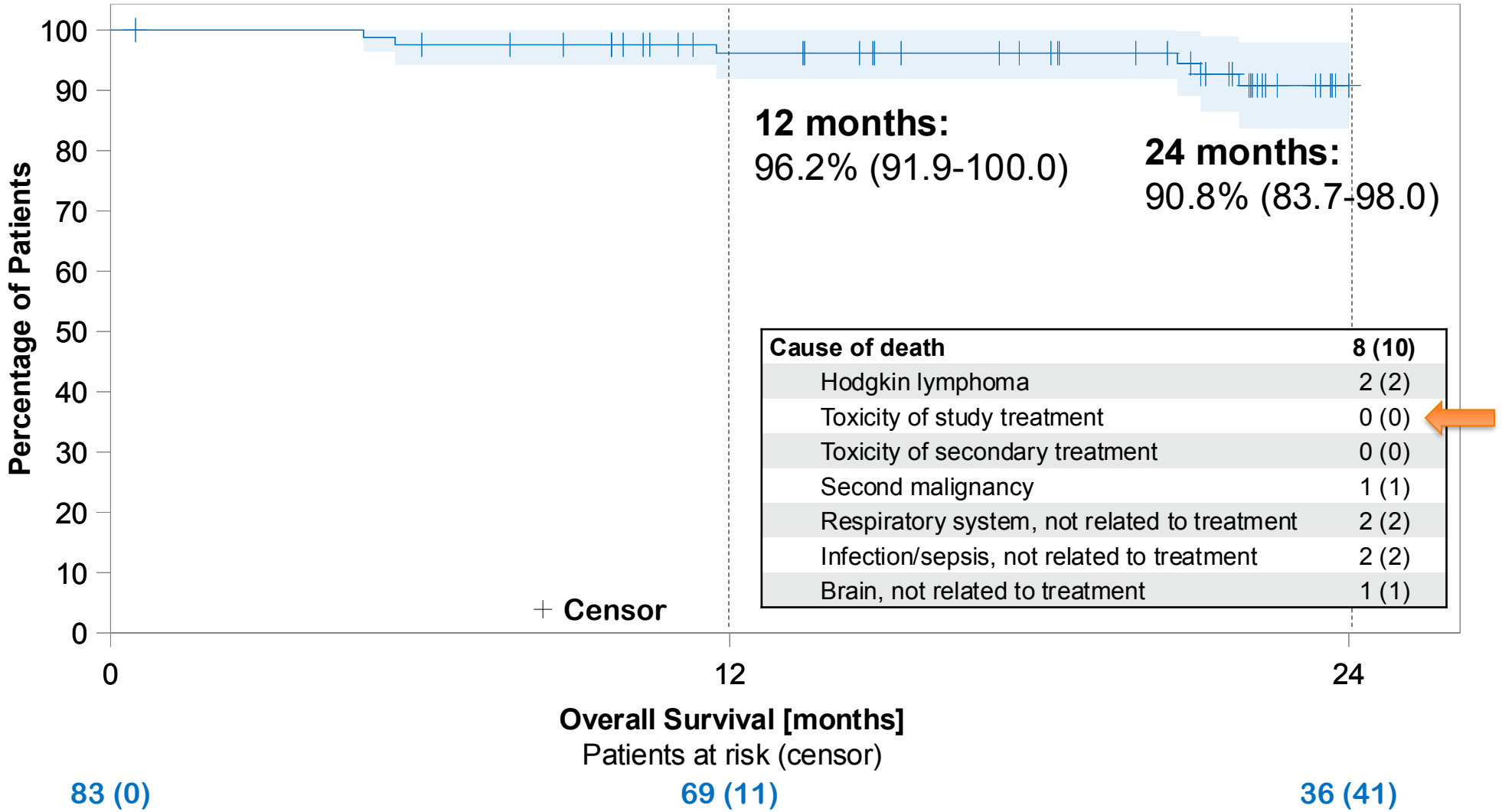
ITT population, mFU 23 months



GHSG

Overall survival

ITT population, mFU 24 months



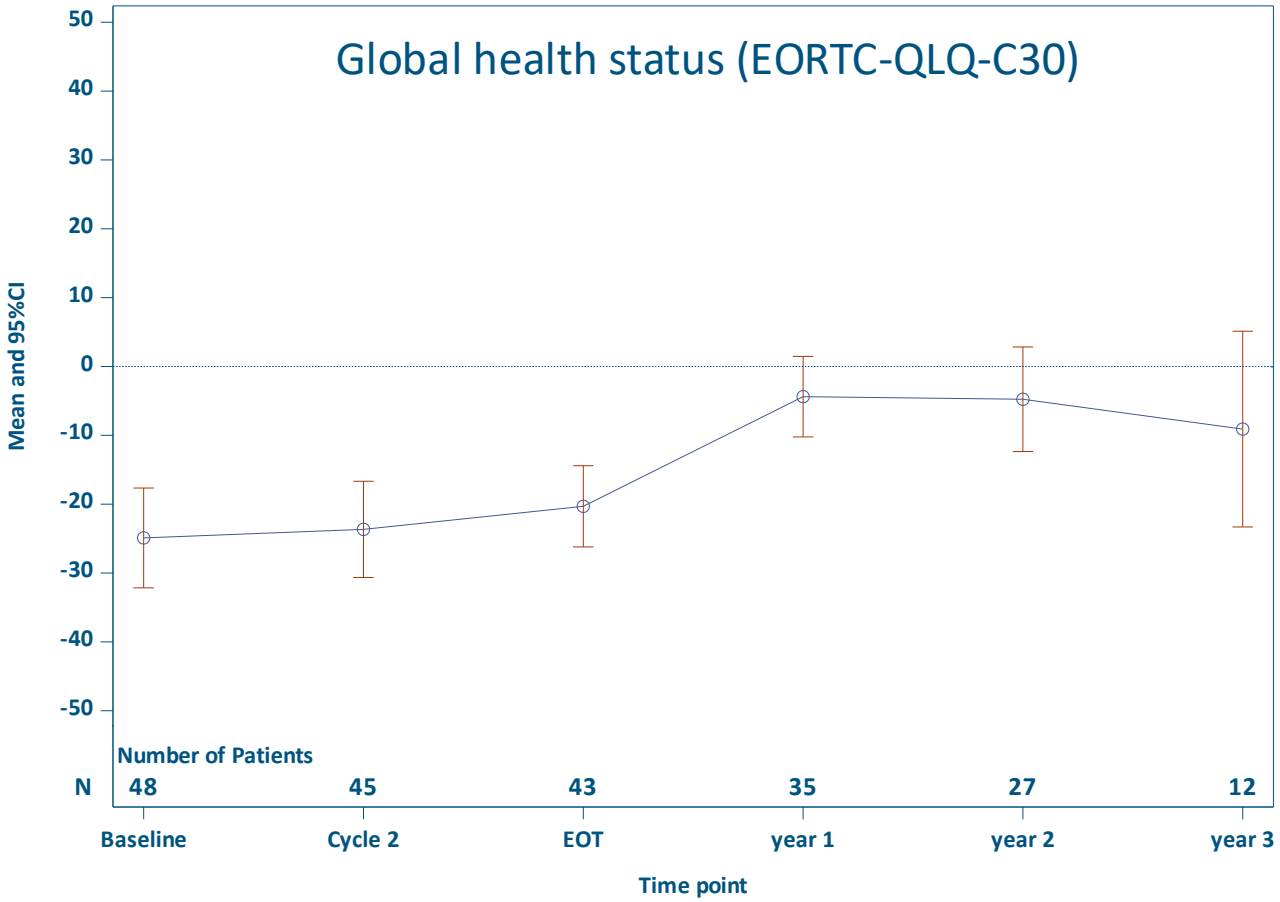
Cause of death	8 (10)
Hodgkin lymphoma	2 (2)
Toxicity of study treatment	0 (0)
Toxicity of secondary treatment	0 (0)
Second malignancy	1 (1)
Respiratory system, not related to treatment	2 (2)
Infection/sepsis, not related to treatment	2 (2)
Brain, not related to treatment	1 (1)

Patients at risk (censor)

0	12	24
83 (0)	69 (11)	36 (41)

GHSG

Patient reported outcomes (PROs)



Dedicated analysis of patient reported outcomes in patients providing separate consent to identify impact on health-related quality of life.

EORTC questionnaires (QLQ-C30, CIPN-20, FA12)

Sex- and age- adjusted differences to reference population of general health status:
Improvement after treatment

Similar improvements in terms of symptom- and functioning scales.

Patients reported normalization of global health status following treatment.

GHSG

Summary & Authors Conclusion

PET-guided BrECADD addresses an unmet need of older patients with AS-cHL:

- Although Treatment with BrECADD frequently requires dose adaptions, it is feasible also in this more vulnerable cohort of patients >60 years of age. No treatment-related mortality was observed.
- PET-guided BrECADD results in a high rate of complete and durable remissions
- The majority of patients (60%) requires only 4x BrECADD, resulting in an abbreviated treatment of only 12 weeks and reduced anthracycline exposure.
- Longitudinal QoL measures including General Health status return to normal after treatment.

The unprecedentedly high 2y-PFS rate above 90% encourages the use of PET-guided BrECADD as first-line treatment option for patients with AS-cHL between 61-75 years

GHSG

GELTAMO

Brentuximab Vedotin - ESHAP Significantly Increases the Metabolic Complete Remission Rate versus ESHAP in Relapsed Classical Hodgkin's Lymphoma. Final Results of the BRESELIBET Prospective Trial.

A. Sureda, J. Núñez Céspedes, MJ Terol, F. Hernández Mohedo, E. Domingo-Doménech, F. de la Cruz, M. Moreno, ME. Amutio, AP. González, R. Córdoba, C. Martínez, S. Romero, M. Bastos, A. Rodríguez, J. Briones, R. Greil, M. Casanova, A. Rubio, I. Avivi, R.I del Campo García, P. Gómez, T. Vassilakopoulos, S. Basic-Kinda, S. Papageorgiou, V. Noriega, JJ Sánchez Blanco, B. Sánchez, I. Zeberio, R. García Sanz.

ISHL13 Meeting, Cologne, Germany, October 2024

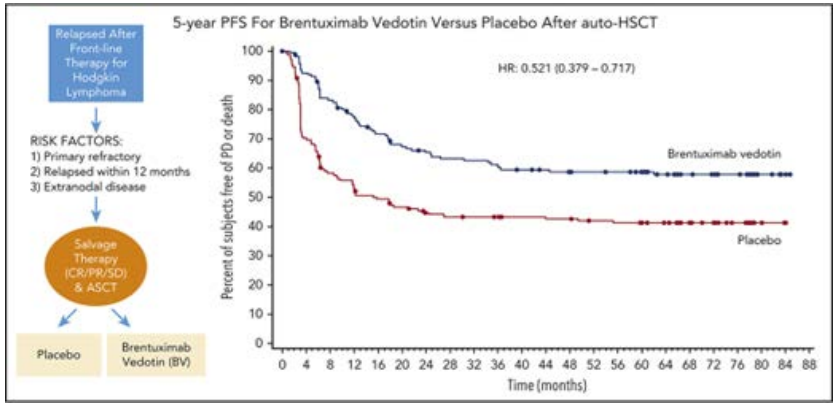
Introduction

- Autologous stem cell transplantation (auto-HCT) is still the standard of care for those patients with relapsed/refractory Hodgkin's lymphoma[1]
- Best salvage treatment strategy for these patients is still unknown
- Complete metabolic remission (mCR) before auto-HCT is the most important prognostic factor to guarantee long-term disease free survival after the procedure[2]
- Phase I/II prospective clinical trials indicate that the combination of brentuximab vedotin (BV) + chemotherapy is feasible and might be associated with a higher mCR rate than chemotherapy alone.[3-5] BRESHAP demonstrated a mCR of 70%[6]

[1] Snowden J et al, BMT 2022; [2] Moskowitz CH et al, Blood 2012; [3] LaCasce AS et al, Br J Haematol 2020;
[4] Kersten MJ et al, Haematol 2021; [5] Moskowitz AJ et al, Lancet 2015; [6] García Sanz R et al, Ann Oncol 2019

Introduction

- Consolidation with BV after auto-HCT has demonstrated to significantly increase progression free survival (PFS) after auto-HCT in patients with high-risk features in the setting of a randomized double blind prospective clinical trial (AETHERA Trial)[1]



- The potential substitution of auto-HCT by BV consolidation in “low-risk” patients has not been tested so far

[1] *Moskowitz CH et al, Blood 2018*

Sureda A et al, ISHL13

Study Design, Objectives, Consort Diagram

Key exclusion criteria:
- Lymphocyte predominant nodular HL
- Prior therapy with BV
- History of PN ≥2
- Prior malignancies

Key inclusion criteria:
- Adult patients (>18 years up to 65 years)
- Diagnosis of cHL
- Primary refractory or 1st relapse (early or late relapse)
- Measurable disease at the time of enrollment
- ECOG 0–2
- Adequate 'standard' laboratory values
- Written informed consent

Primary objective:
- mCR rate after 3 cycles of ESHAP vs BV-ESHAP
- Feasibility of BV consolidation after attaining mCR with second-line therapy

Secondary objectives:
- 2-yr PFS, OS, DOR, TTP
- Hematological and extra-hematological toxicities
- Stem cell collection yield
- QoL

BRESELIBET (ClinicalTrials.gov ID: NCT04378647)

Sureda A et al, ISHL13

Clinical Characteristics of the Patients at the Study Entry (n = 151)

	BRESHAP (n=76)	ESHAP (n=75)	P value
Age (years), median (range)	39 (18-63)	38 (18-65)	0.72
Sex (M/F) (%)	43 (56.6) / 33 (43.4)	45 (60) / 30 (40)	0.67
Histological subtype (%) Nodular sclerosis / Mixed cellularity Lymphocyte depletion / Lymphocyte rich Unclassifiable	 41 (53.9) / 15 (19.7) 1 (1.3) / 3 (3.9) 10 (13.2) / 6 (7.9)	 46 (61.3) / 9 (12) 2 (2.7) / 4 (5.3) 7 (9.3) / 5 (6.6)	0.46
ABVD – based 1L therapy (%)	74 (97.3)	71 (94.6)	0.88
Disease status at study entry (%) Primary refractory dosease Early relapse Late relapse	 28 (36.8) 18 (23.7) 30 (39.5)	 25 (33.3) 26 (34.7) 24 (32.0)	0.31
Ann Arbor Stage (%) I-II / III-IV	 34 (44.7) / 42 (55.3)	 38 (50.7) / 37 (49.3)	0.46
B symptoms (%)	17 (22.4)	20 (26.7)	0.53
Bulky disease (%)	8 (10.5)	5 (6.7)	0.39
Extranodal disease (%) No site / 1 site / > 1 site	 49 (64.5) / 20 (26.3) / 7 (9.2)	 45 (60) / 13 (17.3) / 17 (22.7)	0.055
ECOG Performance Status 0-1 (%)	74 (97.4)	74 (98.7)	> 0.99

M. Male; F. Female

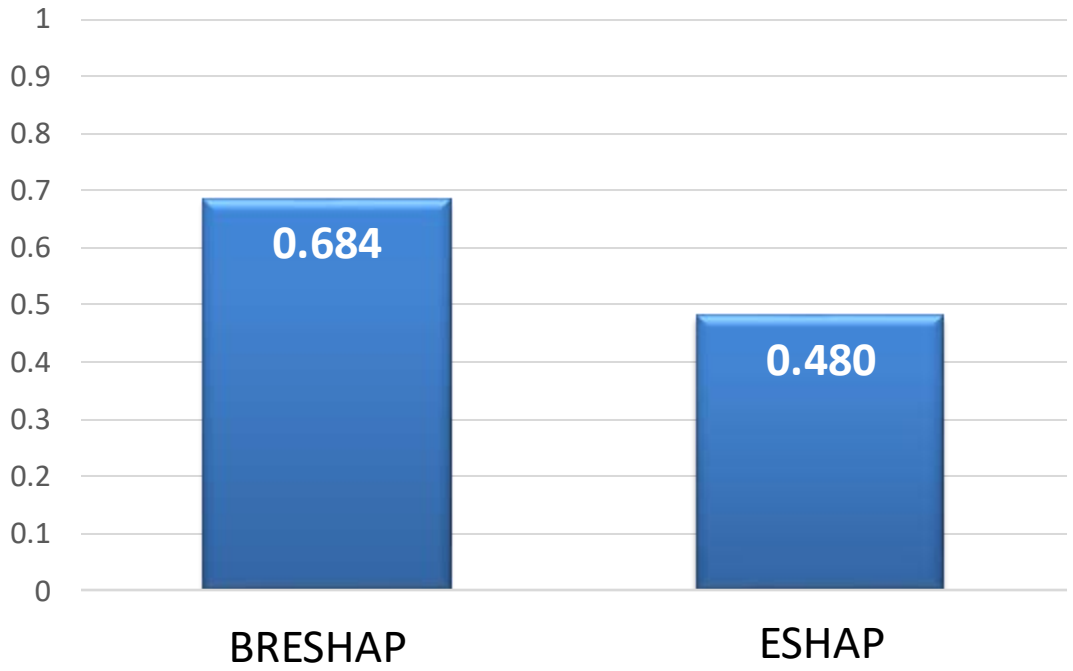
Sureda A et al, ISHL13

Grade 3-4 Adverse Events During Salvage Therapy (>5% patients)

	BRESHAP (n = 76)				ESHAP (n = 75)				Total	
	Grade 3		Grade 4		Grade 3		Grade 4		Any grade	
	N	%	N	%	N	%	N	%	N	%
Hematologic										
Neutropenia	5	6.6	7	9,2	12	16,0	10	13.3	34	22.5
Thrombocytopenia	4	5.3	7	9.2	11	14.7	8	10.7	30	19.9
Anaemia	11	14.5	1	1.3	9	12.0	1	1.3	22	14.6
Non hematologic										
Febrile neutropenia	1	1.3	2	2.6	2	2.7	0	0.0	5	3.3
Hypomagnesaemia	2	2.6	0	0.0	1	1,.3	1	1.3	4	2.6
Increased AST	1	1.3	0	0.0	1	1.3	0	0.0	2	1.3
Asthenia	2	2.6	0	0.0	0	0.0	0	0.0	2	1.3
Pancytopenia	0	0.0	0	0.0	0	0.0	2	2.7	2	1.3
Pulmonary embolism	1	1.3	0	0.0	1	1.3	0	0.0	2	1.3

Sureda A et al, ISHL13

Primary Endpoint & Stem Cell Collection



	BRESHAP (n = 76)	ESHAP (n = 75)	P value
mCR (DS 1-3)	52 (68.4%)	36 (48%)	0.011
No mCR (DS 4–5)	24 (31.6%)	39 (52%)	

Stem cells were collected in 124 patients (82.2%); collection was successful (> 2.0 x 10^6 $CD34^+$ cells / kg) in 93.5% of the patients. No differences between BRESHAP and ESHAP treated patients

Sureda A et al, ISHL13

Multivariate Analysis for the Primary End Point (mCR)

N=151	p-value	OR	95% C.I. for OR	
			Lower	Upper
Extranodal disease	<.001			
Extranodal disease (No vs. 1 site)	.039	2.523	1.046	6.084
Extranodal disease (No vs. >1 site)	<.001	9.674	3.067	30.514
Disease status	.004			
Disease status (Primary refractory vs. Early relapse)	.016	.321	.127	.812
Disease status (Primary refractory vs. Late relapse)	.002	.235	.096	.575
Treatment arm	.029	2.322	1.088	4.952

Sureda A et al, ISHL13

Moving to Consolidation With Brentuximab Vedotin

- N = 80 moved to consolidation therapy with BV
- Number of cycles of BV received: 13 (2 – 16) [median (range)]
- Dose modifications / delays:
  - 52 out of 80 patients had dose modifications and/or delays (65%)
  - In 20 patients, dose delays and dose modifications (38.5%)
- Disease relapses:
  - 14 relapses during consolidation after 10.5 (2 – 16) [median (range)] cycles of BV
  - 2 of them in the follow up phase
- 51 patients have finished consolidation with BV

Sureda A et al, ISHL13

Grade 3-4 Adverse Events During Consolidation Therapy

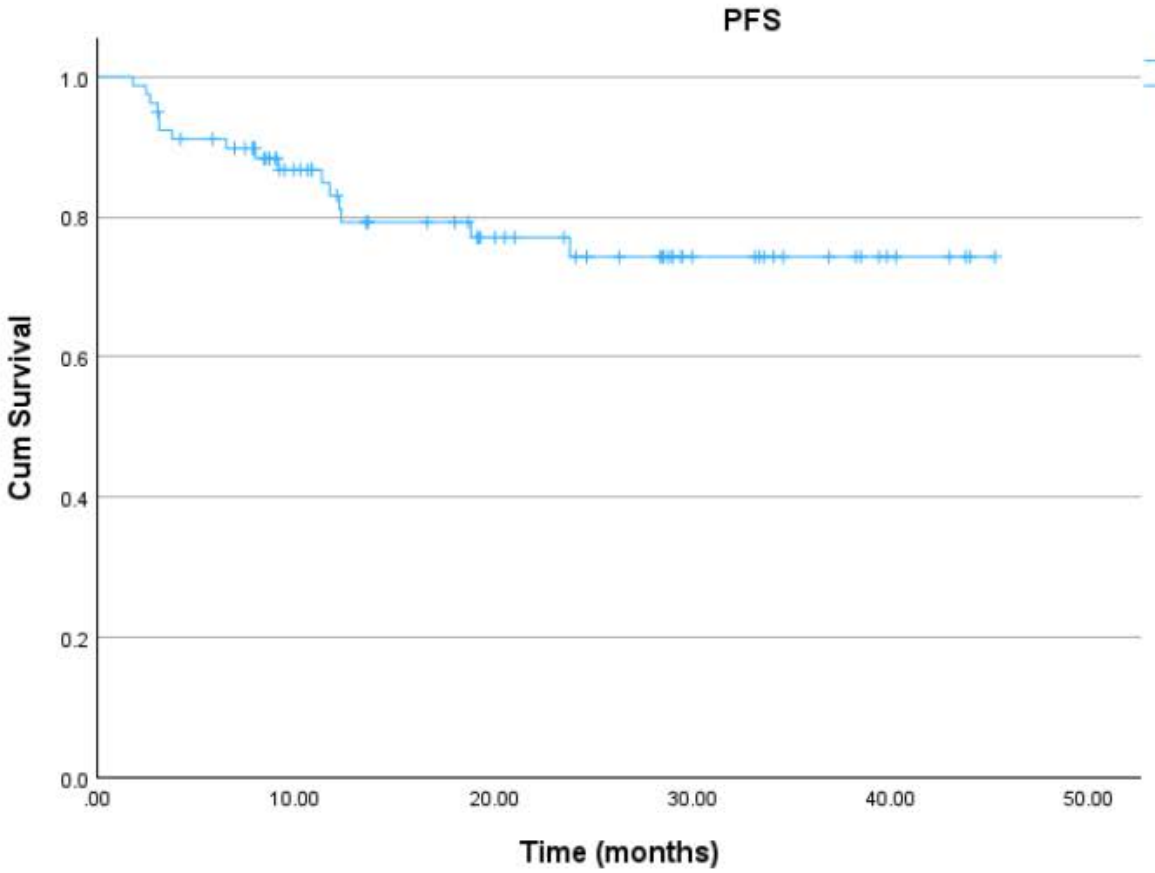
	BRESHAP (n=47)		ESHAP (n=33)				Total (n=80)	
	Grade 3		Grade 3		Grade 4		Any grade	
	N	%	N	%	N	%	N	%
Hematologic								
Neutropenia	1	2.1	5	15.2	0	0.0	6	7.5
Non hematologic								
Peripheral neuropathy	8	17.0	1	3.0	1	3.0	10	12.5

Of the 6 patients with G3-4 neutropenia in the consolidation phase, 1 has discontinued due to AE

Of the 10 patients with G3-4 peripheral neuropathy in the consolidation phase, 9 have discontinued due to AE

Sureda A et al, ISHL13

PFS for Patients Entering Consolidation Phase



Median Follow Up 17.3 (2.5 – 45.5) mo

Time point	Estimate PFS in consolidation phase	95% Confidence Interval	
		Lower Bound	Upper Bound
24 months	74.3%	62.8%	85.8%

Sureda A et al, ISHL13

Author's Conclusions

- BRESELIBET trial is the first prospective randomized clinical trial that demonstrates the superiority of BV in combination with chemotherapy versus chemotherapy alone:
  - BRESHAP significantly increases mCR than ESHAP at the end of salvage therapy
  - No additional toxicity signals
  - No impairment on stem cell collection

- BV consolidation might eventually substitute auto-HCT in patients that achieve a mCR after salvage therapy

Sureda A et al, ISHL13

EORTC
European Organisation for Research and Treatment of Cancer

EORTC-1537-COBRA: VERY EARLY FDG-PET-RESPONSE ADAPTED TARGETED THERAPY FOR ADVANCED HODGKIN LYMPHOMA: A SINGLE-ARM PHASE II STUDY

Martin Hutchings, Anna Sureda Balari, Susana Carvalho, Andrej Vranovsky, Walter Noordzij, Annika Loft, Anne Arens, Wendy Stevens, Arjan Diepstra, Berthe Aleman, Sherida Woei-A-Jin, Maria Viguria, Kirsten Saevels, Liane Te Boome, Sanne Tonino, Paul Meijnders, Eva Domingo Domènech, Anna Caroline Hasselbalch Riley, Sarah Nuyens, Cedric Mallien, Ward Sents, Emanuel Buhrer, Catherine Fortpied, and Wouter Plattel; on behalf of the EORTC Lymphoma Group

13th International Symposium on Hodgkin Lymphoma. Cologne, Germany, 27 October 2024.

