Denver ASH Review

Updates in Lymphoma II

Manali Kamdar, MD,MBBS
Associate Professor of Medicine
Clinical Director of Lymphoma Services
Morton and Sandra Saffer Endowed Chair in Hematology Research
Division of Hematology and Bone marrow Transplantation
University of Colorado, Anschutz Cancer Center

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Disclosures

Research Support/Funding: Novartis
Consultancy: AbbVie, AstraZeneca, Celgene/ Bristol-Myers Squibb, Beigene, Genentech
DMC: Celgene, Genentech

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Highlights of ASH

Diffuse Large B Cell Lymphoma

Hodgkin Lymphoma

Chronic Lymphocytic Leukemia

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Five-year analysis of the POLARIX study: Prolonged follow-up confirms positive impact of polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) on outcomes

Gilles Salles[1], Franck Morschhauser[2], Laurie H. Sehn[3], Alex F. Herrera[4], Jonathan W. Friedberg[5], Marek Trněný[6], Georg Lenz[7], Jeff P. Sharman[8], Charles Herbaux[9], John M. Burke[10], Matthew Matasar[11], Graham P. Collins[12], Yuqin Song[13], Antonio Pinto[14], Shinya Rai[15], Koji Izutsu[16], Calvin Lee[17]*, Saibah Chohan[18], Matthew Sugidono[17], Yanwen Jiang[17], Connie Lee Batlevi[17], Mark Yan[18], Jamie Hirata[17]*, Hervé Tilly[19], Christopher R. Flowers[20]

[1]*Memorial Sloan Kettering Cancer Center, New York, NY, USA;* [2]*University of Lille, Lille, France;* [3]*BC Cancer Centre for Lymphoid Cancer and the University of British Columbia, Vancouver, BC, Canada;* [4]*City of Hope, Duarte, CA, USA;* [5]*Wilmot Cancer Institute, University of Rochester, Rochester, NY, USA;* [6]*Charles University, Prague, Czech Republic;* [7]*University Hospital Münster, Münster, Germany;* [8]*Willamette Valley Cancer Institute and Research Center, Florence, OR, USA;* [9]*University of Montpellier, Montpellier, France;* [10]*Rocky Mountain Cancer Centers/US Oncology, Aurora, CO, USA;* [11]*Rutgers Cancer Institute, New Brunswick, NJ, USA;* [12]*Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom;* [13]*Peking University Cancer Hospital, Beijing, China;* [14]*National Cancer Institute, Fondazione G. Pascale, IRCCS, Naples, Italy;* [15]*Department of Hematology and Rheumatology, Kindai University, Faculty of Medicine, Osaka-Sayama City, Japan;* [16]*National Cancer Center Hospital, Tokyo, Japan;* [17]*Genentech, Inc., South San Francisco, CA, USA;* [18]*Hoffmann-La Roche Ltd, Mississauga, Canada;* [19]*Centre Henri-Becquerel and University of Rouen, Rouen, France;* [20]*M.D. Anderson Cancer Center, Houston, TX, USA*

**This affiliation was active at the time of the analysis*

Presented at the 66th ASH Annual Meeting | December 7–10, 2024

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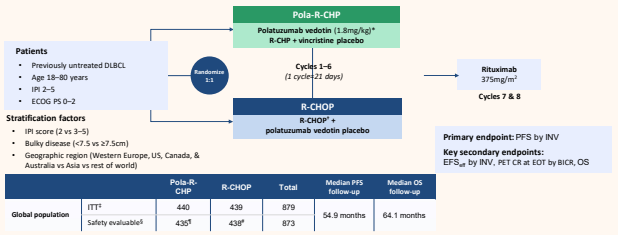
POLARIX study design



		Pola-R-CHP	R-CHOP	Total	Median PFS follow-up	Median OS follow-up
Global population	ITT‡	440	439	879	54.9 months	64.1 months
	Safety evaluable§	435¶	438#	873		

*IV on Day 1; †R-CHOP: IV rituximab 375mg/m², cyclophosphamide 750mg/m², doxorubicin 50mg/m², and vincristine 1.4mg/m² (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5; ‡As randomized population; §As treated population; ¶One patient was randomized to Pola-R-CHP but did not receive polatuzumab vedotin; #One patient was randomized to R-CHOP but did not receive vincristine. BICR, blinded independent central review; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS24, event-free survival (efficacy); EOT, end of treatment; INV, investigator; IPI, International Prognostic Index; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; R, randomized; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.

Tilly H, *et al. N Engl J Med* 2022;386:351–63.

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Baseline characteristics

n (%), unless otherwise stated		Global population	
		Pola-R-CHP (n=440)	R-CHOP (n=439)
Age	Median, years (min–max)	65.0 (19–80)	66.0 (19–80)
	≥65 years	231 (52.5)	236 (53.8)
Sex	Male	239 (54.3)	234 (53.3)
ECOG PS	0–1	374 (85.0)	363 (82.7)*
	2	66 (15.0)	75 (17.1)
IPI at screening	2	167 (38.0)	167 (38.0)
	3–5	273 (62.0)	272 (62.0)
Bulky disease	≥7.5cm	193 (43.9)	192 (43.7)
Baseline lactate dehydrogenase	>1x upper limit of normal	291 (66.1)	284 (64.7)
Ann Arbor stage	III or IV	393 (89.3)	387 (88.2)
Number of extranodal sites	≥2	213 (48.4)	213 (48.5)
NHL histologic diagnosis reported by investigators	DLBCL NOS, ABC, GCB	373 (84.8)†	367 (83.6)
	HGBCL, DHL/THL	43 (9.8)	50 (11.4)
	Other large B-cell lymphoma	24 (5.5)	22 (5.0)
COO centrally reported by NanoString‡	n	330	338
	ABC by NanoString	102 (30.9)	119 (35.2)
	GCB by NanoString	184 (55.8)	168 (49.7)
	Unclassified by NanoString	44 (13.3)	51 (15.1)
	Unknown	110	101

*ECOG PS was not reported for one patient in the R-CHOP arm; †The total percentage for NHL histologic diagnosis in the Pola-R-CHP arm may exceed 100% due to rounding; ‡Based on central review, and percentages are based on biomarker evaluable population (i.e., by excluding patients with unknown status). ABC, activated B cell; COO, cell-of-origin; DHL, double-hit lymphoma; GCB, germinal center B cell; HGBL, high-grade B-cell lymphoma; NOS, not otherwise specified; THL, triple-hit lymphoma.

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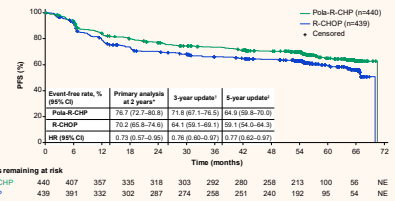
PFS benefit of Pola-R-CHP over R-CHOP is maintained at 5y

PFS in the global ITT population



Event-free rate, % (95% CI)	Primary analysis at 2 years*	3-year update†	5-year update‡
Pola-R-CHP	76.7 (72.7–80.8)	71.8 (67.1–76.5)	64.9 (59.8–70.0)
R-CHOP	70.2 (65.8–74.6)	64.1 (59.1–69.1)	59.1 (54.0–64.3)
HR (95% CI)	0.73 (0.57–0.95)	0.76 (0.60–0.97)	0.77 (0.62–0.97)

Patients remaining at risk

Pola-R-CHP	440	407	357	335	318	303	292	280	258	213	100	56	NE
R-CHOP	439	391	332	302	287	274	258	251	240	192	95	54	NE

At the 5-year follow up, Pola-R-CHP had a **sustained and significant PFS benefit**, confirming results from the primary analysis of PFS at 2 years of follow up (HR 0.73).[1]

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*Data cut-off: June 28, 2021; †Data cut-off: June 15, 2022; ‡Data cut-off: July 5, 2024. CI, confidence interval; HR, hazard ratio; NE, not evaluable.

1. Tilly H, *et al. N Engl J Med* 2022;386:351–63.

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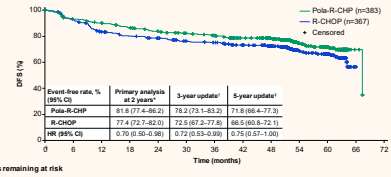
CR obtained after Pola-R-CHP treatment is maintained with 5y follow-up

DFS (DoCR) in the global ITT population



Event-free rate, % (95% CI)	Primary analysis at 2 years*	3-year update†	5-year update‡
Pola-R-CHP	81.8 (77.4–86.2)	78.2 (73.1–83.2)	71.8 (66.4–77.3)
R-CHOP	77.4 (72.7–82.0)	72.5 (67.2–77.8)	66.5 (60.8–72.1)
HR (95% CI)	0.70 (0.50–0.98)	0.72 (0.53–0.99)	0.75 (0.57–1.00)

Patients remaining at risk

Pola-R-CHP	383	347	333	317	301	286	277	251	222	105	79	3	NE
R-CHOP	367	336	295	279	268	253	247	230	206	98	72	NE	NE

Complete remissions are durable and sustained with longer follow-up.