Background

There are still unmet needs in advanced cHL

- Two major advances for advanced stage cHL in the last two decades:
  - PET-response adapted treatment (RATHL, HD 18, etc.)[1,2]
  - Introduction of novel antibody-based agents (brentuximab vedotin, anti-PD1)[3,4]
- In the experimental arm of ECHELON-1 all patients received 6 x A-AVD regardless of early PET results[5]
- For patients <60 years treated in the experimental arm:
  - 3-y PFS was 87.2% in PET2 negative patients
  - 3-y PFS was **69.2% in PET2 positive patients**
- HD21 shows that BrECADD is safer and more effective than BEACOPPesc
  - 4-y PFS for patients in the experimental arm (all BrECADD and <60 years) was **94.3%**[6]

1. Johnson PW, et al. N Engl J Med 2016; 374, 2419-29.
2. Borchmann P. et al. Lancet 2017; 390: 2790-2802.
3. Ansell SM, et al. N Engl J Med 2022; 387: 310-320.
4. Herrera AF, et al. N Engl J Med 2024; 391: 1379-1389.
5. Strauss D, et al. Blood 2020; 135 (10): 735–742
6. Borchmann P, et al. Lancet 2024; 404: 341-352.

EORTC
European Organisation for Research and Treatment of Cancer

Objectives and study design

Open label, multi-center, single-arm phase II trial

Primary Objective

To use early FDG-PET/CT to optimise the balance between efficacy and toxicity in advanced stage Hodgkin lymphoma patients treated with BV-containing regimens

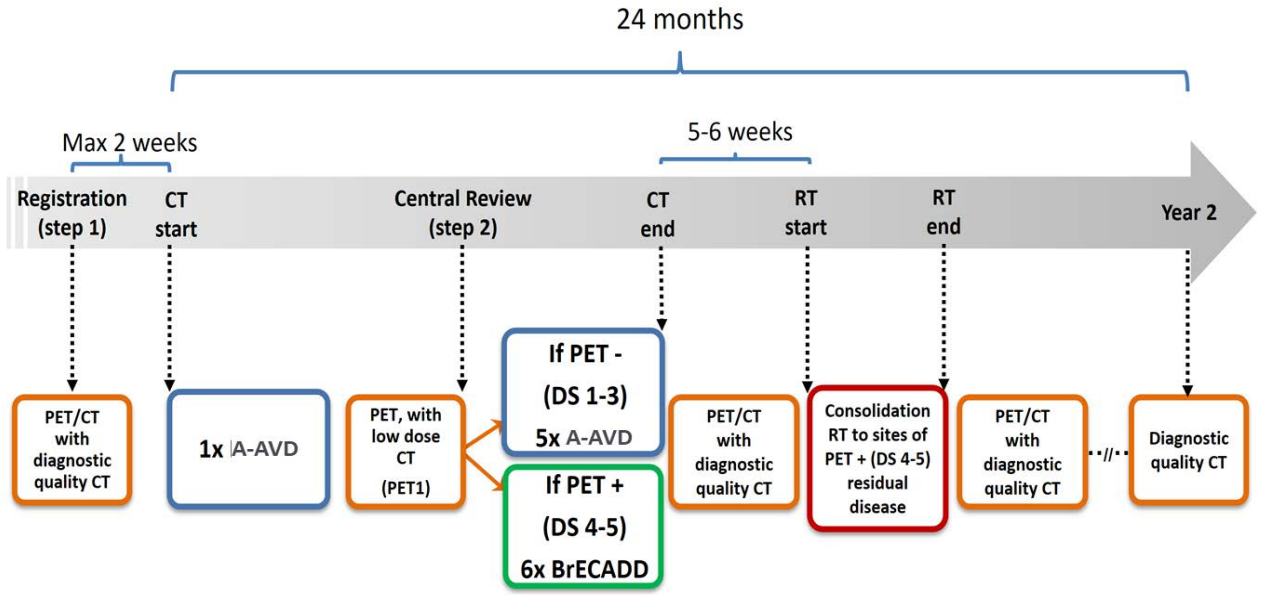
Primary Endpoint

Modified progression-free survival rate at 2 years after start of treatment (2yr-mPFS)*

The study was designed to reject an 80% or less 2yr-mPFS rate

mPFS:

- Progressive disease (PD)
- Start of new treatment for cHL when not in CR at the end of protocol treatment
- Death due to any cause



Primary analysis conducted when all patients had 2 years of follow-up

Median follow-up = 30.1 months; inter-quartile range = (24.6 - 36.4)

EORTC
European Organisation for Research and Treatment of Cancer

Central review of PET1 and radiotherapy plans

- **A real-time central review** of FDG-PET scans (baseline and after 1 cycle of BrAVD) was performed by a panel of 3 experts, using the 5-point Deauville Criteria
- PET1 was performed, centrally uploaded, quality controlled, scored, adjudicated, and reported to the treating physician within a time window of three working days and in time for the next treatment on C2D1

- **Post-chemotherapy radiotherapy plans** similarly underwent real-time central quality control by a panel of expert lymphoma radiation oncologists, before radiotherapy was delivered to the patients

EORTC
European Organisation for Research and Treatment of Cancer

CONSORT

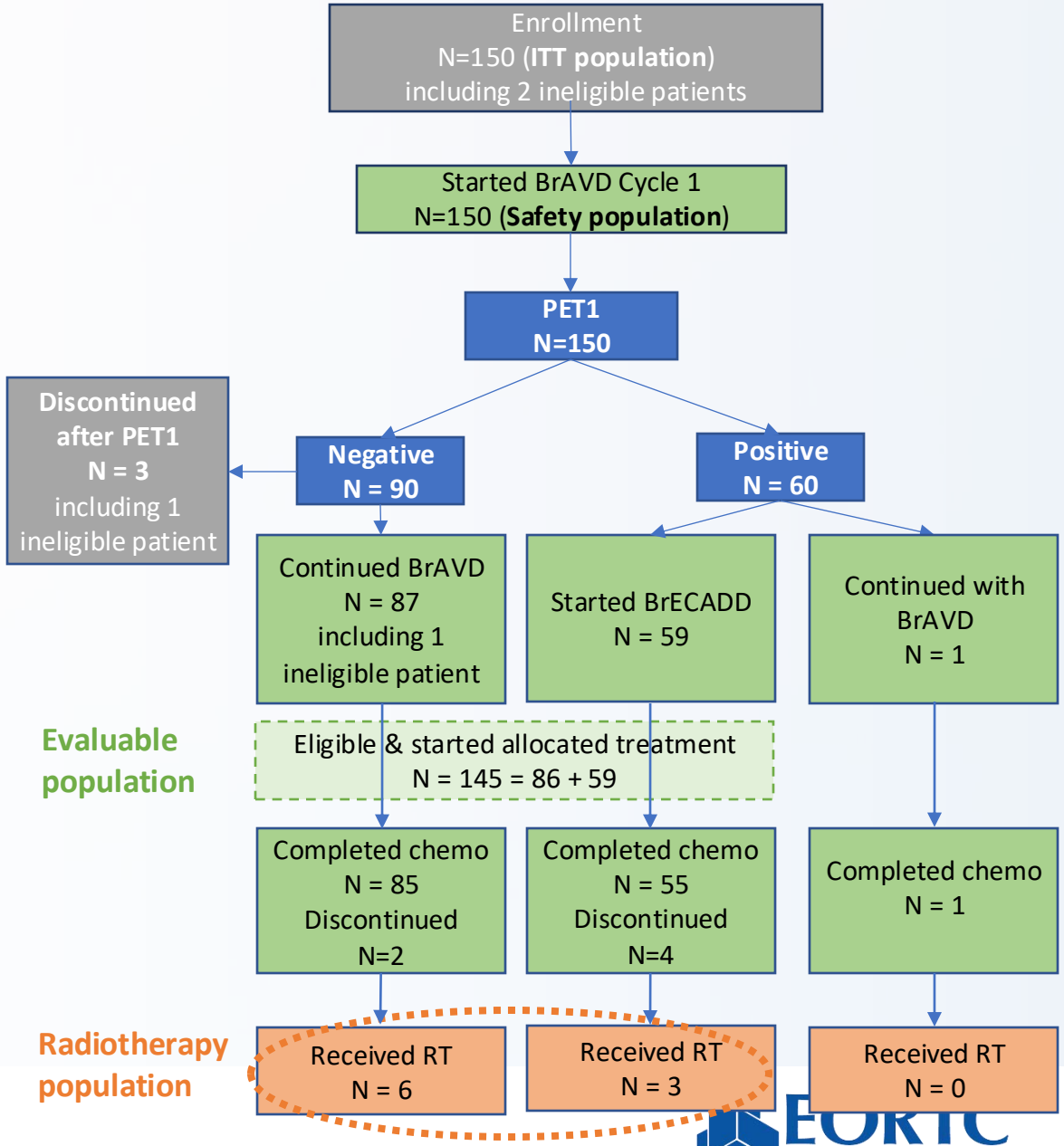
Previously untreated classical Hodgkin lymphoma

- Stage III – IV
- Stage IIB with large mediastinal mass and/or extranodal lesion(s) (GHSG)

Patient characteristics

- 55% male
- 60% with stage IV disease

- 150 patients included at 16 sites in 2 years
  - August 2019 – August 2021
- 145 evaluable patients
  - → eligible and continued per protocol after PET1
- 9 patients discontinued treatment prematurely
  - 1 due to progressive disease
  - 5 due to toxicity
  - 3 due to other reasons (misunderstanding by investigator, COVID19 lockdown, withdrawal of consent)



EORTC
European Organisation for Research and Treatment of Cancer

Adverse events

149/150 patients experienced on-treatment adverse events:

- 63% reporting grade 3-4 AEs
- 55% treatment-related AEs grade 3-4
- 30% reported SAEs
- 1 new malignancy (BCC)
- No grade 5 AEs reported

Toxicity signals highly comparable with Echelon-1 and HD21

AEs with an incidence of ≥15% in all patients	All grades	Grade 3-4
Peripheral sensory neuropathy	53%	6%
Nausea	43%	1%
Constipation	37%	3%
Neutropenia	36%	35%
Fatigue	35%	1%
Anemia	25%	12%
Vomiting	21%	1%
Abdominal pain	19%	1%
Diarrhoea	19%	1%
Peripheral motor neuropathy	18%	3%
Bone pain	18%	0%
Insomnia	17%	0%
Fever	16%	1%
Oral mucositis	16%	1%
Myalgia	15%	0%

EORTC
European Organisation for Research and Treatment of Cancer

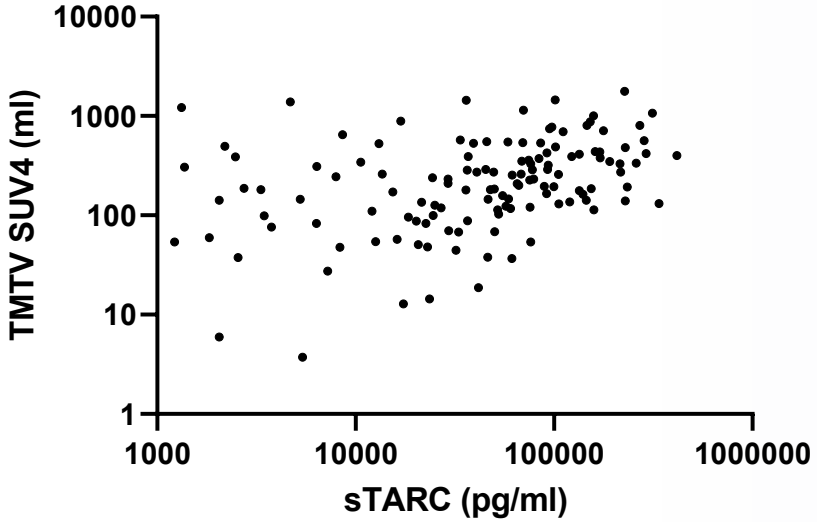
Efficacy

145 eligible patients who continued the allocated treatment after PET1

- Complete metabolic response rate at end of treatment: **91.0%** (95% CI: 85.2-95.1%)
- 16 patients experienced a mPFS event (all were PFS events)
- The mPFS rate at 2 years was 89.5% (80% 2-sided exact CI: 85.7-92.4%).
  - 2-year mPFS was 88.3% in PET1 negative patients
  - **2-year mPFS was 91.3% in PET1 positive patients**
- No deaths have occurred

EORTC
European Organisation for Research and Treatment of Cancer

TARC before, during, and after treatment

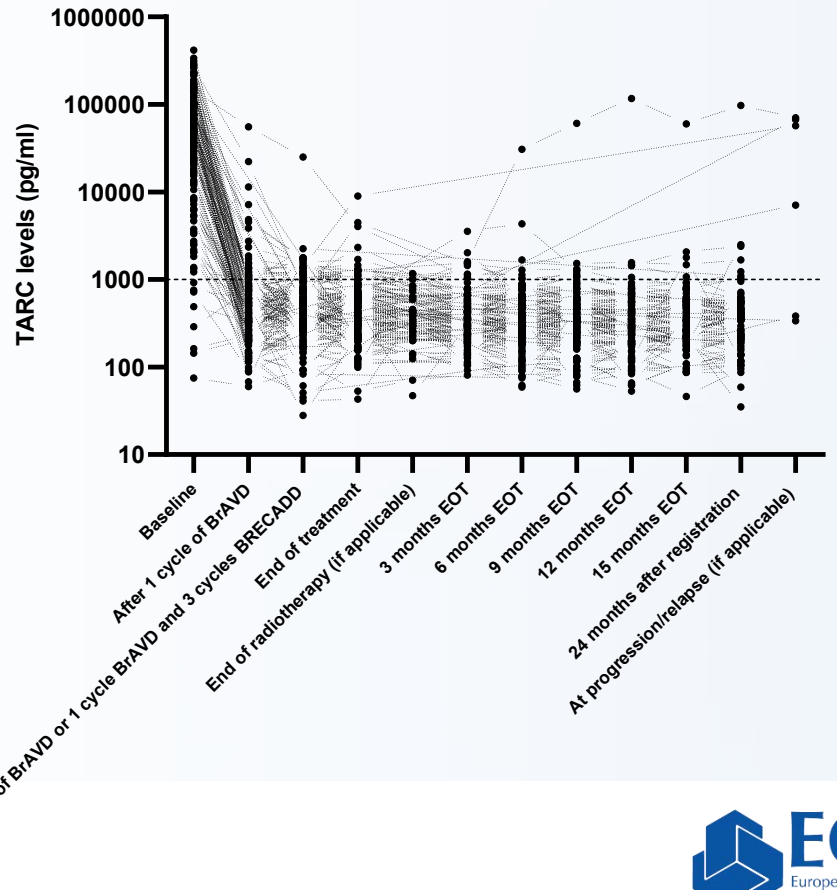


Correlation of sTARC and TMTV (SUV4 cut-off) at diagnosis

Spearman's correlation r = 0.401

p < 0.0001

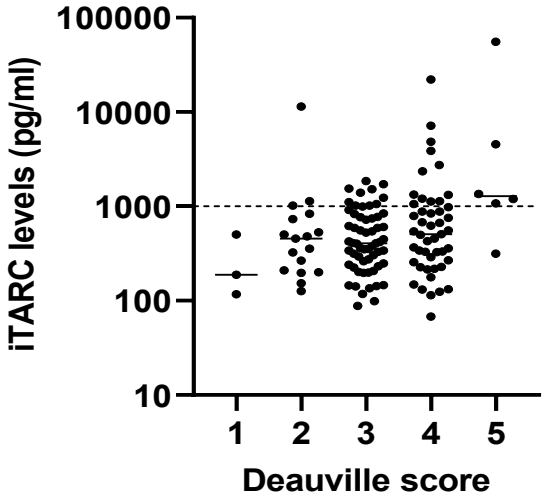
Dynamics of sTARC before, during and after treatment

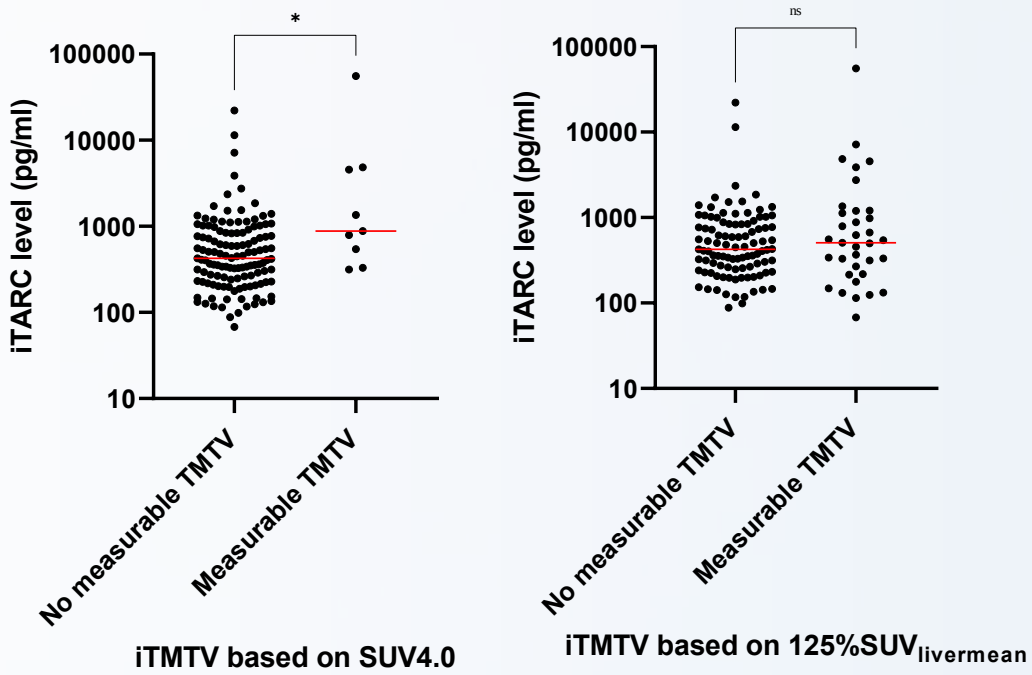


EORTC
European Organisation for Research and Treatment of Cancer

Most patients with Deauville 4 after 1 cycle are negative for TARC and MTV

TARC levels after one cycle according to Deauville score





iPET positive patients with and without measurable total metabolic tumour volume

Deauville score	TMTV positive (SUV4)	TMTV negative (SUV4)	TMTV positive (125% $SUV_{livermean}$)	TMTV negative (125% $SUV_{livermean}$)
4 (n = 54)	6	48	35	19
5 (n = 6)	4	2	5	1

TARC levels in all patients after one cycle divided into measurable or no measurable TMTV

EORTC
European Organisation for Research and Treatment of Cancer

Authors Conclusions

- Treatment adaptation based on a very early FDG-PET/CT leads to very high efficacy in advanced stage HL patients receiving BV-containing first-line treatment while sparing most patients intensive chemotherapy
- Early PET-response adapted therapy improves outcomes - also on the backbone of A-AVD
- No new safety signals observed
- We investigate the value of TARC as a marker of pre-treatment disease burden, early response, and recurrence

EORTC
European Organisation for Research and Treatment of Cancer

Impact of Treatment-Related Morbidity on Health-Related Quality of Life in Patients with Advanced-Stage Classical Hodgkin Lymphoma Receiving Multiagent Therapy: Findings from the HD21 Study

Fjoralba Kristo, MD, MPH[1]; Flora Mazerolle, MSc[2]; Thibaud Alin, MSc[2]; Antoine Regnault, PhD[2]; Justin Ferdinandus, MD[3]; Karolin Behringer, MD[3]; Janina Jablonski, MSc[3]; Peter Borchmann, MD[3]; Ajibade Ashaye, MD, MBA, MPH MSc[1]

[1]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [2]Modus Outcomes, a company of THREAD, Lyon, France; [3]German Hodgkin Study Group and Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf, University of Cologne, Cologne, Germany

Background

- The German Hodgkin Study Group (GHSG) HD21 trial evaluated the efficacy and safety of BrECADD in advanced-stage, classical Hodgkin lymphoma (cHL), and showed reduced toxicity profile and higher progression-free survival compared to eBEACOPP[1].
- HD21 study demonstrated reduction of treatment-related morbidity (TRMB), with at least one TRMB reported in 42% vs. 59% of participants treated with BrECADD vs. eBEACOPP respectively[1].
- TRMB included severe acute hematological and nonhematological toxicities that can result in dose delay or reduction.