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*Data cut-off: June 28, 2021; †Data cut-off: June 15, 2022; ‡Data cut-off: July 5, 2024; §CR assessment occurred at the 0-month timepoint. CR, complete remission; DFS, disease-free survival; DoCR, duration of complete remission.

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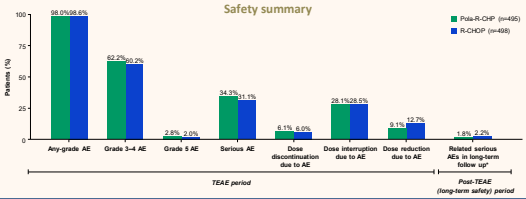
Pola-R-CHP shows a favorable benefit–risk profile compared with R-CHOP in the expanded population

Safety summary



Safety profile remained comparable between treatment arms, with no increased risks with long-term follow-up. There was no substantial change in the proportion of patients with AEs (≥5%) compared with the global population.

Data cut-off: July 5, 2024. *TEAEs are defined as new or worsening AE from the first dose of study drug through 90 days after the last dose of any study drug or prior to NALT, whichever is earlier. After this TEAE period, the post-TEAE period (i.e. long-term safety follow up) reporting requirement is only for serious AEs that the investigator believes to be related to prior study drug treatment. AE, adverse event; TEAE, treatment-emergent adverse event.

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Take Home Points:

Pola-R-CHP is established as a standard of care in IPI 2+ newly diagnosed DLBCL

5-year follow-up of POLARIX showed sustained and significant PFS and DFS benefits for patients receiving Pola-R-CHP versus R-CHOP

Numerically fewer deaths, especially lymphoma-related deaths, fewer subsequent treatments, were observed in patients receiving Pola-R-CHP compared with R-CHOP

No new safety signals were noted

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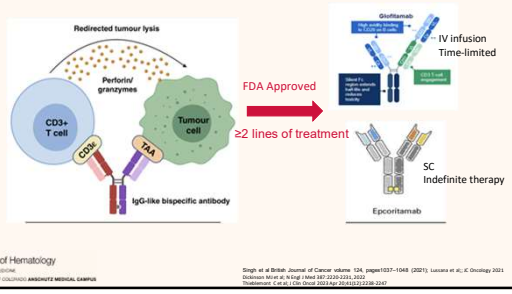
Anti-CD20/CD3 Bispecific T Cell Engager (BiSp) therapies approved in R/R LBCL after failure of ≥2 lines of treatment



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Singh et al British Journal of Cancer volume 124, pages1037–1048 (2021); Lucuna et al; JC Oncology 2021
Dickinson M et al, N Engl J Med 387:2220-2231, 2022
Thieblemont, C et al, J Clin Oncol 2023 Apr 20;41(12):2238-2247

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Fixed-duration glofitamab monotherapy continues to demonstrate durable responses in patients with relapsed or refractory large B-cell lymphoma: 3-year follow-up from a pivotal Phase II study

Michael Dickinson,[1] Carmelo Carlo-Stella,[2] Franck Morschhauser,[3] Emmanuel Bachy,[4] Guillaume Cartron,[5] Paolo Corradini,[6] Nancy L. Bartlett,[7] Gloria Iacoboni,[8] Cyrus Khan,[9] Mark Hertzberg,[10] Lorenzo Falchi,[11] Joshua Brody,[12] Marek Trněný,[13] Estefania Mulvihill,[14] Aurelien Berthier,[14] Alessia Bottos,[14] James Relf,[15] Fabiola Bene Tchaleu,[16] Linda Lundberg,[14] Martin Hutchings[17]

[1]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, Australia; [2]Humanitas University and IRCCS Humanitas Research Hospital, Milan, Italy; [3]Hôpital Claude Huriez and CHU de Lille, Lille, France; [4]Centre Hospitalier Lyon Sud, Lyon, France; [5]CHU de Montpellier, Montpellier, France; [6]University of Milan and Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [7]Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]Allegheny Health Network, Pittsburgh, PA, USA; [10]Prince of Wales Hospital and University of New South Wales, Sydney, Australia; [11]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [12]Tisch Cancer Institute, New York, NY, USA; [13]Charles University, Prague, Czech Republic; [14]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [15]Roche Products Ltd, Welwyn Garden City, UK; [16]Genentech, Inc., South San Francisco, CA, USA; [17]Rigshospitalet, Copenhagen, Denmark

Presented at the 66th ASH Annual Meeting | December 7–10, 2024

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Study design

Pivotal single-arm Phase II study in patients with R/R LBCL and ≥2 prior therapies

Key inclusion criteria

- DLBCL NOS, HGBCL, transformed FL, or PMBCL
- ECOG PS 0–1
- ≥2 prior therapies, including:
  - Anti-CD20 antibody
  - Anthracycline