This post-hoc analysis explored the impact of TRMB on participants' HRQoL

Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

1. Borchmann P. et al. *Lancet*. 2024;404(10450):341-352

Methods

- 1,500 patients randomized (1:1) to receive BrECADD vs. escalated BEACOPP (eBEACOPP) in a 4 or 6 cycles 21-day treatment cycles in HD21 study (NCT02661503)
  - A high proportion of participants without baseline PRO value were excluded

Treatment-related morbidity

Acute nonhematological toxicity

Cardiac, gastrointestinal, hepatobiliary, nervous system, renal and urinary, and respiratory/thoracic/mediastinal disorders of grade 3 and 4

Hematological toxicity

Anemia, thrombocytopenia, and infections of grade 4

Health-related quality of Life

EORTC QLQ-C30 collected over treatment period (after 2 cycles, at restaging after chemotherapy) and follow-up (up to 5 years)

- Statistical analyses
  - Description of the QLQ-C30 physical function (PF), global health/quality of life (GH/QL) and fatigue (FA) scores according to participants' experience of TRMB
  - Multivariable linear regression analyses of these PRO scores according to TRMB, adjusted for age, sex and baseline PRO score

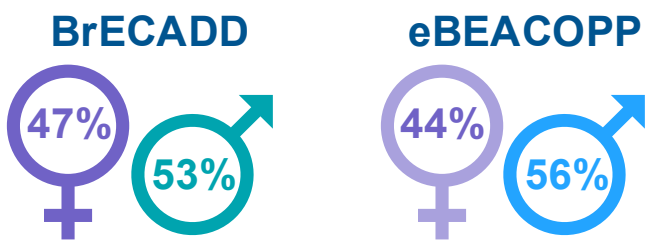
Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Demographic and Disease Characteristics

Similar median (range) **age** in both arms

31 (18-60) **years**

Similar proportion of males and females

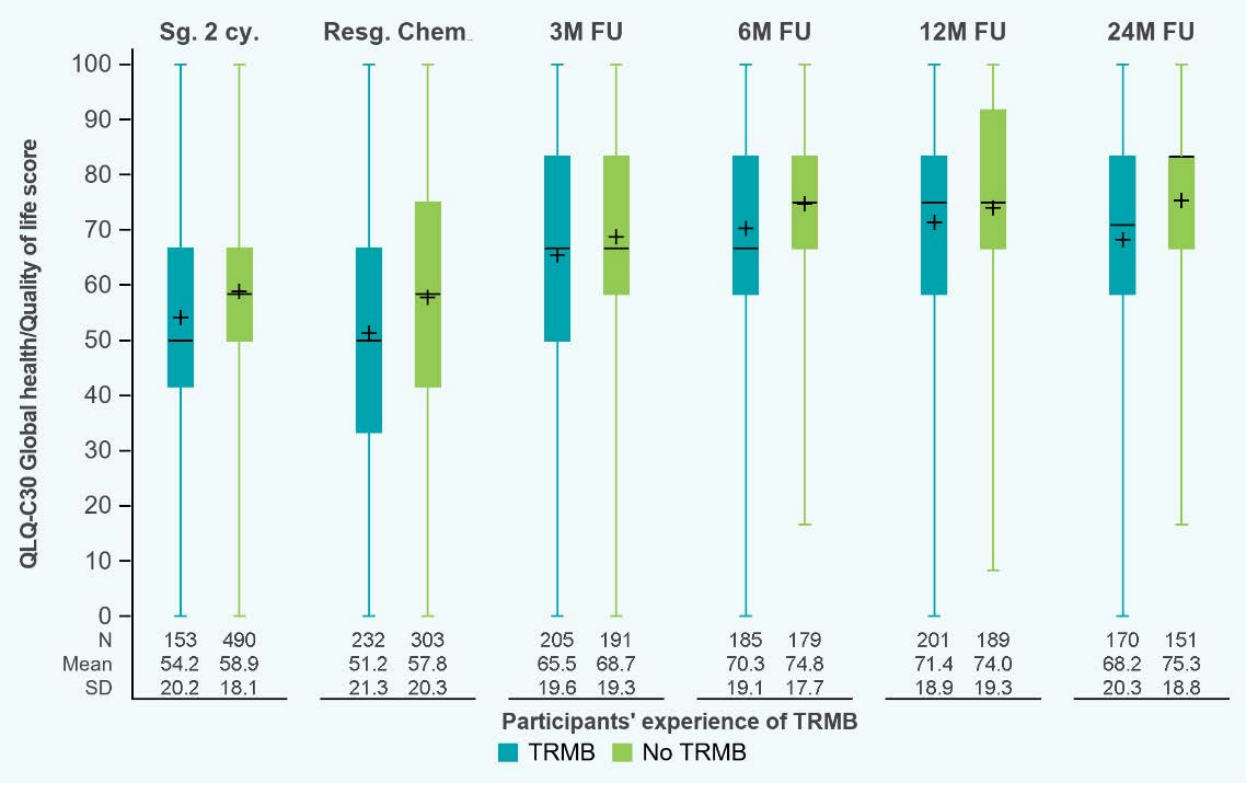


Characteristic	BrECADD N=360	eBEACOPP N=372
Ann Arbor stage, n(%)		
Class IIb	59 (16%)	53 (14%)
Class IIIa	65 (18%)	84 (23%)
Class IIIb	83 (23%)	87 (23%)
Class IVa	50 (14%)	57 (15%)
Class IVb	103 (29%)	91 (25%)
IPS score, n(%)		
0-2	205 (57%)	216 (58%)
3-7	155 (43%)	156 (42%)
ECOG-PS at baseline, n (%)		
0 – Fully active	238 (66%)	263 (71%)
1 – Symptoms ambulatory	116 (32%)	105 (28%)
2 – In bed <50% of daytime	6 (2%)	4 (1%)

Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Impact of TRMB on participants' global health/quality of life

Figure 1a: Impact of TRMB on general health/quality of life as assessed by the EORTC QLQ-C30 GH/QL score



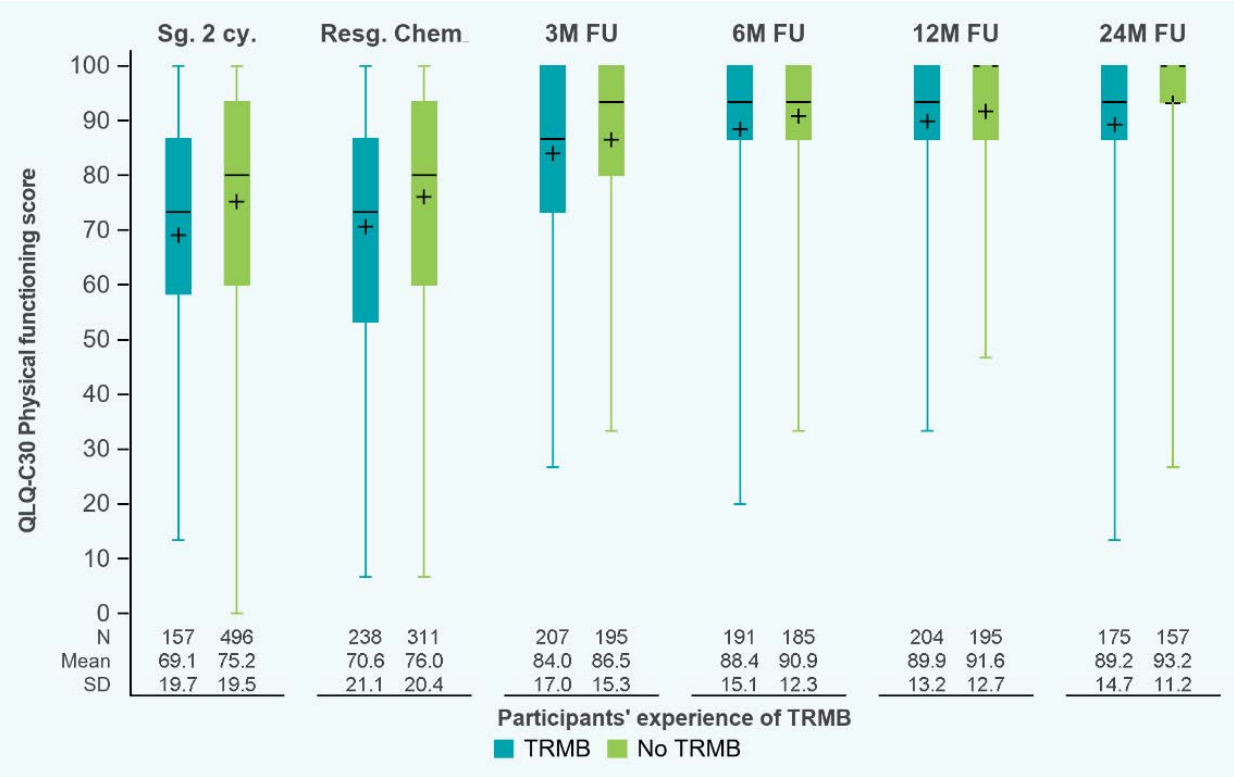
Higher score =
Better quality of life

Legend: Box for each score: interquartile range (Q1-Q3); +: mean; —: median; bottom and top bars: score range (minimum and maximum).
Abbreviations: 3M FU: 3-month follow-up; 12M FU: 12-month follow-up; 24M FU: 24-month follow-up; N: number of participants; Resg. Chemo: restaging after chemotherapy visit; SD: standard deviation; Sg. 2 cy.: staging after 2 cycles visit

Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Impact of TRMB on participants' physical functioning

Figure 1b: Impact of TRMB on physical functioning as assessed by the EORTC QLQ-C30 PF score



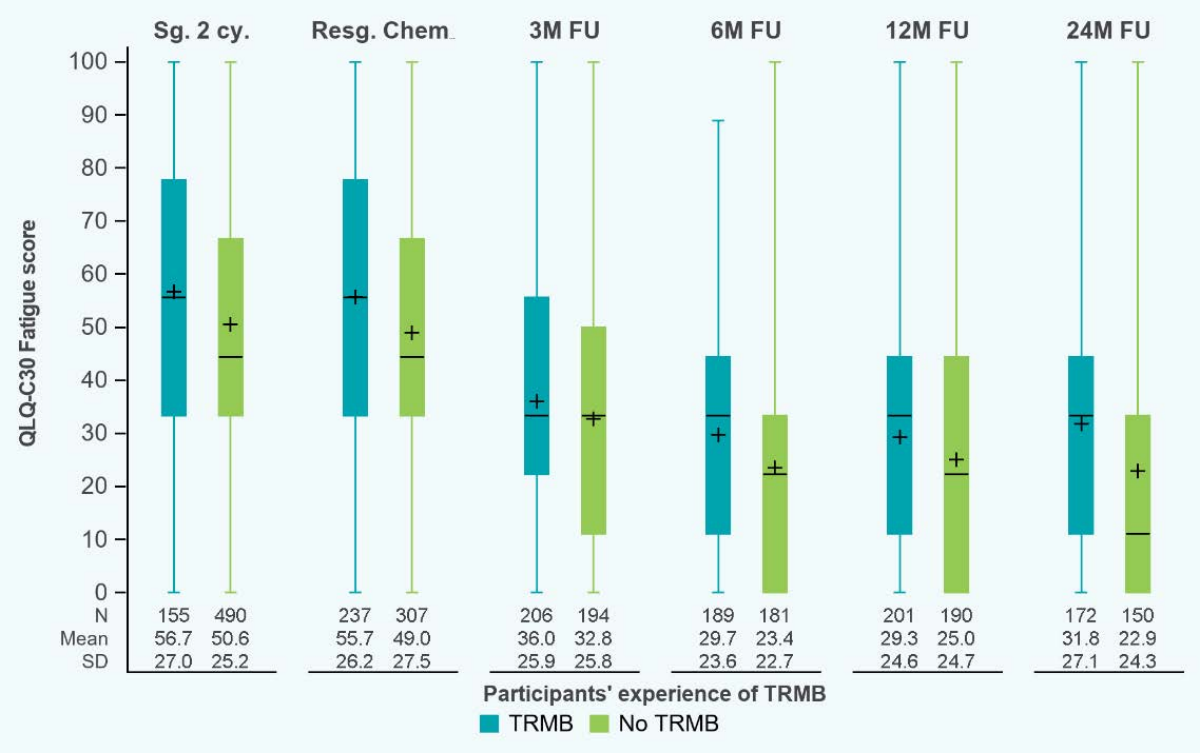
Higher score = Better physical functioning

Legend: Box for each score: interquartile range (Q1-Q3); +: mean; —: median; bottom and top bars: score range (minimum and maximum).
Abbreviations: 3M FU: 3-month follow-up; 12M FU: 12-month follow-up; 24M FU: 24-month follow-up; N: number of participants; Resg. Chemo: restaging after chemotherapy visit; SD: standard deviation; Sg. 2 cy.: staging after 2 cycles visit; TRMB: treatment-related morbidities.
Direction of the QLQ-C30 PF score: a higher score indicates better physical functioning.

Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Impact of TRMB on participants' levels of fatigue

Figure 1c: Impact of TRMB on levels of fatigue as assessed by the EORTC QLQ-C30 FA score



Higher score = More (worse) Fatigue

Legend: Box for each score: interquartile range (Q1-Q3); +: mean; —: median; bottom and top bars: score range (minimum and maximum).
Abbreviations: 3M FU: 3-month follow-up; 12M FU: 12-month follow-up; 24M FU: 24-month follow-up; N: number of participants; Resg. Chemo: restaging after chemotherapy visit; SD: standard deviation; Sg. 2 cy.: staging after 2 cycles visit; TRMB: treatment-related morbidities.
Direction of the QLQ-C30 FA score: a higher score indicates more fatigue.

Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Multivariable analysis exploring the impact of TRMB on participants' HRQoL

Table 2: Multivariable analysis of the EORTC QLQ-C30 GH/QL, PF, and FA scores according to participants' experience of TRMB

PRO score, adjusted mean difference estimate in participants who experienced TRMB as compared to those who did not	Staging after 2 cycles	Restaging after chemotherapy	3-month FU	12-month FU	24-month FU
QLQ-C30 PF score	-3.6*	-3.5*	-1.0	-0.8	-2.1
QLQ-C30 GH/QL score	-3.4*	-5.4*	-2.4	-2.1	-5.8*
QLQ-C30 FA score	3.7*	4.5*	0.2	2.6	5.4*

Positive results (p-value below 0.05) are identified by a *, not adjusted for multiplicity of the tests.

Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Author's Conclusion

- Participants who experienced TRMB events reported poorer overall health, physical functioning, and more fatigue than those who did not at the end of treatment period.
- These findings describe a detrimental effect of TRMB events on patients' quality of life, including physical function and fatigue. While the impact of TRMB events was expected to naturally decrease after treatment discontinuation, a negative effect was still observed at 24-month FU.
- Treatments associated with fewer TRMB events are not only relevant clinically but can also improve patients' experience in advanced stage cHL, suggesting that TRMB is also a patient-relevant endpoint.

Kristo F, et al. Poster Presentation 4426. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Estimation of Health State Utility Values for Patients Undergoing First-line Treatment for Advanced Stage Classical Hodgkin Lymphoma in the HD21 Trial

Christopher G Pelligra, MS[1], Fjoralba Kristo, MD, MPH[2], Yutian Mu, MS[3], Justin Ferdinandus, MD[4], Karolin Behringer, MD[4], Janina Jablonski, MSc[4], Peter Borchmann, MD[4], Ajibade Ashaye, MD, MBA, MPH, MSc[2]

[1]Evidera, Atlanta, GA, USA. [2]Takeda Development Center Americas, Inc., Cambridge, MA, USA. [3]Evidera, Waltham, MA, USA. [4]German Hodgkin Study Group and Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf, University of Cologne, Cologne, Germany

Background

- HD21 (NCT02661503) is an ongoing phase 3, randomized, open-label study of first-line therapy for advanced classical Hodgkin lymphoma.
- Patients received 4 or 6 cycles of either of the following treatments: BrECADD or eBEACOPP.
- In HD21, BrECADD has shown a more favorable toxicity profile and improved PFS compared with eBEACOPP [1].
  - Health-related quality of life was assessed using the EORTC QLQ-C30.
- However, preference-based utility measures required for health economic evaluations were not administered.
  - One such instrument is the EQ-5D-3L, a self-administered questionnaire with five dimensions and three levels for each (“no problems”, “some problems” or “extreme problems” [2]).

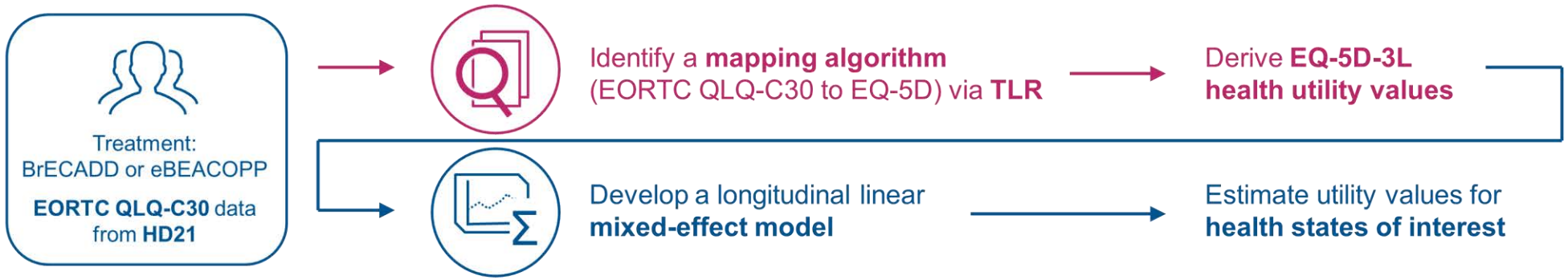
BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; PFS, progression-free survival.

[1] Borchmann P, Ferdinandus J, Schneider G, et al. Lancet. 2024;404(10450):341-352. [2] EuroQoL, https://euroqol.org/information-and-support/euroqol-instruments/eq-5d-3l.

Objectives

- To identify and apply an appropriate algorithm to map the collected EORTCQLQ-C30 data to EQ-5D-3L utility values.
- To estimate utility values for health states of interest.

Study design



EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Methods

- A TLR was conducted in the Embase, Medline, and HERC databases to identify relevant studies mapping the EORTC QLQ-C30 to the EQ-5D.
  - Studies of adults with Hodgkin lymphoma and other blood cancers where EORTC QLQ-C30 was directly or indirectly mapped to EQ-5D, and which were in English, were included.
- Once an appropriate mapping model was identified, it was applied to the HD21 EORTC QLQ-C30 data to derive EQ-5D-3L health utility scores using the UK value set [1]. The UK value set was chosen to reflect preferences of the UK general population.
- All analyses were conducted on the EQ-5D-evaluable population, which consisted of all patients in the intent-to-treat analysis set who had non-missing calculated EQ-5D-3L health utility values at baseline and at least one post-baseline assessment.

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; HERC, Oxford Health Economic Research Centre; TLR, targeted literature review.

[1] Dolan P. Modeling valuations for EuroQol health states. Med Care. 1997 Nov;35(11):1095-1108.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Methods

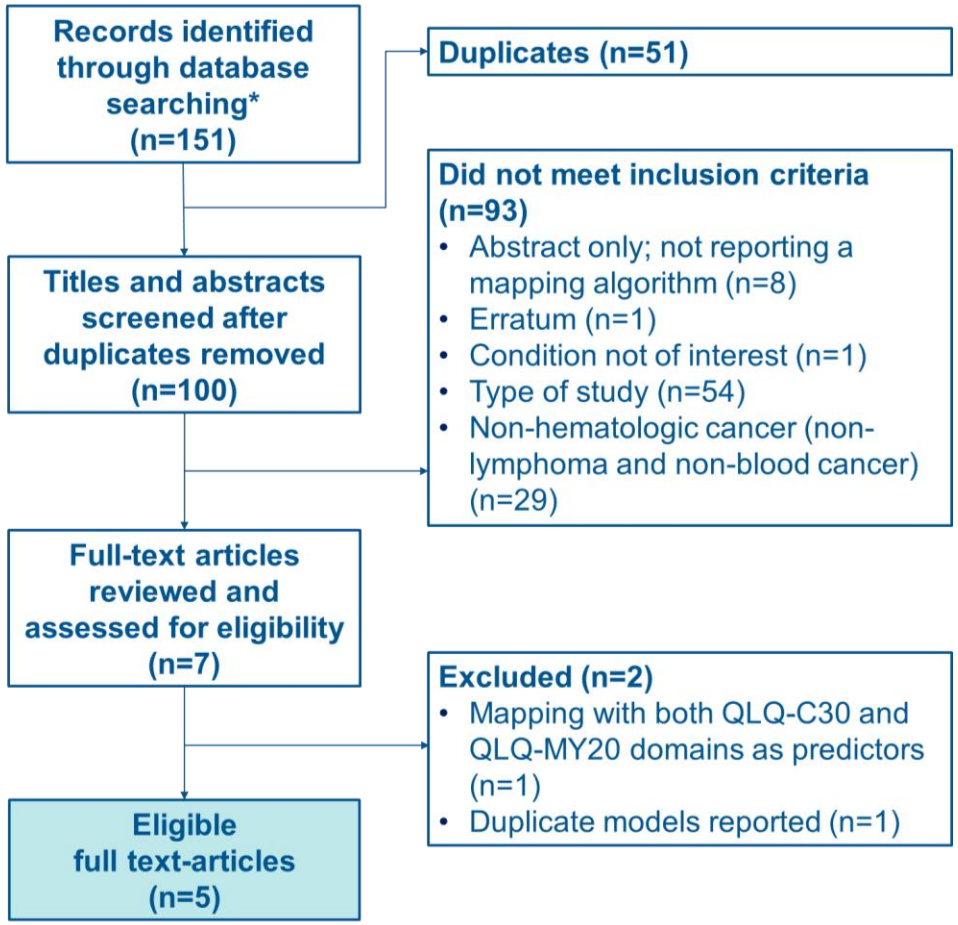
- A longitudinal linear mixed-effect model was used to estimate health utility values for five health states of interest: Progression-free on BrECADD, progression-free on eBEACOPP, progression-free off BrECADD, progression-free off eBEACOPP, and progressed.
  - On-treatment was defined as visits while patients were undergoing chemotherapy, while off-treatment was defined as visits after completion of chemotherapy.
  - Progression-free was defined as visits prior to central review confirmation of investigator-assessed progression, while progressed was defined as visits after central review confirmation of investigator-assessed progression and before censoring.
  - The model included EQ-5D-3L health utility as the dependent variable and the following covariates: treatment arm (BrECADD/eBEACOPP), on/off-treatment, BrECADD on treatment (interaction term; yes/no), progressive disease (yes/no), age (continuous), and baseline utility (continuous).
- Least-square mean (95% CI) utility values were estimated for the health states.

BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; CI, confidence intervals; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

TLR

- The TLR (search date: 25 Jan 2024) identified 151 records, of which five full-text articles were eligible for inclusion.
  - Of these, the study by Young et al. 2015 (PMID: 25997920) [1] was chosen as the most appropriate due to its large sample (N=771, of which 74% had myeloma), wide usage in the literature, and use of an indirect approach for the EQ-5D-3L, which allowed for flexibility in the country value sets to be used.



*Includes one record identified from the HERC database.
HERC, Oxford Health Economic Research Centre; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-MY20, Quality of Life Questionnaire myeloma module; Quality of Life Questionnaire Core 30; TLR, targeted literature review.

[1] Young TA, Mukuria C, Rowen D, Brazier JE, Longworth L. Med Decis Making. 2015 Oct;35(7):912-926.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Baseline characteristics and instrument completion rates

- In HD21, 751 patients were randomized to BrECADD and 749 to eBEACOPP (intent-to-treat population).
  - Of these, 343 patients receiving BrECADD and 347 receiving eBEACOPP formed the EQ-5D-evaluable population.
  - Completion rates were low (49% of the intent-to-treat population)
- Demographic and disease characteristics were generally comparable between treatment groups and between the intent-to-treat and EQ-5D-evaluable populations, except that the latter consisted of mostly (99.9%) patients from Germany, where the QLQ-C30 was mainly administered.

BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Observed health utility values

- At baseline, mean (95% CI) EQ-5D-3L utility values were similar for the BrECADD (0.62 [0.59–0.66]) and eBEACOPP (0.65 [0.62–0.68]) treatment groups.
  - In both groups, after patients completed chemotherapy, mean health utility values increased and remained stable across visits while patients remained progression-free.

BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Model-based analysis of health utility values

- On/off-treatment, age, and baseline utility score were significant predictors of utility (P<0.05).

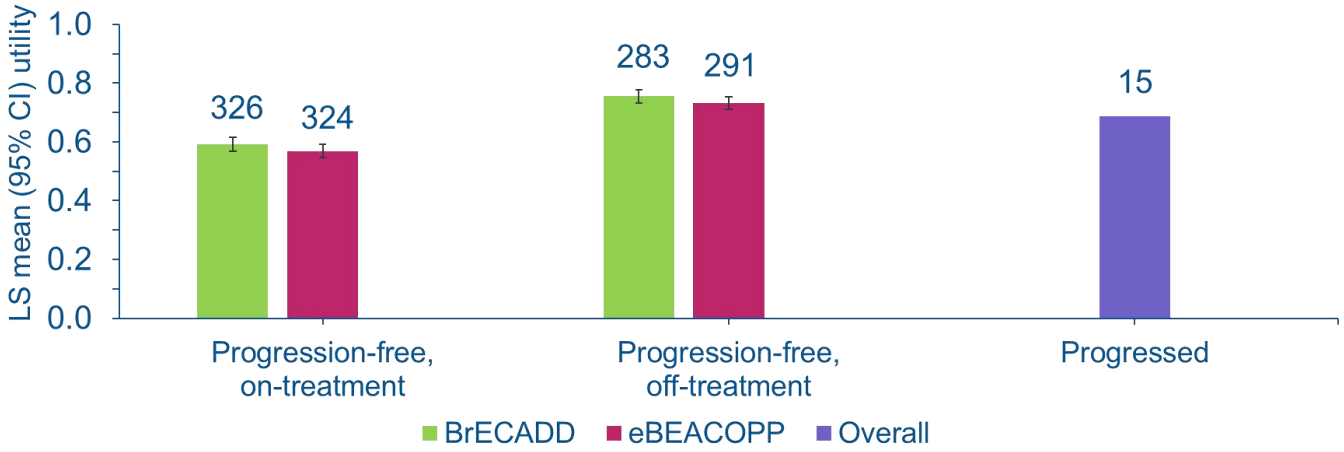
Covariate	Coefficient (95% CI)	P-value	Standard error
Intercept	0.732 (0.710, 0.754)	<0.001	0.011
Treatment arm (BrECADD vs eBEACOPP)	0.023 (–0.008, 0.055)	0.143	0.016
On/off-treatment (on treatment vs off-treatment)	–0.162 (–0.181, –0.144)	<0.001	0.009
BrECADD on treatment (interaction term; yes/no)	–0.001 (–0.027, 0.025)	0.927	0.013
Progressive disease (yes vs no)	–0.056 (–0.130, 0.018)	0.138	0.038
Centered age (mean = 33.8 years)	–0.006 (–0.007, –0.004)	<0.001	0.001
Centered baseline utility score (mean = 0.637)	0.312 (0.261, 0.362)	<0.001	0.026

Model-estimated coefficients. Coefficients for discrete variables indicate the difference in utility between each level. Coefficients for centered continuous variables indicate the difference in utility for one-unit difference from the mean (i.e., mean age or baseline utility). Shading indicates P<0.05.
BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; CI, confidence interval; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Model-based analysis of health utility values

- Progression-free utility estimates were similar for BrECADD vs eBEACOPP, but they were higher off-treatment (i.e., after completing chemotherapy) vs on-treatment.
  - The utility estimate for the progressed state fell between the progression-free on-treatment and off-treatment estimates.



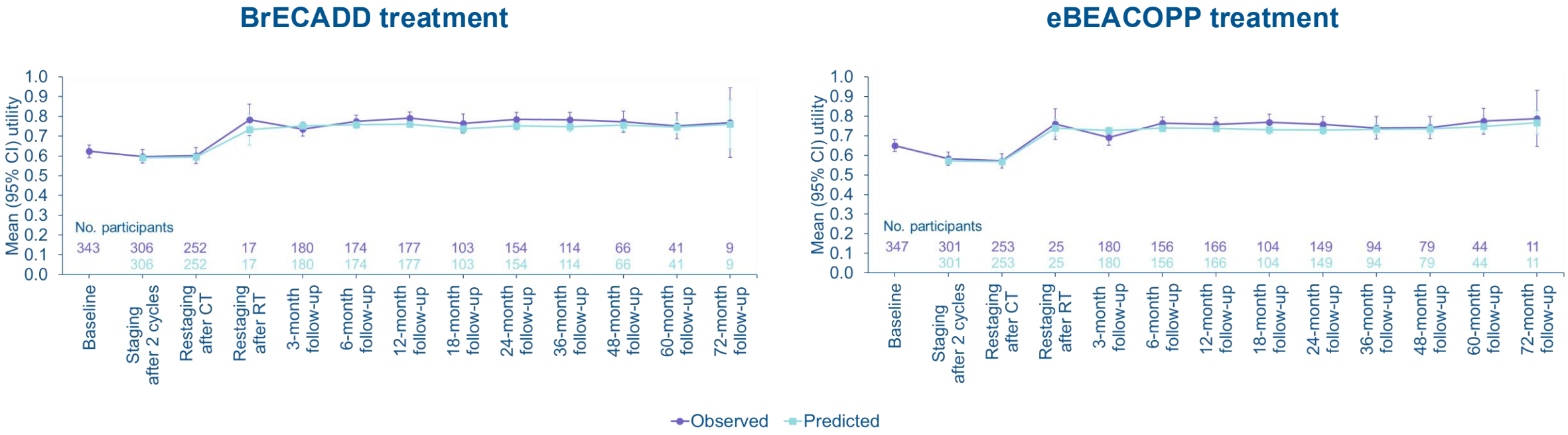
Health state	On treatment		Off treatment	
	BrECADD	eBEACOPP	BrECADD	eBEACOPP
Progression-free	0.59 (0.57, 0.62)	0.57 (0.55, 0.59)	0.76 (0.74, 0.78)	0.73 (0.71, 0.76)
Progressed	Not applicable		0.69 (0.61, 0.76)	

Values shown are the LS mean (adjusted for covariates) [95% CI] in the EQ-5D-evaluable population. Numbers above the bars indicate participants.
BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; CI, confidence interval; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; LS, least-square.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Model-based analysis of health utility values

- The mean predicted by the linear mixed-effect model aligned closely with the mapped values for both treatment arms.



BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; CI, confidence interval; CT, chemotherapy; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; RT, radiotherapy.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Author's Conclusions

- Completion of chemotherapy with either BrECADD or eBEACOPP resulted in improved utility in the progression-free state.
- Therefore, the improvement of PFS by BrECADD observed in the HD21 study could lead to an increase in quality-adjusted survival in adults with advanced stage Hodgkin lymphoma.
- Reported utilities can be used to inform a UK cost-effectiveness model.

BrECADD, brentuximab vedotin in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone; eBEACOPP, escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; PFS, progression-free survival.

Pelligra CG, et al. Poster Presentation 2346. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Patient-Reported Chemotherapy-Induced Peripheral Neuropathy (CIPN) in Advanced-Stage Classical Hodgkin Lymphoma Treated with BrECADD and eBEACOPP in the HD21 Trial

Fjoralba Kristo, MD, MPH[1]; Flora Mazerolle, MSc[2]; Thibaud Alin, MSc[2]; Antoine Regnault, PhD[2]; Justin Ferdinandus, MD[3]; Karolin Behringer, MD[3]; Janina Jablonski, MSc[3]; Peter Borchmann, MD[3]; Ajibade Ashaye, MD, MBA, MPH MSc[1]

[1]Takeda Development Center Americas, Inc., Cambridge, MA, USA; [2]Modus Outcomes, a company of THREAD, Lyon, France; [3]German Hodgkin Study Group and Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf, University of Cologne, Cologne, Germany

Background and Objectives

- Chemotherapy-induced peripheral neuropathy (CIPN) is a common dose-limiting side effect experienced by patients treated with chemotherapy and can manifest through sensory, motor, and autonomic neuropathy symptoms. Sensory symptoms are usually predominant and likely increase with improved survival[1,2]
- The German Hodgkin Study Group HD21 study showed that BrECADD improved tolerability and progression-free survival compared with escalated BEACOPP (eBEACOPP) as first-line treatment for newly diagnosed advanced-stage classical Hodgkin lymphoma[3]

This exploratory post-hoc analysis investigated patient-reported CIPN sensory symptoms, and its impact on participants' health-related quality of life (HRQoL) in patients treated with BrECADD and eBEACOPP.

Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

1. Younes A. et al. *J Clin Oncol*. 2012;30(18):2183-9
2. Staff NP. et al. *Ann Neurol*. 2017;81(6):772-81
3. Borchmann P. et al. *Lancet*. 2024;404(10450):341-352

Methods

- 1,500 patients randomized (1:1) to receive BrECADD vs. escalated BEACOPP (eBEACOPP) in a 4 or 6 cycles 21-day treatment cycles in HD21 study (NCT02661503)
  - A high proportion of participants without baseline PRO value were excluded

Patient-Reported Outcome (PRO) data collection

- Treatment period (after 2 cycles, at restaging after chemotherapy)
- Follow-up (3-month, 6-month, then every 6-month up to 2 years, and every year 2 to 5 years)

European Organisation for Research and Treatment of Cancer (EORTC)

Quality of Life questionnaire – Core 30 items (QLQ-C30)	Quality of Life Questionnaire – 20-item Chemotherapy-Induced Peripheral Neuropathy module (QLQ-CIPN20)

- Descriptive statistical analyses
  - Description of responses to QLQ-CIPN20 items during the treatment and follow-up (FU) periods
  - Description of the QLQ-C30 global health/quality of life (GH/QL) and fatigue (FA) scores in patients who reported CIPN sensory symptoms and those who did not

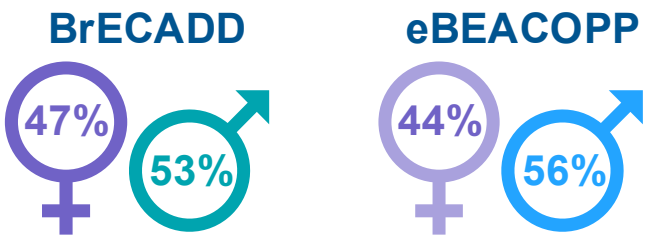
Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Demographic and Disease Characteristics

Similar median (range) **age** in both arms

31 (18-60) **years**

Similar proportion of males and females



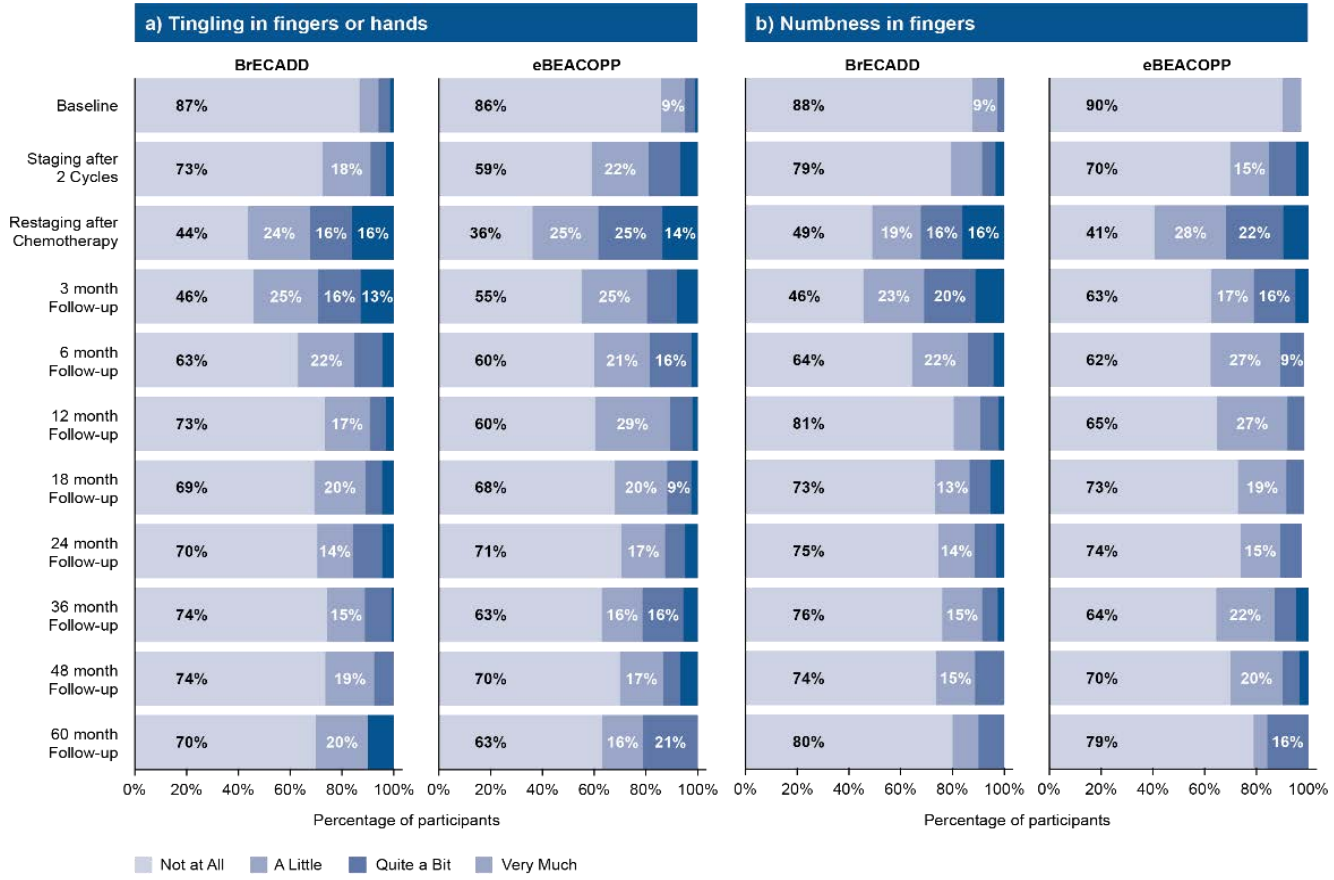
Characteristic	BrECADD N=360	eBEACOPP N=372
Ann Arbor stage, n(%)		
Class IIb	59 (16%)	53 (14%)
Class IIIa	65 (18%)	84 (23%)
Class IIIb	83 (23%)	87 (23%)
Class IVa	50 (14%)	57 (15%)
Class IVb	103 (29%)	91 (25%)
IPS score, n(%)		
0-2	205 (57%)	216 (58%)
3-7	155 (43%)	156 (42%)
ECOG-PS at baseline, n (%)		
0 – Fully active	238 (66%)	263 (71%)
1 – Symptoms ambulatory	116 (32%)	105 (28%)
2 – In bed <50% of daytime	6 (2%)	4 (1%)

Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Participants' Experience of CIPN Sensory Symptoms Over Time Across Arms

CIPN-related sensory symptoms (tingling and numbness in fingers or hands) were most frequently reported at restaging after chemotherapy and at 3-month FU

Figure 1: Tingling in fingers or hands (a) and numbness in fingers (b) experienced by participants as assessed by the EORTC QLQ-CIPN20

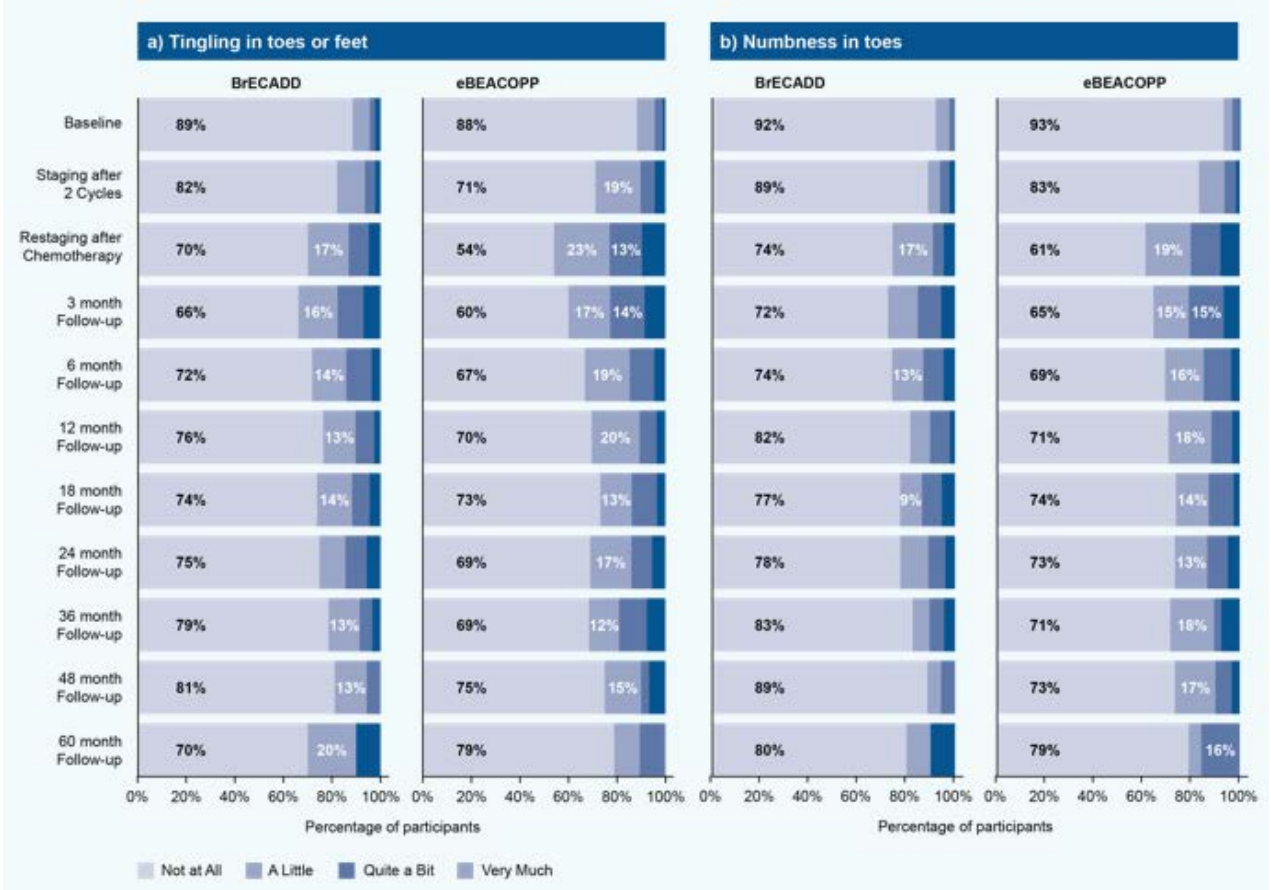


Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Participants' Experience of CIPN Sensory Symptoms Over Time Across Arms

CIPN-related sensory symptoms (tingling and numbness in toes or feet) were most frequently reported at restaging after chemotherapy and at 3-month FU

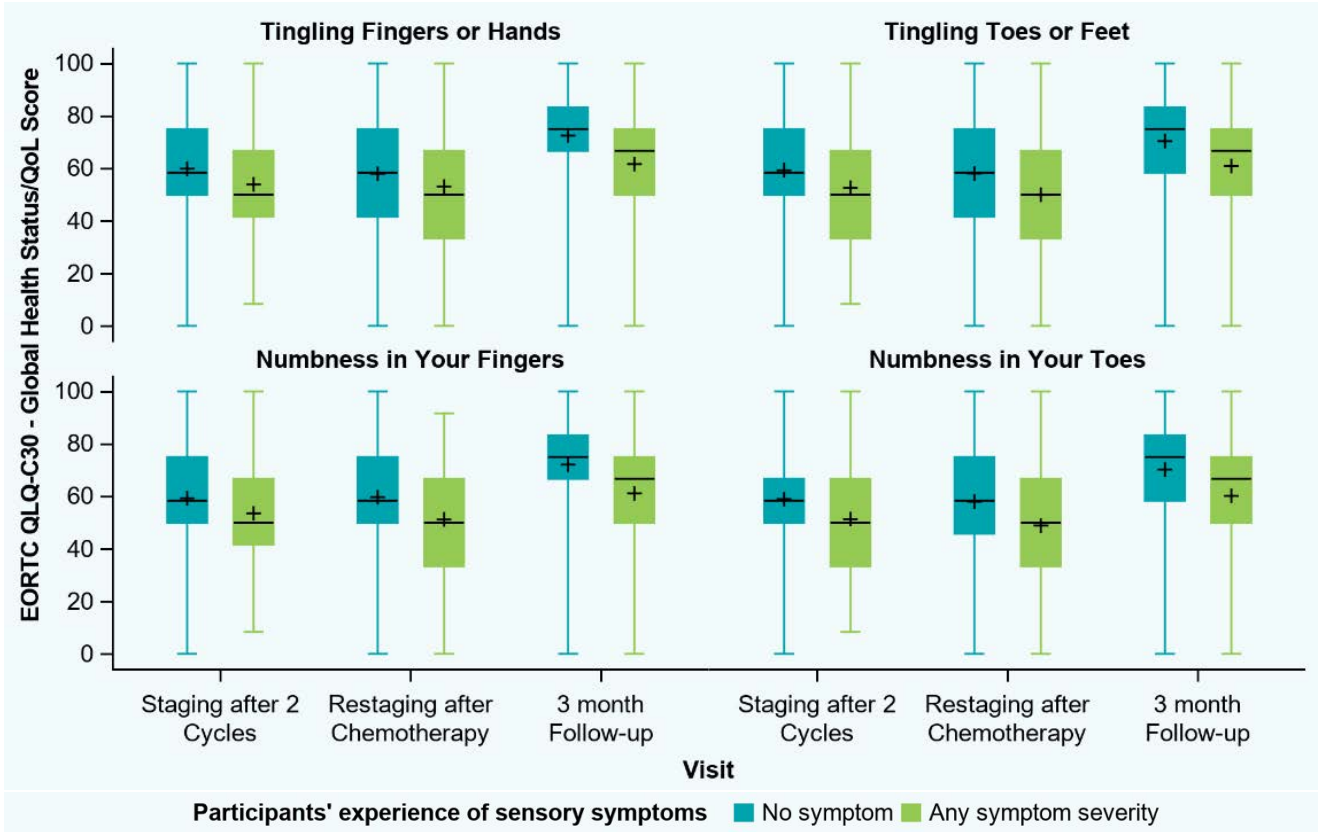
Figure 2: Tingling in toes or feet (a) and numbness in toes (b) experienced by participants as assessed by the EORTC QLQ-CIPN20



Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Impact of CIPN-Related Sensory Symptoms on Participants' Health-Related Quality of Life

Figure 3a: Impact of CIPN-related sensory symptoms on participants' global health/quality of life as assessed by the EORTC QLQ-C30 GH/QL score



Higher score = Better quality of life

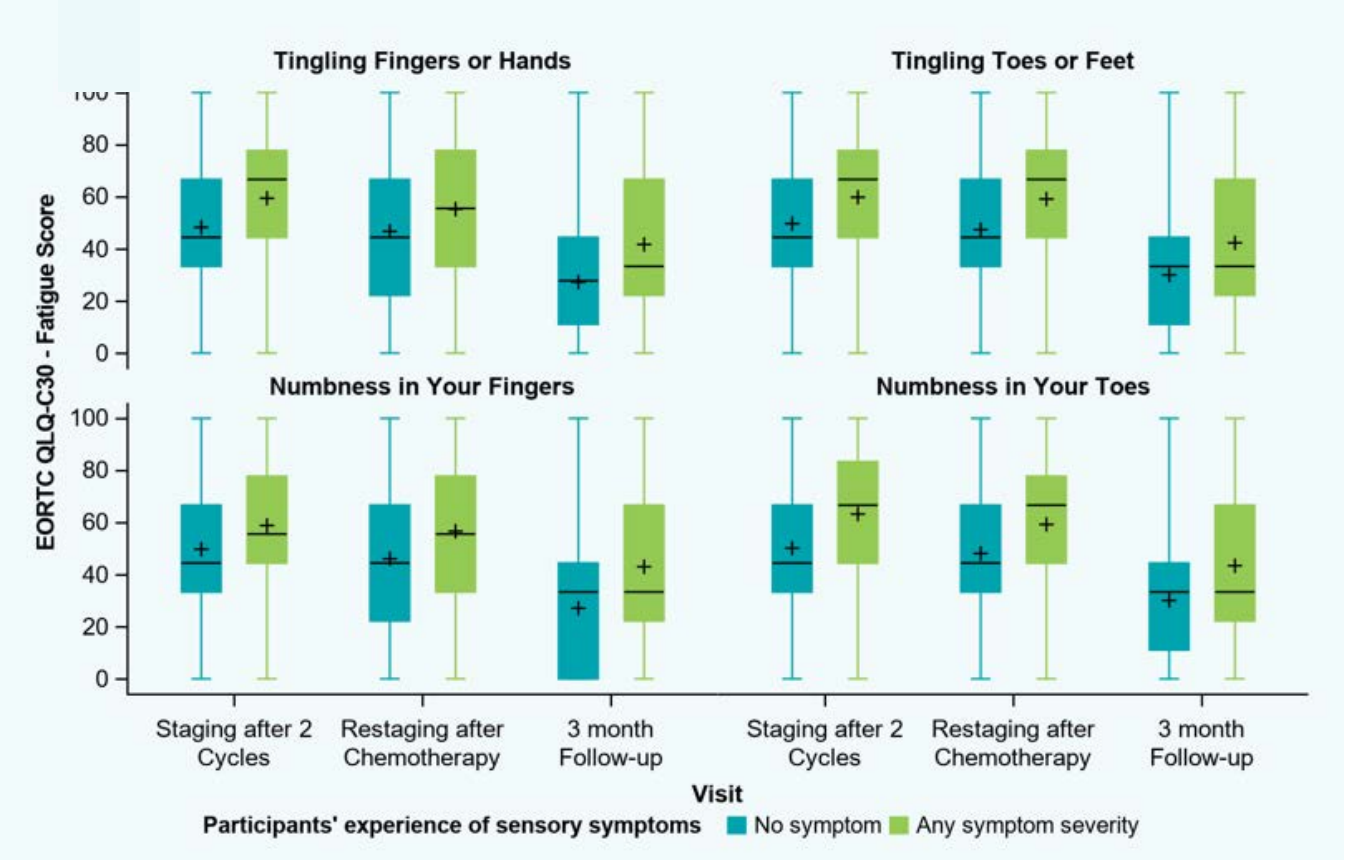
Higher score = Better quality of life

Legend: Box for each score: interquartile range (Q1-Q3); +: mean; —: median; bottom and top bars: score range (minimum and maximum).

Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Impact of CIPN-Related Sensory Symptoms on Participants' Fatigue

Figure 3b: Impact of CIPN-related sensory symptoms on participants' fatigue



Legend: Box for each score: interquartile range (Q1-Q3); +: mean; —: median; bottom and top bars: score range (minimum and maximum).

Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Author's Conclusions

- CIPN-related sensory symptoms, especially tingling and numbness in hands and feet, were reported by an increased proportion of patients at the end of the treatment period, and in the early follow-up assessments, in both BrECADD and eBEACOPP arms. Symptoms related to lower extremities generally occurred less frequently with BrECADD.
- Detrimental impact of CIPN-related sensory symptoms was observed on patient quality of life and fatigue

These analyses suggest that multiagent regimen treatments for newly diagnosed advanced-stage cHL associated with fewer CIPN-related sensory symptoms could also prevent the decrement in patient's health-related quality of life.

Kristo F, et al. Poster Presentation 1662. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024.

Effectiveness and safety for re-treatment with brentuximab-vedotin (BV) in patients with relapsed/refractory (R/R) CD30+ malignancies: A retrospective medical chart review study in Spain. The BELIEVE Study. NCT:04998331-Poster 2376

Ramón García-Sanz[1], Anna Sureda-Balari[2] Eva Domingo-Domenech[2], Francisco J. Capote[3], Antonio Gutierrez[4], Antonia Rodriguez[5], Marta Grande[6,7], and Lourdes Baeza-Montañez[6].

1. Hospital Universitario Gregorio Marañón, Madrid, Spain; 2. Institut Catala D'oncologia, Hospital Duran i Reynals. IDIBELL. L'Hospitalet de Llobregat, Barcelona, Spain; 3. Hospital Universitario Puerta del Mar, Cádiz, Spain; 4. Hospital Son Espases IdISBa, Palma de Mallorca, Spain; 5. Hospital Universitario 12 de Octubre, Madrid, Spain; 6. Medical Department, Takeda Farmacéutica España S.A, Madrid, Spain and 7. Universidad de Alcalá, Alcalá de Henares, Madrid, Spain.

Background

- **BV is a CD30-directed antibody-drug conjugate** indicated in patients with [1]:
  - Previously untreated Hodgkin lymphoma (HL) or anaplastic large cell lymphoma (ALCL)
  - R/R classical Hodgkin lymphoma (cHL)
  - Systemic anaplastic large cell lymphoma (sALCL)
  - CD30+ cutaneous T cell lymphoma (CTCL), including mycosis fungoides and primary cutaneous anaplastic large cell lymphoma.
- Although there are limited data on R/R patients who received BV retreatment, they showed promising clinical results[2-5].

To describe the effectiveness and safety of BV retreatment in R/R patients with CD30+ malignancies in a real-world setting in Spain.

BV: brentuximab-vedotin; RR: relapsed/refractory. 1. Takeda. Adcetris® (brentuximab vedotin) SmPc. 2023. https://www.ema.europa.eu; 2. Bartlett, NL et al. *J Hematol Oncol*. 2014;7:24; 3. Fukuhara, N et al. *Leuk Lymphoma*. 2020;61:176-80; 4. Sano, D et al. *Blood*. 2022;140:12003-04; 5. Sano, D et al. *Curr Oncol*. 2024;31:2598-609; 6. Mitteldorf, C et al. Poster A-133 Presented at EORTC-CLTG Annual Meeting, 9–11 October 2024, Lausanne, Switzerland

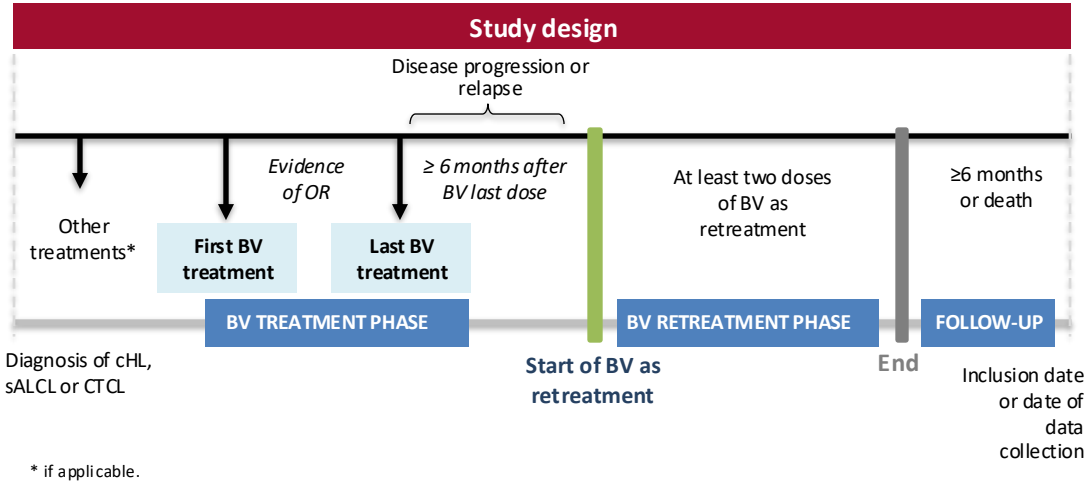
Garcia-Sanz R, et al. Poster Presentation 2376. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Methods

- **The BELIEVE study is a noninterventional, retrospective medical chart review conducted in 30 Spanish sites (2014-2022).**

Adult patients with CD30+ malignancies (cHL, sALCL and CTCL) treated with BV (evidence of objective response, OR) and having received ≥2 doses of BV as retreatment were included.

Follow up was up to ≥6 months, treatment discontinuation due to death, or toxicity.



BV: brentuximab-vedotin; cHL: classical Hodgkin lymphoma; CTCL: cutaneous T cell lymphoma; sALCL: systemic anaplastic large cell lymphoma

Garcia-Sanz R, et al. Poster Presentation 2376. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results: Patient Characteristics

- **43 patients were evaluable:** 16 cHL, 13 sALCL and 14 CTCL.

- Most patients (84%) received treatments between the first course of BV and BV retreatment.
- The median time from first BV treatment to retreatment initiation was 18 months.
- The median duration from diagnosis to end of follow-up was 6.26 (1.78–20.41) years

The median number of cycles during first BV was similar to the ones at BV retreatment: 6 (4-10)

- **cHL:** 4.5 (2-18)
- **sALCL**: 6 (2-20)
- **CTCL:** 7 (3-14)

20.9% of patients with one **allogenic transplant** after BV retreatment

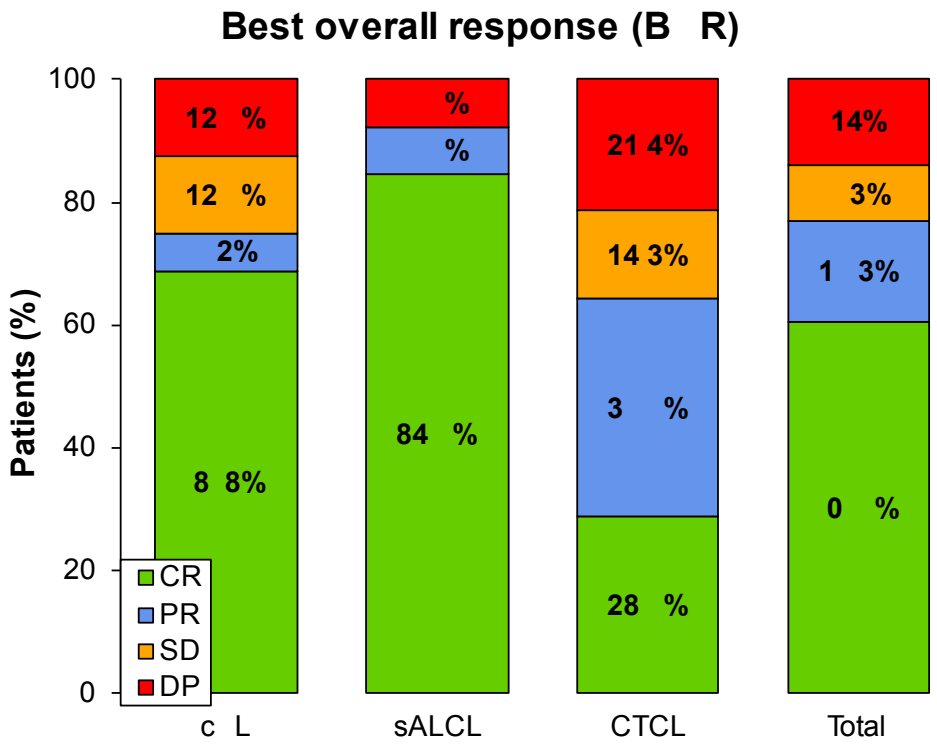
- **cHL:** 25% (n=4)
- **sALCL:** 23.1% (n=3)
- **CTCL**: 14.3% (n=2)

	Total patients n=43
Mean age, years (range)	46.2 (18.0-76.0)
Male, %	58.1%
Clinical stage (Ann Arbor) at BV retreatment, n	
Stage I	3
Stage II	8
Stage III	4
Stage IVa	5
Stage IVb	5
Missing	18
ECOG PS grade 0-1, %	91.8%
Treatments between the first BV and BV retreatment, n (range)	1.6 (1.0 – 5.0)
Median time between first BV and BV retreatment, months (range)	18 (7–108)
Transplants before BV retreatment, n	
1 autologous transplant	0
2 autologous transplants in tandem	0
2 allogenic transplant	1

BV: brentuximab-vedotin; cHL: classical Hodgkin lymphoma; CTCL: cutaneous T cell lymphoma; sALCL: systemic anaplastic large cell lymphoma; SD: standard deviation; ECOG PS: Eastern Cooperative Oncology Group Performance Status .

Garcia-Sanz R, et al. Poster Presentation 2376. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results: best overall response (BOR)

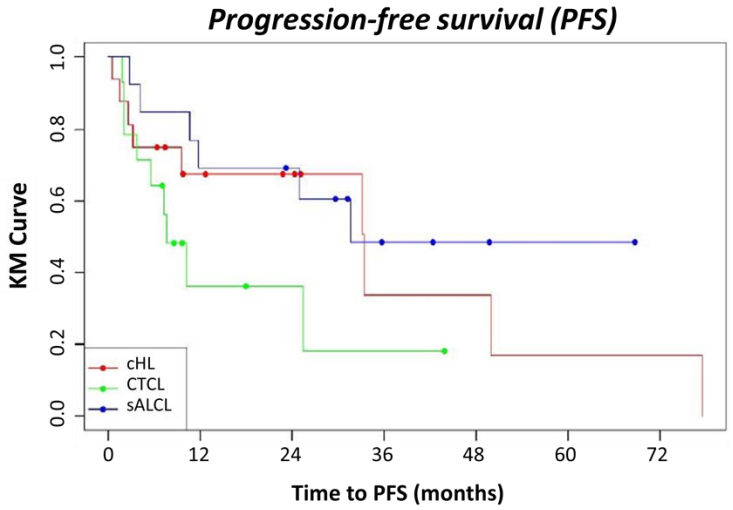


- A total of **77% patients achieved overall response:**
  - 26 (61%) CR, 7 (16%) PR and progression was observed in 6 patients (14%).
- Overall, the median time to achieve CR was 4 (0.6-24.3) months.

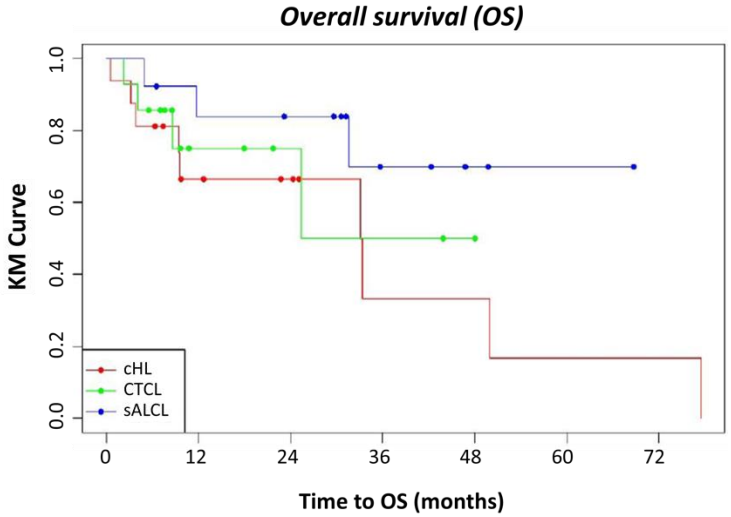
BOR: best overall response; BV: brentuximab-vedotin; CR: complete response; cHL: classical Hodgkin lymphoma; CTCL: cutaneous T cell lymphoma; DP: disease progression; PR: partial response; sALCL: systemic anaplastic large cell lymphoma; SD: stable disease

Garcia-Sanz R, et al. Poster Presentation 2376. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results: survival



- The **PFS was 9.6 months** (0.5-77.5) and was reported by **55.8% of patients**.



- **OS was reported for 27 patients (62.8%),** including 7 cHL (43.8%), 10 sALCL patients (76.9%) and 10 CTCL (71.4%)
- Overall, the median KM time to death was 50.0 (0.5-77.5) months: 33.1 (0.5-77.5) in cHL group, - (4.9 - 31.6) months in sALCL group and 25.4 (2.3-25.4) in CTCL group.

BV: brentuximab-vedotin; cHL: classical Hodgkin lymphoma; CTCL: cutaneous T cell lymphoma; OS: overall survival; PFS: progression-free survival; sALCL: systemic anaplastic large cell lymphoma; KM: Kaplan-Meier

Garcia-Sanz R, et al. Poster Presentation 2376. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results: safety and treatment characteristics

AEs related to BV retreatment

45%

N=18

- In total, 18 patients experienced AEs related to BV retreatment, mainly peripheral sensory neuropathy.

Severe AEs

19%

N=8

- Overall, 8 patients experienced severe AEs: 1 (2.3%) peripheral motor neuropathy, 3 (7%) peripheral sensory neuropathy, 1 (2.3%) neutropenia and 3 (7%) others with clinical relevance.

- **No grade 5 events were reported during retreatment**

The **median initial dose of BV retreatment** was the same as in the first course of BV, **1.8 mg/kg**, and was also constant in the three cohorts.

- Eight (19%) patients had an initial dose adjustment mostly due to peripheral neuropathy.
- During retreatment, 5 patients had a dose adjustment of 1.2 mg/kg: 1 in CTCL group and 4 sALCL patients.

AE: adverse event; BV: brentuximab-vedotin; cHL: classical Hodgkin lymphoma; CTCL: cutaneous T cell lymphoma; OS: overall survival; PFS: progression-free survival; sALCL: systemic anaplastic large cell lymphoma.

Garcia-Sanz R, et al. Poster Presentation 2376. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Author’s Conclusions

- The BELIEVE study is the first real word evidence study in Spain that assesses the role of BV as retreatment.
- Adverse events were manageable with dose modification or interruption.
- BV retreatment seems to be a promising and tolerable treatment alternative.

BV: brentuximab-vedotin

Garcia-Sanz R, et al. Poster Presentation 2376. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

P-4435

BV-CHP in Previously Untreated Patients With CD30-Positive Adult T-Cell Leukemia-Lymphoma: A Multicenter Real-World Retrospective Study

Junya Makiyama[1], Masahito Tokunaga[2], Motoaki Shiratsuchi[3], Takanori Toyama[4], Satoshi Oka[5], Ilseung Choi[6], Takahiro Yoshida[7], Kiyoshi Okazuka[7], Atae Utsunomiya[2]

[1]Department of Hematology, Sasebo City General Hospital, Sasebo, Japan; [2]Department of Hematology, Imamura General Hospital, Kagoshima, Japan; [3]Department of Hematology, Iizuka Hospital, Iizuka, Japan; [4]Department of Internal Medicine, Miyazaki Prefectural Nobeoka Hospital, Nobeoka, Japan; [5]Department of Hematology and Blood Transfusion, Kochi Health Sciences Center, Kochi, Japan; [6]Department of Hematology and Cell Therapy, NHO Kyushu Cancer Center, Fukuoka, Japan; [7]Japan Medical Affairs, Japan Oncology Business Unit, Takeda Pharmaceutical Company Limited, Tokyo, Japan

Methods
Study Design

Medical records of patients from 6 sites in Japan

Primary endpoint: ORR[a] for BV-CHP
Key secondary endpoints: OS and PFS

Patients aged ≥18 years with previously untreated CD30-positive ATL, treated with BV-CHP

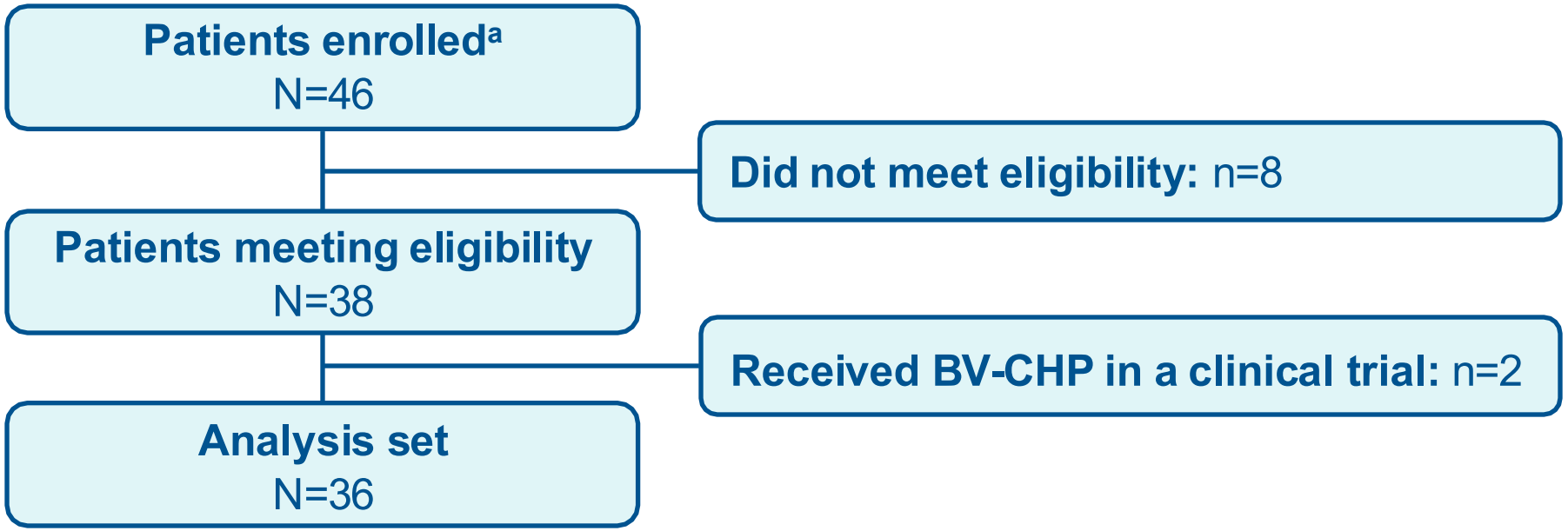
AEs tracked for up to 4 weeks post-treatment

CD30 positivity determined via immunohistochemistry or flow cytometry

This study was conducted in accordance with Ethical Guidelines for Medical and Biological Research Involving Human Subjects.
[a] Response and progression were assessed using the JCOG version of the ATL response criteria.
AE, adverse event; ATL, adult T-cell leukemia-lymphoma; BV-CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisolone; JCOG, Japan Clinical Oncology Group; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Methods
Patient Disposition Flowchart



Patients who started BV-CHP treatment between April 2020 and January 2024 were included in the analysis set.
[a] From 6 sites.
BV-CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisolone.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results

Patient Demographics and Baseline Characteristics

Characteristics	Analysis Set (N=36)
Age, years	
Median (range)	71 (53–92)
≤70	13 (36.1)
>70	23 (63.9)
Sex, n (%)	
Male	12 (33.3)
Female	24 (66.7)
ECOG PS	
0–1	32 (88.9)
2	4 (11.1)
Ann Arbor clinical stage	
I	0
II	2 (5.6)
III	9 (25.0)
IV	23 (63.9)
Unknown	2 (5.6)

Characteristics	Analysis Set (N=36)
ATL subtypes	
Acute	19 (52.8)
Lymphoma	17 (47.2)
Simplified ATL-PI[9]	
Low risk	11 (30.6)
Intermediate risk	19 (52.8)
High risk	6 (16.7)
Duration of follow-up, days	
Median (range)	372.5 (74–1253)
Number of cycles of BV-CHP	
Median (range)	3 (1–6)
Relative dose intensity of BV, %	
Median (range)	86.9 (57.8–123.5)
CD30 expression[a], %	
Median (range)	40.8 (7.1–91.4)

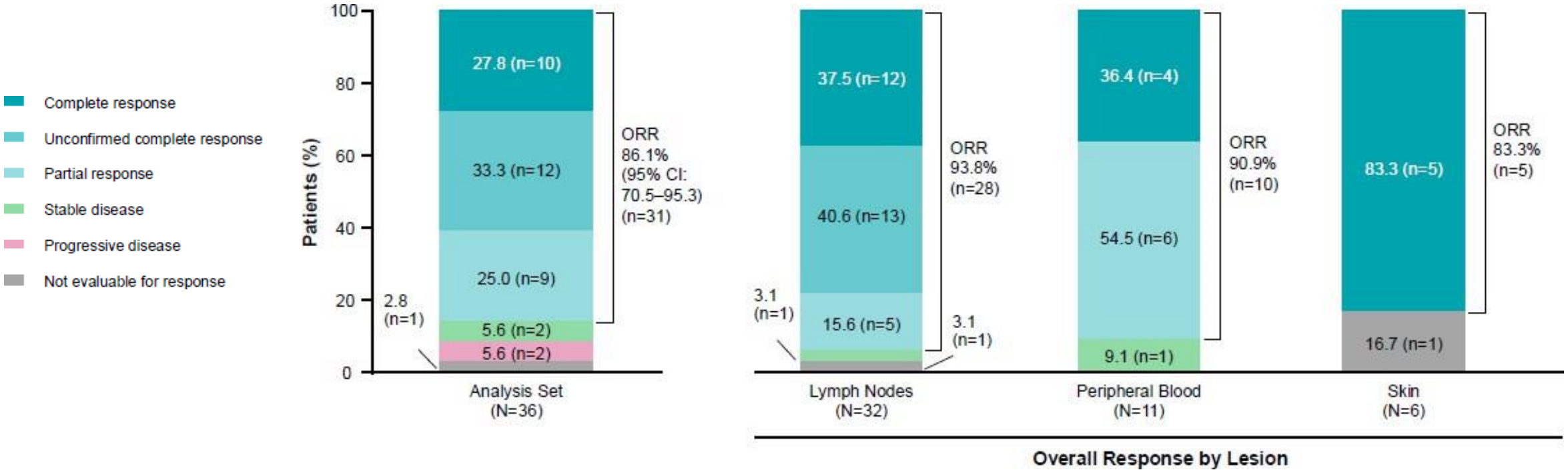
Data are n (%) unless stated otherwise.

[a] In all patients, CD30 positivity was confirmed through either immunohistochemistry or FCM; the quantitative results from the 20 patients measured using FCM showed a CD30 positivity rate of 40.8%.

ATL, adult T-cell leukemia-lymphoma; ATL-PI, prognostic index for acute and lymphoma type ATL; BV, brentuximab vedotin; BV-CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisolone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FCM, flow cytometry.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results
Summary of Overall Response

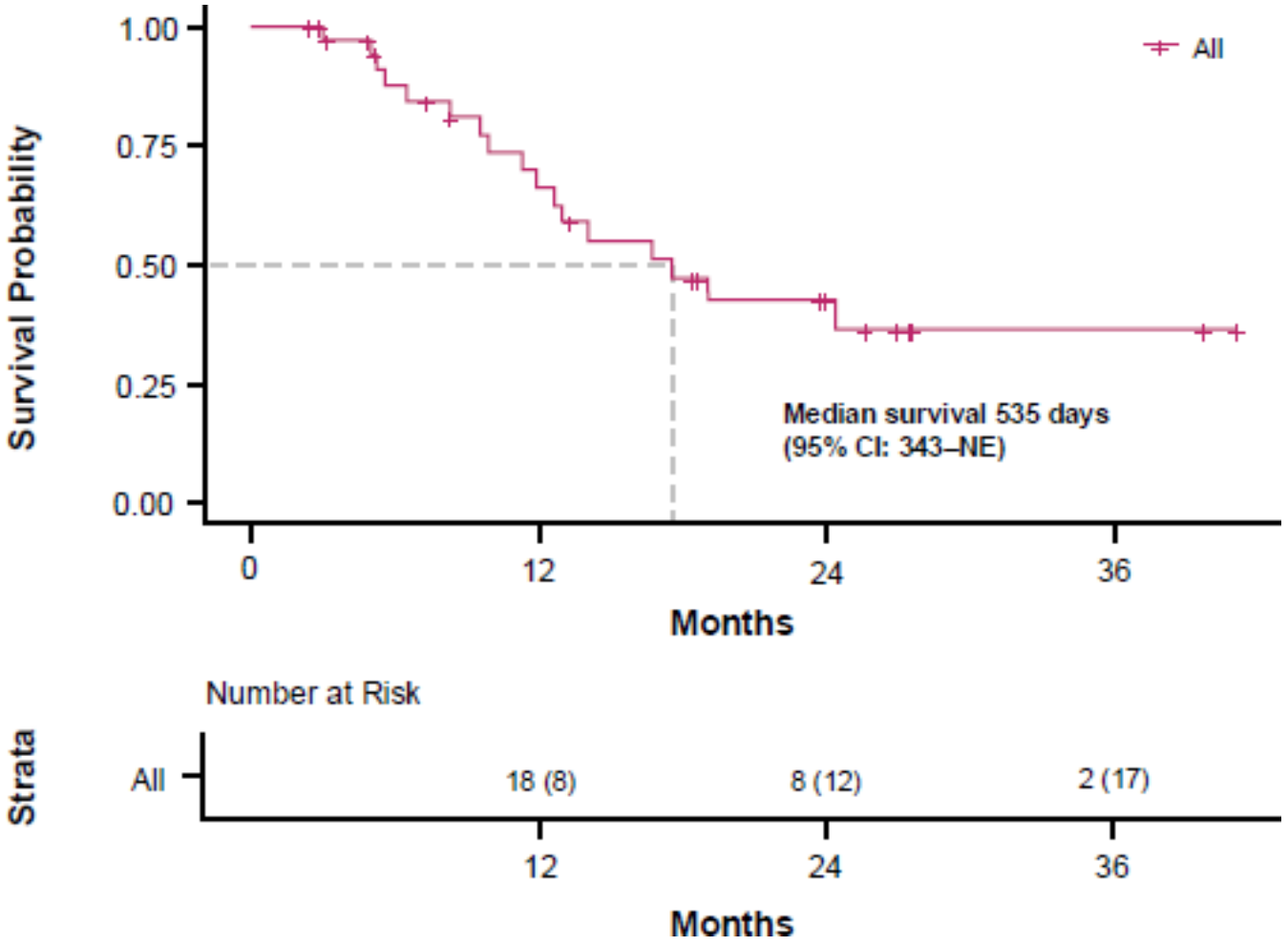


Total percentages may not add up to 100% due to rounding; ORR may not add up to sum of responses due to rounding.
CI, confidence interval; ORR, overall response rate.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results

Overall Survival in the Analysis Set (N=36)

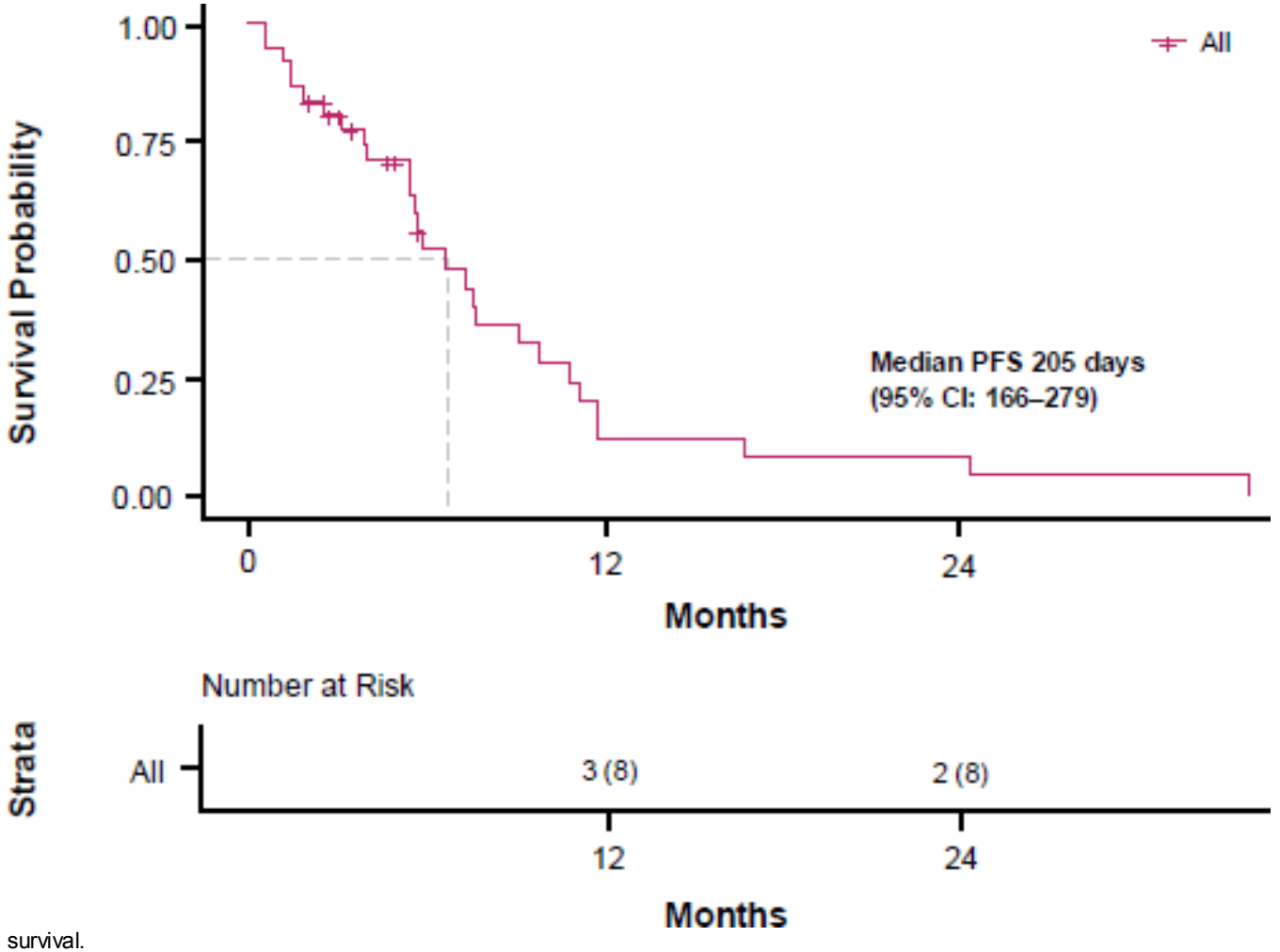


CI, confidence interval; NE, not estimable.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results

Progression-Free Survival in the Analysis Set (N=36)

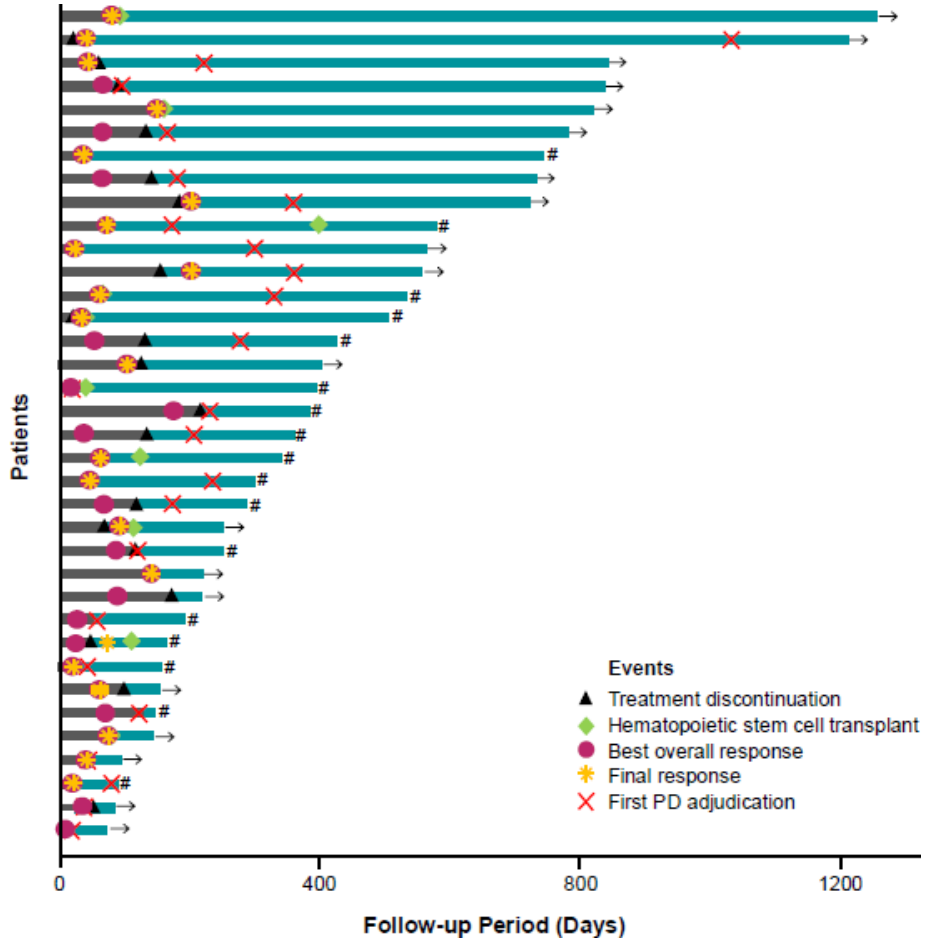


CI, confidence interval; PFS, progression-free survival.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

RESULTS

Swimmer Plot of Clinical Course for Individual Patients



Note 1: The period highlighted in dark gray on the bar represents the BV-CHP administration period, and the remaining periods are highlighted in teal.
Note 2: If the patient is censored, it is marked as →, and if the patient is death, it is marked as '#'.
BV-CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisolone; PD, progressive disease.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results

Summary of Adverse Events in the Analysis Set (N=36)

Details	Any Grade[a]	Grade ≥3
Patients with any TEAEs	32 (88.9)	32 (88.9)
Hematologic		
Neutropenia[b]	28 (77.8)	28 (77.8)
Febrile neutropenia	14 (38.9)	14 (38.9)
Thrombocytopenia[c]	7 (19.4)	4 (11.1)
Anemia	4 (11.1)	1 (2.8)
Leukopenia	2 (5.6)	1 (2.8)
Non-hematologic		
Peripheral neuropathy[d]	4 (11.1)	0
Herpes zoster	3 (8.3)	2 (5.6)
Sepsis	2 (5.6)	2 (5.6)
COVID-19 infection	2 (5.6)	2 (5.6)
CMV infection	2 (5.6)	2 (5.6)
Interstitial lung disease	2 (5.6)	1 (2.8)

- Of 36 patients, 7 discontinued BV due to adverse events (AEs).
  - AEs that lead to discontinuation were myelosuppression, skin disorder, infection, and interstitial pneumonia.
- Peripheral neuropathy occurred in 4 patients (3 with grade 2 and 1 with grade 1).
  - 1 patient had a BV dose reduction due to peripheral neuropathy.
- All AEs were resolved or improved, with no treatment-related deaths.

Data are n (%).
AEs were coded to a System Organ Class and Preferred Term using the Medical Dictionary for Regulatory Activities Version 26.1.
[a] Only AEs occurring in ≥5% of patients are reported for any grade; [b] Includes the Preferred Terms neutropenia and neutrophil count decreased; [c] Includes the Preferred Terms thrombocytopenia and platelet count decreased; [d] Includes the Preferred Terms peripheral neuropathy and peripheral sensory neuropathy.
AE, adverse event; BV, brentuximab vedotin; CMV, cytomegalovirus; TEAE, treatment-emergent adverse event.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results

Demographics and Baseline Characteristics for Stem Cell Transplanted/Non-transplanted Patients

Characteristics	SCT Patients (n=11)	Non-SCT Patients (n=25)
Age, years		
Median (range)	65 (61–72)	75 (53–92)
Sex, n (%)		
Male	2 (18.2)	10 (40.0)
Female	9 (81.8)	15 (60.0)
ECOG PS		
0–1	11 (100.0)	21 (84.0)
2	0	4 (15.0)
ATL subtypes		
Acute	6 (54.5)	13 (52.0)
Lymphoma	5 (45.5)	12 (48.0)
Ann Arbor clinical stage		
I	0	0
II	0	2 (8.0)
III	3 (27.3)	6 (24.0)
IV	8 (72.7)	15 (60.0)
Unknown	0	2 (8.0)
Simplified ATL-PI[9]		
Low risk	4 (36.4)	7 (28.0)
Intermediate risk	6 (54.5)	13 (52.0)
High risk	1 (9.1)	5 (20.0)

Data are n (%) unless stated otherwise.
ATL, adult T-cell leukemia-lymphoma; ATL-PI, prognostic index for acute and lymphoma type ATL; ECOG PS, Eastern Cooperative Oncology Group Performance Status; SCT, stem cell transplantation.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Results

Outcomes in Stem Cell Transplanted/Non-Transplanted Patients Following BV-CHP Therapy

- Of the 36 patients, 11 received allogeneic stem cell transplantation (10 with cord blood and 1 with peripheral blood).
- The disease status before transplantation was 2 complete response, 8 partial response, and 1 stable disease following a median of 3 cycles of BV-CHP (range, 1–6).
- Acute graft-versus-host disease was observed in 2 of 11 patients, including grade 1 in 1 patient and grade 4 in 1 patient.
- The median PFS after initiation of BV-CHP was 234 (95% CI: 168–343) days and 180 (95% CI: 96–279) days in transplanted and non-transplanted patients, respectively.

BV-CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisolone; CI, confidence interval; PFS, progression-free survival.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Discussion

- In this real-world study, BV-CHP demonstrated an overall response rate (ORR) of 86.1% with a median PFS of 6.7 months (205 days), which is comparable to regimens like mLSG15 + mogamulizumab (ORR 86%; PFS 8.5 months) and mLSG15 alone (ORR 75%; PFS 6.3 months).[5]
- AEs were manageable, including non-hematologic toxicity.
  - Compared with mogamulizumab, BV-CHP had a low incidence of acute graft-versus-host disease, and no evident effect on subsequent treatments was observed.[6,10]
- Graft-versus-host disease frequency varies by transplant type, graft source, and human leukocyte antigen (HLA) disparity.
  - This study's limitations include a higher proportion of cord blood transplants and no HLA disparity data.

Author's Conclusions

- In this multicenter retrospective study, BV-CHP demonstrated a favorable ORR with acceptable tolerability.
- All AEs were manageable, and no new safety signals were observed.
  - However, high rates of neutropenia and febrile neutropenia were observed, suggesting that granulocyte colony-stimulating factor primary support might be indicated for these patients.
- These data support BV-CHP as a potential standard first-line therapy for CD30-positive ATL.

Makiyama J, et al. Poster Presentation 4435. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-10, 2024

Brentuximab Vedotin, Cyclophosphamide, Doxorubicin and Prednisone (BCAP) First-Line Treatment of Advanced-Stage Hodgkin Lymphoma in OlderPatients: Final Results of the GHSG-NLG Phase II BVB Trial

Brockelmann PJ, et al.
Abstract #3054

Paul J. Bröckelmann[1,2*], Boris Böll[1*], Daniel Molin[3] Gundolf Schneider[1], Sirpa Leppä[4], Julia Meissner[5], Peter Kamper[6], Martin Hutchings[7], Jacob Haaber Christensen[8], Ulf Schnetzke[9], Michael Fuchs[1], Dennis A. Eichenauer[1], Bastian von Tresckow[1,10], Helen Kaul[1], Peter Borchmann[1], Alexander Fossså[11]

1 University Hospital of Cologne and German Hodgkin Study Group (GHSG), Cologne, Germany; 2 Max Planck Institute for Biologyof Ageing, Cologne, Germany; 3 Uppsala, Sweden and Nordic Lymphoma Group (NLG); 4 Helsinki, Finland and NLG; 5 Heidelberg, Germany; 6 Aarhus, Denmark and NLG; 7 Copenhagen, Denmark; 8 Odense, Denmark; 9 Jena, Germany; 10 Essen, Germany; 11 Oslo, Norway and NLG. *Equal Contribution,

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

Introduction and Aim

- The incidence of classic Hodgkin lymphoma (cHL) in the elderly is increasing, outcomes among elderly patients with advanced-stage disease are historically poor, and prospective clinical trials dedicated to this vulnerable population are scarce.
- We evaluated the combination of the antibody-drug conjugate brentuximab vedotin (BV) with an anthracycline-containing chemotherapy in first-line.

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

Methods and Patients

- The international GHSG-NLG intergroup phase II BVB trial (NCT02191930) evaluated six cycles of BCAP, consisting of BV (1.8mg/kg on day 1), cyclophosphamide (750mg/m2 d1), doxorubicin (50mg/m2 d1) and prednisone (100mg/day 2-6) as first-line treatment for advanced-stage cHL patients ≥60 years. Consolidative radiotherapy of 30 Gy was recommended for PET-positive residuals after end of systemic treatment (EOT; Figure 1).

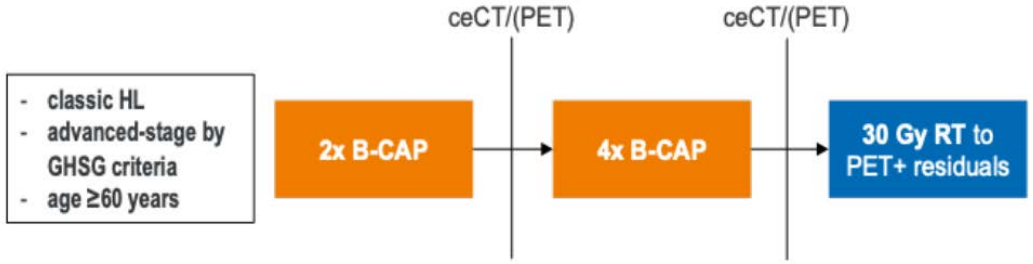


Figure 1: Study Flow Chart

- Primary endpoint was objective response rate (ORR) determined by computed tomography (CT) after completion of B-CAP

- A total of 49 evaluable patients were recruited between 11/2015 and 09/2017 and characteristics are summarized in Table 1.

Age	Median: 66 years; range: 60 – 84; IQR: 64 – 70 years 4 patients (8%) were ≥ 75 years old
Sex	Female: 23 (47%), male 26 (53%)
Ann Arbor stage	IIB: 2 (4%) IIIA: 7 (14%), IIIB: 8 (16%) IVA: 7 (14%), IVB: 25 (51%)
GHSG risk factors	LMM: 5 (10%) EN-disease: 7 (14%) ≥3 nodal areas: 38 (78%) Elevated ESR: 32 (65%)
IPS (n=48)	1: 3 (6%), 2-3: 21 (44%), 4-7: 24 (50%)
ECOG status	0: 13 (27%), 1: 30 (61%), 2: 4 (8%), 3: 2 (4%)
CIRS-G sum score	0: 6 (12%), 1-3: 25 (51%), 4-7: 18 (37%)
cHL subtype (n=35)	NS: 18 (51%), MC: 12 (34%), LR: 1 (3%), NOS: 4 (11%)

Table 1: Patient Characteristics

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

Results

- With primary G-CSF support documented in 98% of patients, the maximum dose level was maintained in 86% of patients, and the mean relative dose intensity was 93%.
- Most patients experienced hematological toxicities (any G: 92%, G3: 8%, G4: 53%); i.e. neutropenia (G3/4: 61%), anemia (G3/4: 18%) and thrombocytopenia (G3/4: 10%).
- Febrile neutropenia occurred in 27% and infections in 61% (G3: 29%, G4: 2%, G5: 2%) of patients, respectively.
- Neuropathy increased with accumulating B-CAP exposure, was mostly sensory and reported in 67% of patients (G2: 20%, ≥G3: 0). Dose-reduction or omission of BV occurred in 3 patients each.

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

Results (cont.)

- After 2 cycles B-CAP, 94% had an objective response including 34% with CR (Figure 2A).
- The predefined primary endpoint was met with a CT-based ORR at EOT of 98% (95%CI: 90.5-100; CR: 44%), respectively (Figure 2B).

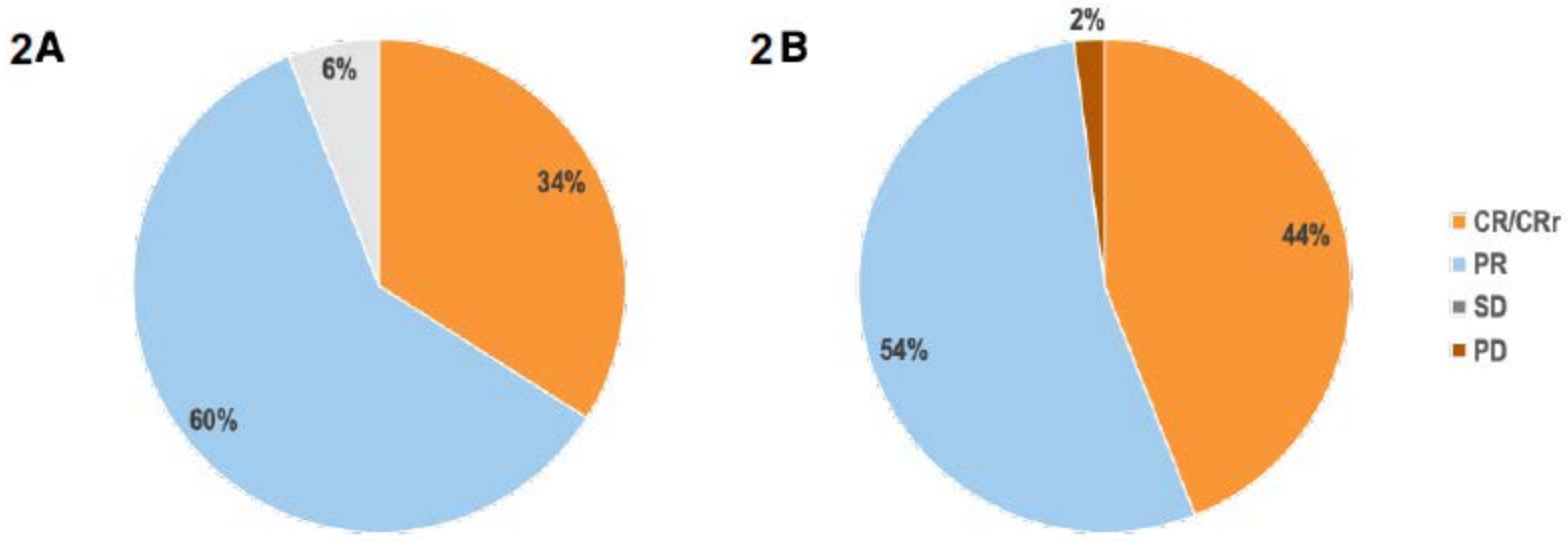


Figure 2: **(A)** ceCT-based remission status after 2x B-CAP **(B)** ceCT-based remission status at EOT. Abbreviations: ceCT: contrast-enhanced computed tomography, CR/CRr: complete remission (with residuals), PR: partial remission, SD: stable disease, PD: progressive disease.

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

Results (cont.)

- Positron emission tomography (PET) after the last cycle showed metabolic CR in 31/48 evaluable patients (65%).
- Ten patients (20%) received consolidative 30 Gy radiotherapy to PET+ residues.
- With a median follow-up of 35 months, 16 patients (33%) experienced tumor progression or relapse and 9 (18%) died, mostly from cHL (6 patients, 12%).
- 3-year PFS (Figure 3A) and OS are 64% (95%CI: 50-79) and 91% (95%CI: 82-99), with more favorable 3-year PFS observed in patients achieving a metabolic CR (82%) compared to patients with metabolic PR (33%; HR 6.7, 95%CI 2.3-19.7; Figure 3B).

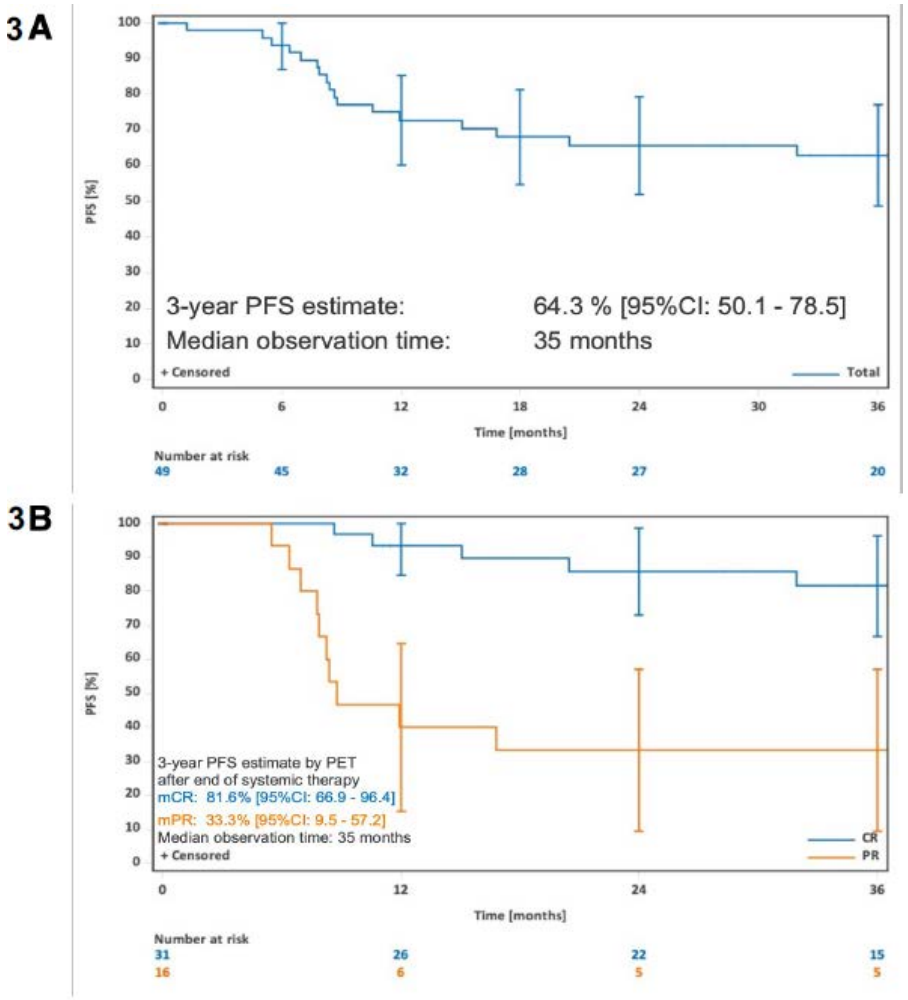


Figure 3: (A) PFS of the ITT population **(B)** PFS stratified by metabolic response at EOT in patients with available PET-based restaging after up to 6x B-CAP. Abbreviations: mCR: metabolic CR, mPR: metabolic PR.

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

Results (cont.)

- Exploratory analyses of patient-reported outcomes (PRO) are ongoing and preliminary results indicate normalization of global health status measured by the EORTC QLQ-C30 questionnaire to age and sex-matched reference values after EOT (Figure 4).
- Additionally, resolution of pre-existing and on-treatment symptoms and an improvement in functioning scales is observed in most patients.

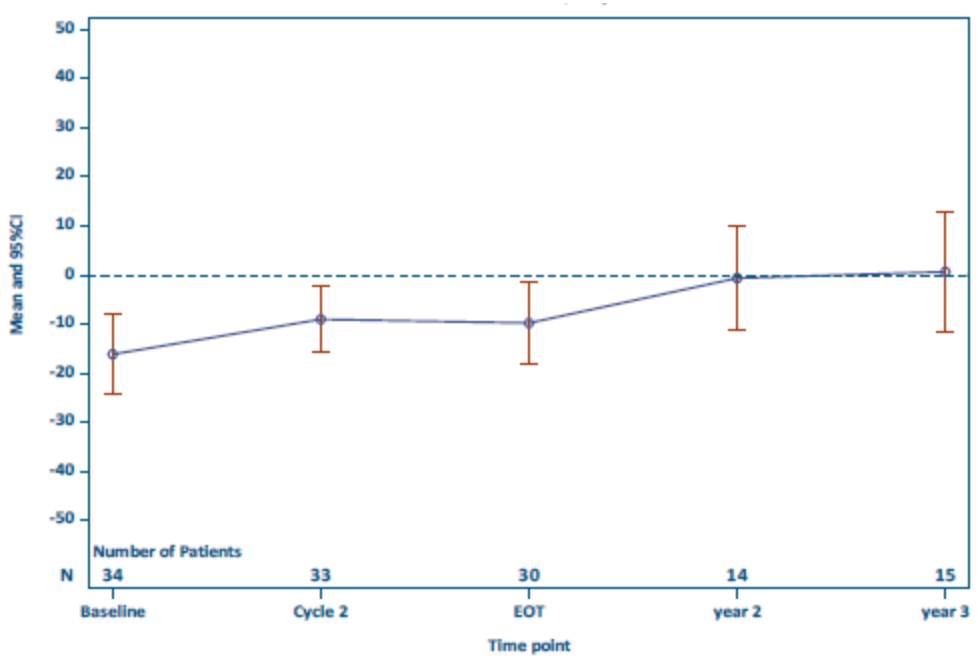


Figure 4: Longitudinal trajectory of the age- and sex-normalized general health status by EORTC QLQ-C30 questionnaire in n=34 patients with evaluable baseline documentation

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

Author’s Conclusion

- The B-CAP regimen is a feasible and effective treatment option for older patients with advanced-stage cHL, resulting in high response rates already after 2 cycles and favorable 3-year PFS in patients achieving a metabolic CR.

Brockelmann PJ, et al. Poster Presentation 3054. Presented at American Society of Hematology (ASH) Annual Meeting 2024, San Deigo, December 7-12, 2024.

PET-Guided BrECADD in Older Patients with Advanced-Stage Classic Hodgkin Lymphoma:

Results from a Phase 2 Part of the GHSG HD21 Trial

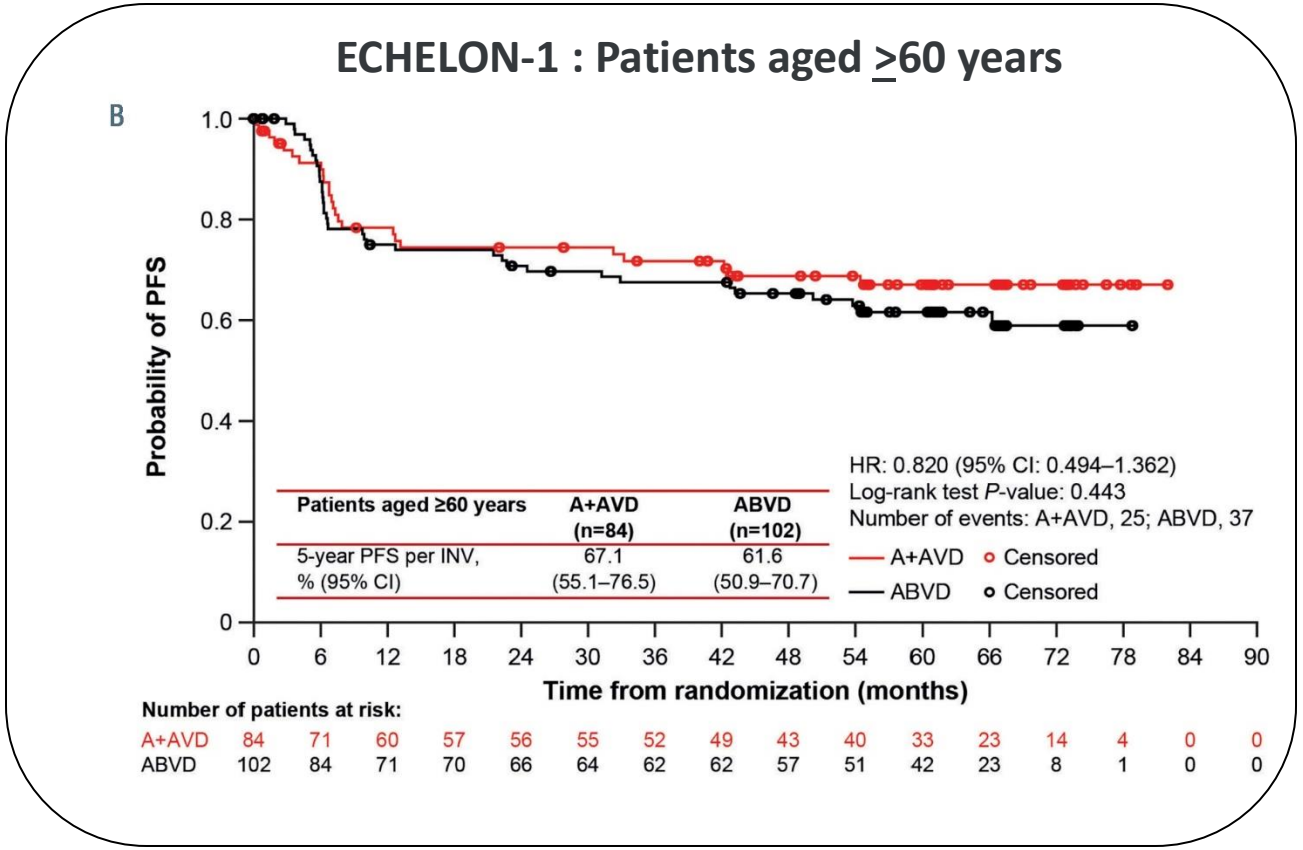
Justin Ferdinandus, Helen Kaul, Alexander Fosså, Andreas Hüttmann, Felix Keil, Yon-Dschun Ko, Felicitas Hitz, Michaela Schwarz, Corinna Trenker, Andrea Kerkhoff, Peter Staib, Kai Wille, Irmgard Dresel, Dennis Hahn, Bernd Hertenstein, Peter Moosmann, Ulrich Mey, Stefan Balabanov, Tasman Armytage, Fernando Roncolato, Johannes C. Hellmuth, Stefanie Kreissl, Michael Fuchs, Gundolf Schneider, Hishan Tharmaseelan, Dennis A. Eichenauer, Bastian von Tresckow, Peter Borchmann, Paul J. Bröckelmann on behalf of GHSG HD21 Investigators

Background

Older patients with advanced-stage Hodgkin Lymphoma (AS-cHL) have inferior outcomes and fewer treatment options.

- eBEACOPP is not feasible with a treatment-related mortality of approx. 15%.[2]

- 5y-PFS of A-AVD (67%) and ABVD (62%) is insufficient.[1]



➢ **High unmet need for effective treatment options in patients with AS-cHL older than 60 years.**

GHSG

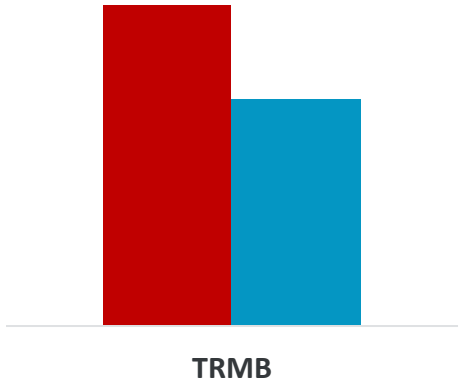
1 Wongso, D et al., JCO 2013
2 Evens, AM et al., Hemasphere 2022

Rationale

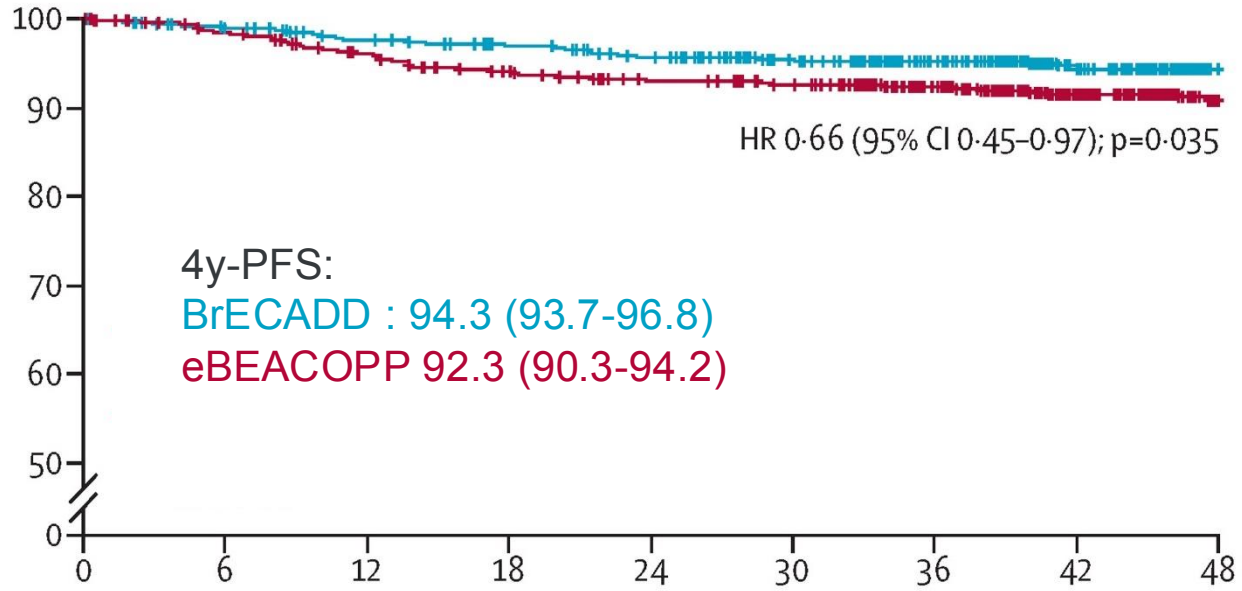
Co-primary Endpoints of GHSG HD21:

Borchmann et al. @ ASH 2022

Treatment-related morbidity (TRMB):
59% (eBEACOPP) vs. 42% (BrECADD)
RR 0.70 (0.63 – 0.78)



Borchmann et al. @ ASH 2023



➢ **Is BrECADD feasible and effective in older patients with AS-cHL?**

GHSG

Borchmann, P et al., Lancet, 2024

Study Design

Prospective, international, multicenter, single-arm add-on cohort to the HD21 trial

N=85
Age 61-75

2 x BrECADD

Interim PET/CT staging

PET2 neg. → **2x BrECADD**

PET2 pos. → **4x BrECADD**

Restaging

RT 30Gy to PET+ residuals

Trial objectives

- Primary: Estimate efficacy of PET-guided BrECADD defined as CR rate after chemotherapy (primary endpoint).
- Secondary: Further explore efficacy, safety and feasibility of PET-guided BrECADD in older patients with AS-cHL

GHSG

Baseline Characteristics

ITT population (n=83)

Characteristic		No. (%)
Age	Median (IQR, range)	67 (63 – 70, 61 – 75)
Sex	Female	32 (39)
	Male	51 (61)
CIRS-G Sum Score	Mean (SD)	3.7 (2.7)
	Median (range)	3 (0 – 10)
Comorbidities	Absent	11 (13)
	Present	72 (87)
ECOG	0	39 (47)
	1	29 (35)
	2	15 (18)
Frailty[1]	0 (fit)	43 (52%)
	1-2 (unfit)	38 (46%)
	3 (frail)	2 (2%)
Ann Arbor Stage	II	3 (4)
	III	35 (42)
	IV	45 (54)
IPS	0-2	22 (27)
	3-7	61 (73)

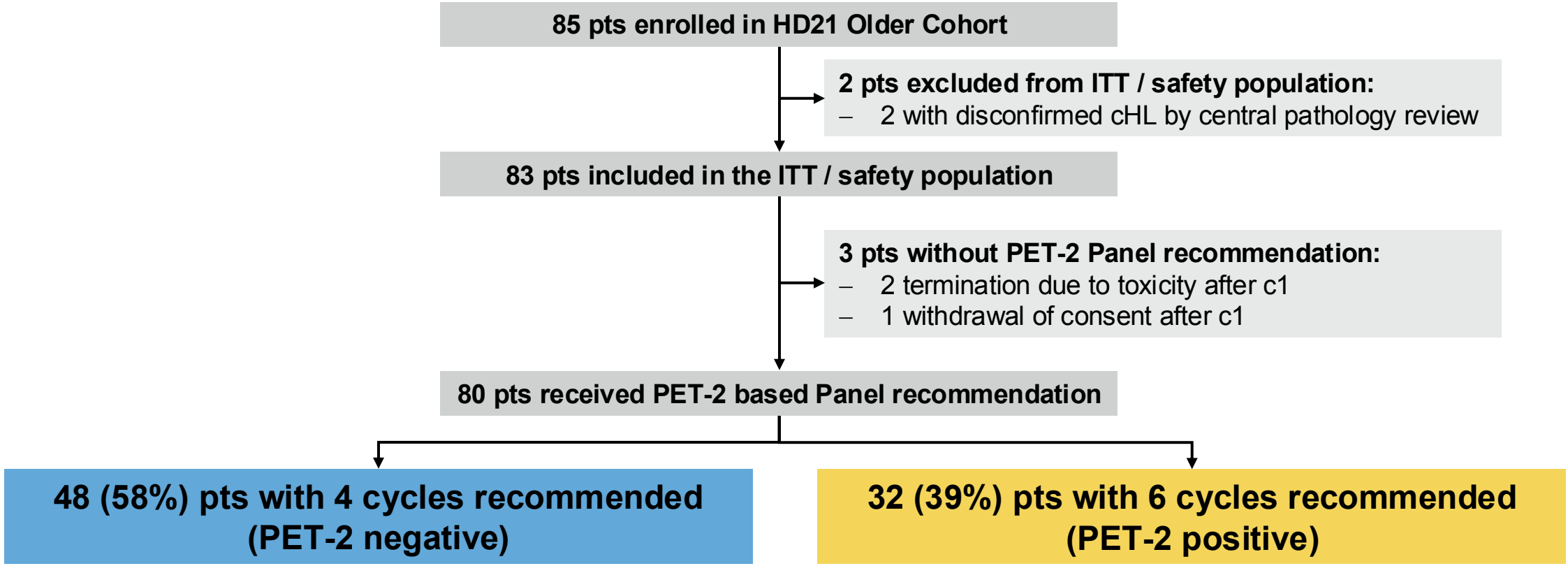
Summary

- 83 patients included in the ITT cohort.
- Median age: 67 years (range: 61-75)
- A majority had IPS ≥3 (73%)
- Almost all presented with comorbidities (87%).
- Mean Cumulative Illness Rating Scale-Geriatric (CIRS-G) score of 3.7 (SD 2.6).
- Approx. half of the cohort unfit or frail.[1]

GHSG

1 Lia K et al, @ISHL13

Trial flowchart

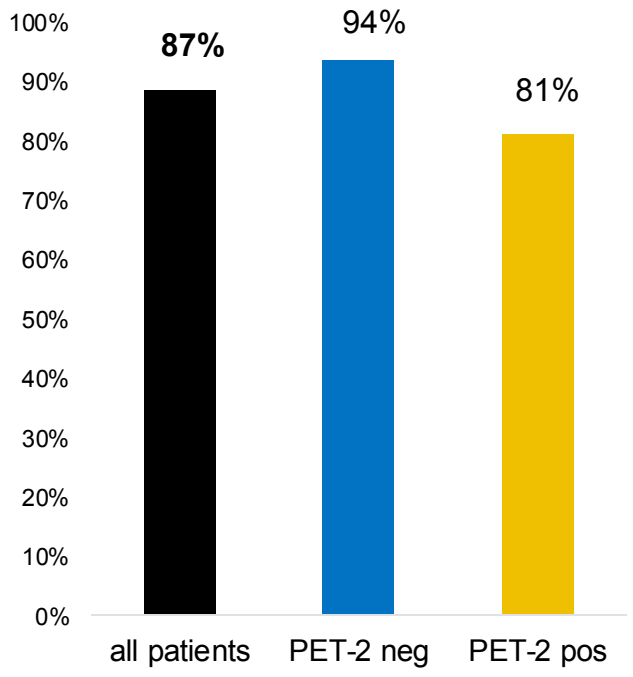


➢ **A majority of patients achieved CR in PET2 and was scheduled for 4 cycles of BrECADD.**

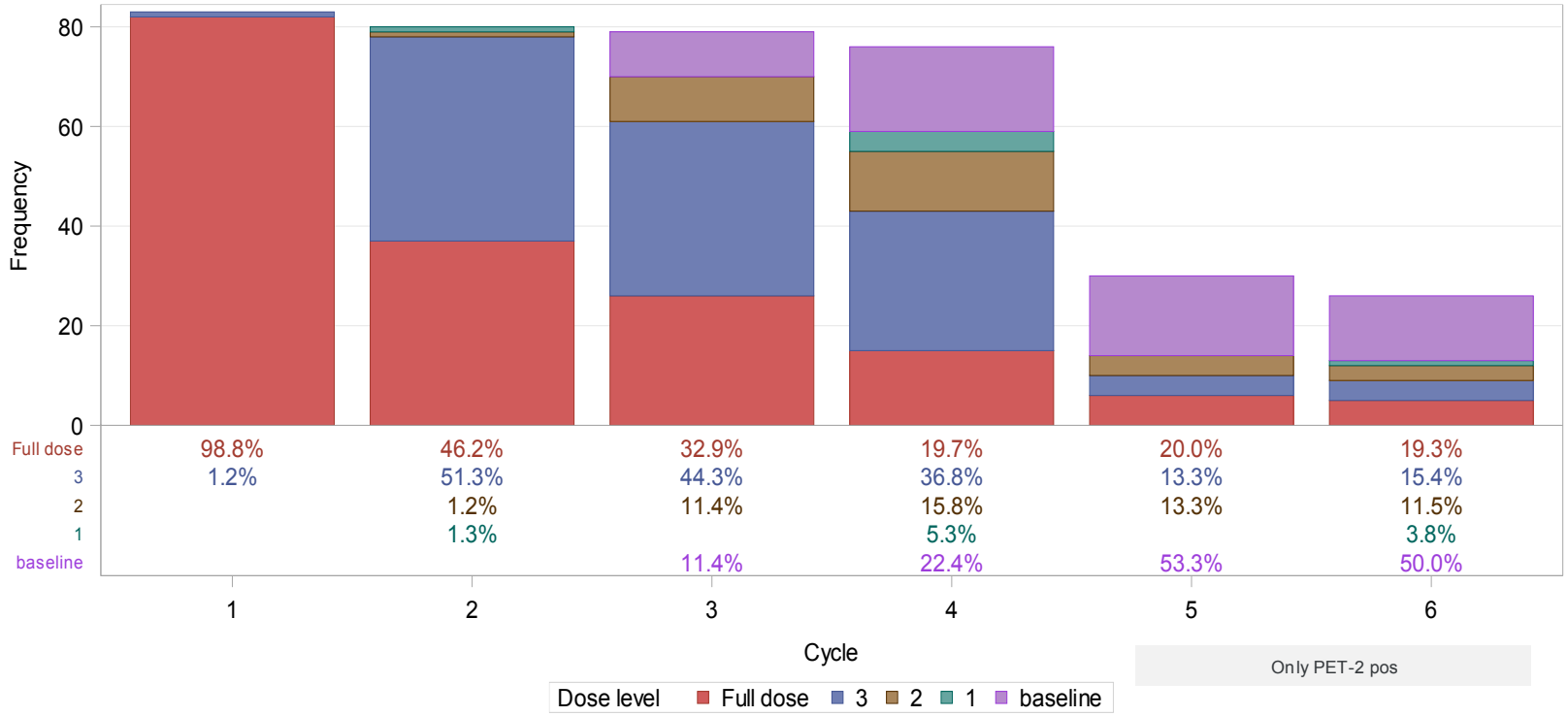
GHSG

Treatment completion and dose levels

Treatment completion rate



Dose levels



- High treatment completion rate: 87% of entire cohort
- Supported by pre-defined, per-protocol dose reductions

GHSG

Adverse Events

Summary

- Most common higher grade toxicities were hematologic, incl. anemia (69%) and thrombocytopenia (86%).
- Neutropenic fever occurred in 46 (55%) patients.
- Grade 2 sensory PN occurred in 9 (11%); one (1%) patient had G3.
- No Grade 5 toxicity

Adverse event*	Any Grade (%)	Grade ≥ 3 (%)
Anemia	81 (98)	57 (69)
Thrombocytopenia	78 (94)	71 (86)
Leukopenia	81 (98)	80 (96)
Neutropenic fever	46 (55)	46 (55)
Infection	55 (65)	39 (47)
Cardiac disorders	23 (28)	2 (2)
Gastrointestinal disorders	60 (72)	19 (23)
Nausea	30 (36)	4 (5)
Mucositis	47 (57)	14 (17)
Peripheral sensory neuropathy**	33 (40)	1 (1)
Nervous system disorder (other than neuropathy)	24 (29)	3 (4)
Renal and urinary disorders	12 (15)	3 (4)
Respiratory, thoracic and mediastinal disorders	37 (45)	5 (6)
Skin and subcutaneous tissue disorders	35 (42)	1 (1)
Hematological TRMB1 event (%)	60 (72)	
Organ TRMB[1] event (%)	28 (34)	
Any TRMB[1] event (%)	66 (80)	

* Frequency ≥10%, ** PNP G2 or higher in 11 (12%) pts. TRMB = Treatment-related morbidity

GHSG

1 Borchmann P et al *Lancet* 2024

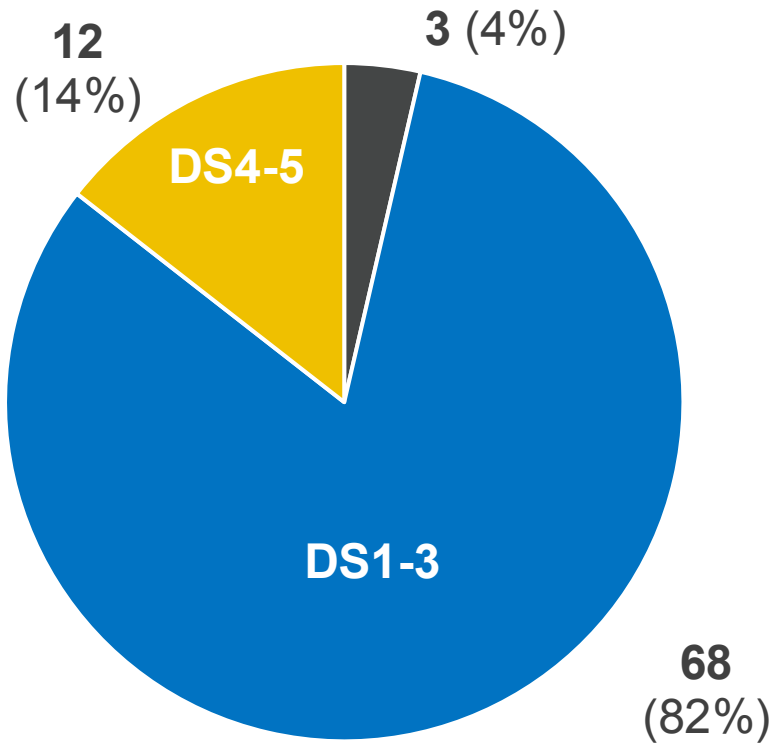
Primary Endpoint: CR Rate after Chemotherapy

CR rate after Chemotherapy: 68/83 patients (82%; 95%CI 72 – 90)

- 4 cycles: 45/48 patients (94%; 95%CI 83 – 99)
- 6 cycles: 23/32 patients (72%; 95%CI 53 – 86)

Non-CR due to:

- Non-CR (DS4-5) at EOT by central review (N=12)
- No response assessment available (N=3)

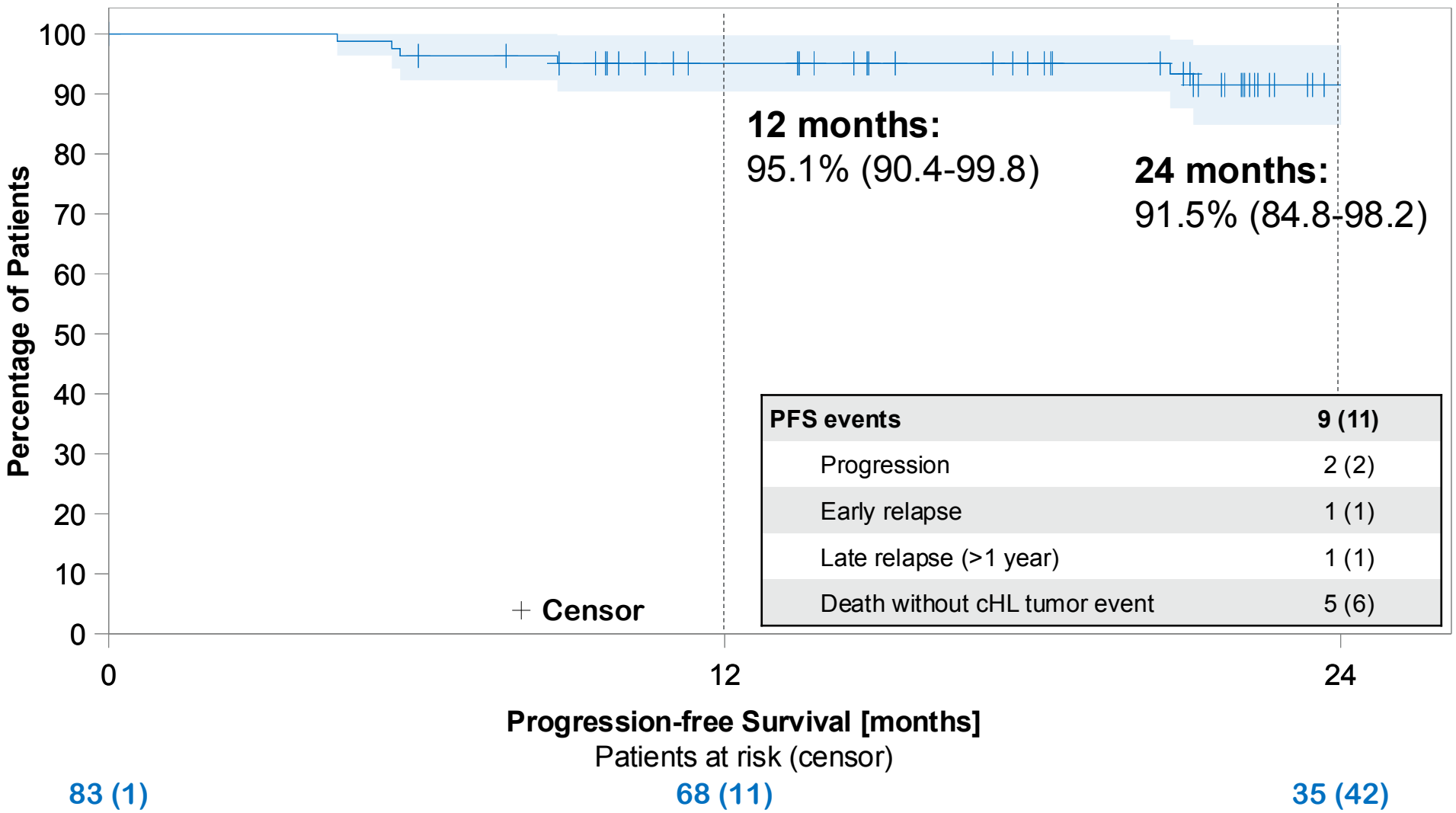


Most patients (82%) were in CR after receiving PET-guided BrECADD.

GHSG

Progression-free survival

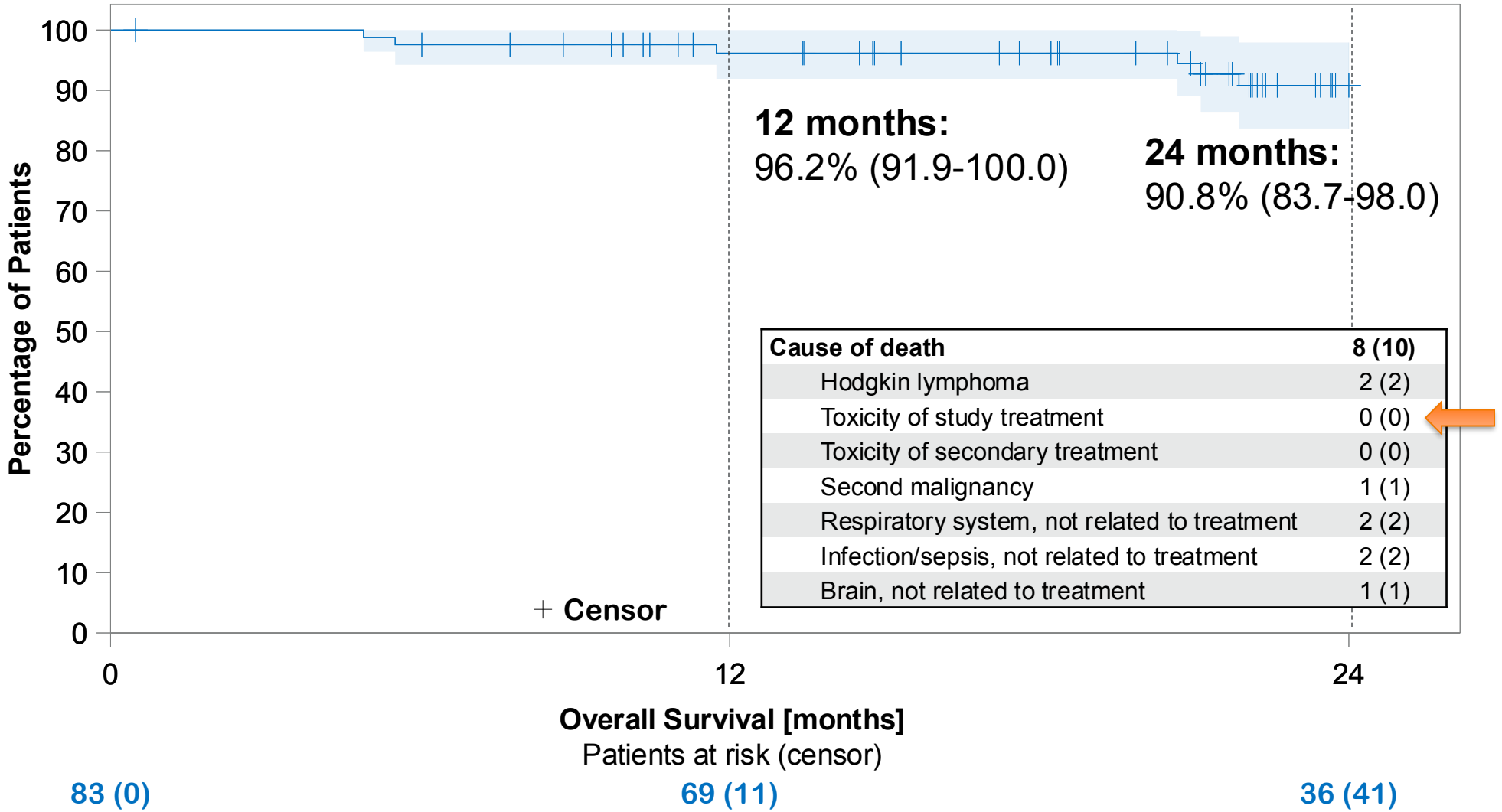
mFU 23 months



GHSG

Overall survival

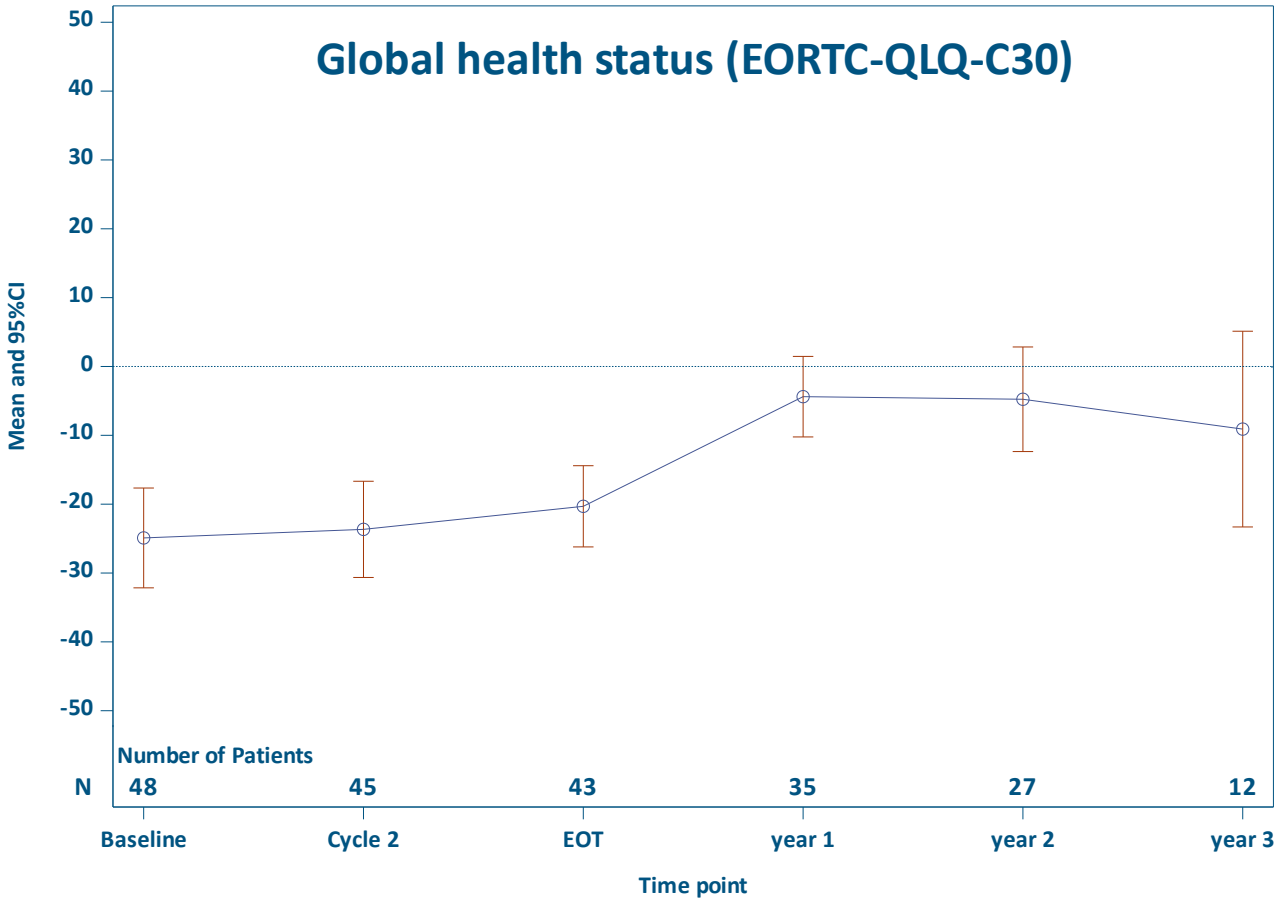
mFU 24 months



Cause of death	8 (10)
Hodgkin lymphoma	2 (2)
Toxicity of study treatment	0 (0)
Toxicity of secondary treatment	0 (0)
Second malignancy	1 (1)
Respiratory system, not related to treatment	2 (2)
Infection/sepsis, not related to treatment	2 (2)
Brain, not related to treatment	1 (1)

GHSG

Health-related Quality of Life



Dedicated analysis of patient reported outcomes in patients providing separate consent to identify impact on health-related quality of life.

EORTC questionnaires (QLQ-C30, CIPN-20, FA12)

Sex- and age- adjusted differences to reference population of general health status by QLQ-C30: Improvement after treatment

Similar improvements in terms of symptom- and functioning scales.

Initially impaired HRQoL improved already during treatment and normalized during follow-up

GHSG

Author's Conclusion

PET-guided BrECADD addresses an unmet need for older patients with AS-cHL:

- With high treatment completion rates and no treatment-related mortality, BrECADD is feasible in this vulnerable cohort when following pre-defined dose adjustments
- PET-guided BrECADD results in a high rate of complete and durable remissions
- The majority of patients (60%) requires only 4x BrECADD, resulting in a short treatment of only 12 weeks and limited anthracycline exposure (<200mg/m^2)
- Initially impaired HRQoL measures improve during and return to normal after 4-6x BrECADD

The unprecedentedly high 2y-PFS rate above 90% encourages the use of PET-guided BrECADD as first-line treatment option for patients with AS-cHL between 61-75 years

GHSG

Additional Brentuximab Vedotin Data

Select each congress tab to review additional abstracts

ASCO 2024 | EHA 2024 | ISHL 2024 | ASH 2024

- The randomized study GHSG HD21 shows superior tolerability and efficacy of BrECADD versus BEACOPP in advanced stage classical Hodgkin lymphoma. Borchmann P, et al. ASCO 2024. *J Clin Oncol*;42(S17); **abstract LBA7000**

Additional Brentuximab Vedotin Data

Select each congress tab to review additional abstracts

ASCO 2024 | **EHA 2024** | ISHL 2024 | ASH 2024

- Real-Life Treatment Practice and Clinical Outcomes in Egyptian Classical Hodgkin Lymphoma Patients: The PROFILE Study. Azim HA, et al. EHA 2024. *HemaSphere* 2024;8(S1); **abstract PB2937**
- An Abbreviated Course of A+AVD Followed by Nivolumab Consolidation for Frontline Therapy in Patients with Limited Stage Hodgkin Lymphoma. Park SI, et al. EHA 2024. *HemaSphere* 2024;8(S1); **abstract S244**
- EORTC-1537-Cobra: Very early FDG-PET-response adapted targeted therapy for advanced Hodgkin lymphoma: a single-arm phase II study. Hutchings M, et al. EHA 2024. *HemaSphere* 2024;8(S1); **abstract S226**
- Phase I-II study combining Brentuximab Vedotin with R-DHAP and autologous stem cell transplantation in CD30 positive diffuse large B-cell lymphoma patients: results of the HOVON 136 study. Lugtenburg PJ, et al. EHA 2024. *HemaSphere* 2024;8(S1); **abstract P1168**
- Bendamustine and Adcetris in untreated hodgkin lymphoma of the elderly: long-term results of the HALO trial. Gallamini A, et al. EHA 2024. *HemaSphere* 2024;8(S1); **abstract P1086**
- Brentuximab Vedotin - ESHAP Significantly Increases the Metabolic Complete Remission Rate versus ESHAP in Relapsed Classical Hodgkin's Lymphoma. Final Results of the BRESELIBET Prospective Trial. Sureda A, et al. EHA 2024. *HemaSphere* 2024;8(S1); **abstract P1093**

Additional Brentuximab Vedotin Data

Select each congress tab to review additional abstracts

ASCO 2024 | EHA 2024 | **ISHL 2024** | ASH 2024

- Brentuximab vedotin, Cyclophosphamide, Doxorubicin and Prednisone (B-CAP) First-Line Treatment of Older Patients with Advanced-Stage Hodgkin Lymphoma: Final Results of the GHSG-NLG Phase II BVB Trial. Brockelmann PJ, et al. ISHL 2024. *Hemasphere* 2024;8(S2); **abstract P081**
- Brentuximab vedotin monotherapy is a feasible and effective treatment in elderly and frail patients with classical Hodgkin lymphoma: Results of the prospective GHSG-NLG phase II BVB trial. Fossa A, et al. ISHL 2024. *Hemasphere* 2024;8(S2); **abstract P080**

Additional Brentuximab Vedotin Data

Select each congress tab to review additional abstracts

ASCO 2024 | EHA 2024 | ISHL 2024 | **ASH 2024**

- PET-guided BrECADD in Older Patients with Advanced-Stage Classical Hodgkin Lymphoma: The Older Cohort of the International GHSG HD21 Trial. Ferdinandus J, et al. ASH 2024. **abstract 568**
- The Addition of Brentuximab Vedotin to ESHAP Significantly Increases the Rate of Metabolic Complete Remissions Vs Chemotherapy Alone. in Patients with Relapsed/Refractory Classical Hodgkin's Lymphoma. Final Results of a Phase IIb Prospective Randomized Clinical Trial (BRESELIBET). Sureda Balari AM, et al. ASH 2024. **abstract 3049**
- Brentuximab Vedotin, Cyclophosphamide, Doxorubicin and Prednisone (B-CAP) First-Line Treatment of Advanced-Stage Hodgkin Lymphoma: Final Results of the GHSG-NLG Phase II Bvb Trial. Brockelmann PJ, et al. ASH 2024. **abstract 3054**
- Updated Analysis of Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine for Nonbulky, Early-Stage Classical Hodgkin Lymphoma. Abramson JS, et al. ASH 2024. **abstract 460**
- Dose-Dense Brentuximab Vedotin Plus Ifosfamide, Carboplatin, and Etoposide (ICE) in Second Line Treatment of Relapsed/Refractory Classical Hodgkin Lymphoma: 5-Year Long Term Follow up. Lynch RC, et al. ASH 2024. **abstract 3043**
- A Randomized Phase 2 Study Incorporating Nivolumab and Brentuximab Vedotin into Radiation-Free Treatment of Early Stage Classic Hodgkin Lymphoma. LaCasce AS, et al. ASH 2024. **abstract 459**
- Interim PET-Adapted De-Escalation Chemotherapy Regimen for Advanced Stage Classical Hodgkin Lymphoma Using Brentuximab Vedotin, Pembrolizumab, Doxorubicin, and Dacarbazine: Phase 2 Safety and Efficacy Study. Lee HJ, et al. ASH 2024. **abstract 1674.3**