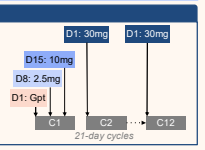
Glofitamab IV administration

Fixed-duration treatment:

- Q3W
- Up to 12 cycles (8.5 months)

CRS mitigation:

- Obinutuzumab IV pre-treatment (1000mg)
- C1 step-up dosing
- Monitoring after first glofitamab dose (2.5mg)



Endpoints

- **Primary**: CR rate (as best response) by IRC*
- **Key secondary**: ORR†, DoR†, DoCR†, PFS, OS

Analyses

- **Landmark**: PFS and OS by response (CR at EOT)
- **Biomarker:** ctDNA kinetics, immune recovery (B-cell, IgG and IgM)

*By PET-CT (Lugano criteria)[1]. †By IRC and investigator.
C, cycle; CRS, cytokine release syndrome; ctDNA, circulating tumor DNA; D, day; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; DoCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; FL, follicular lymphoma; Gpt, obinutuzumab pre-treatment; HGBCL, high-grade B-cell lymphoma; Ig, immunoglobulin; IV, intravenous; IRC, independent review committee; IV, intravenous; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival; PET-CT, positron emission tomography-computed tomography; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; Q3W, three-weekly.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

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Baseline characteristics

n (%)*		All patients (N=154)†
Median age, years (range)		66 (21–90)
Male		100 (64.9)
ECOG PS‡	0	69 (44.8)
	1	84 (54.5)
Ann Arbor stage	I/II	35 (22.7)
	III/IV	116 (75.3)
NHL subtype	DLBCL NOS	110 (71.4)
	trFL	28 (18.2)
	HGBCL	10 (6.5)
	PMBCL	6 (3.9)
Bulky disease	>6cm	64 (41.6)
	>10cm	19 (12.3)

n (%)*	All patients (N=154)†
Median number of prior lines, n (range)	3 (2–7)
2 prior lines	61 (39.6)
≥3 prior lines	93 (60.4)
Prior CAR-T	51 (33.1)
Refractory to prior CAR-T§	46 (29.9)
Prior ASCT	29 (18.8)
Refractory to any prior therapy	138 (89.6)
Refractory to last line of prior therapy	130 (84.4)
Refractory to first line of prior therapy	90 (58.4)
Refractory to any prior anti-CD20	128 (83.1)

The patient population was heavily pre-treated and highly refractory to prior therapy

Clinical cut-off date: May 17, 2024. *Unless otherwise specified. †Safety-evaluable population (all treated patients; one patient enrolled in the intention-to-treat population did not receive any study drug and was excluded from the safety-evaluable population); ‡ECOG PS 2, n=1 (0.6%); one patient had an ECOG PS of 1 at enrolment, but deteriorated before the receipt of study treatment; § Patients who had no response or relapsed within 6 months.
ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T-cell therapy; NHL, non-Hodgkin lymphoma; trFL, transformed follicular lymphoma.

1. Dickinson M, et al. N Engl J Med 2022;387:2220–31.

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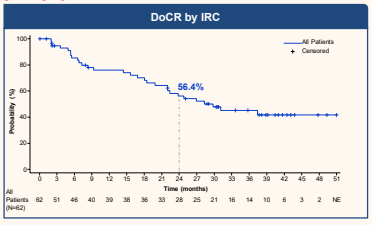
Complete responses remained durable following fixed-duration glofitamab

	(N=155)*
CR rate, n (%) [95% CI]	62 (40) [32.2–48.2]
ORR, n (%) [95% CI]	80 (52) [43.5–59.7]
Median DoCR, months (95% CI)	29.8 (22.0–NE)
24-month DoCR, % (95% CI)	56.4 (42.9–69.8)
Ongoing CRs, n/N (%)	33/62 (53.2)
Median CR follow-up, months (range)	37.7 (0–51)

DoCR by IRC



- Median time on study: 41.0 months (range: 0–52)

An estimated 56.4% of patients with a CR at any time remained in remission at 24 months

All responses in the table are based on the best overall response; *Intention-to-treat population; CI, confidence interval; NE, not estimable.

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Safety summary

- **CRS[a] remained the most common AE**
  - Occurred in 64.3% of patients
  - Mostly Grade 1 (48.1%) or Grade 2 (12.3%); Grade 3 (2.6%) and Grade 4 (1.3%) events were uncommon
- **The incidences of AEs and SAEs have previously been reported[1,2]**
  - Two new Grade ≥3 AEs were reported: neutropenia (Grade 3) and adenocarcinoma pancreas (Grade 4)
- **No new ICANS or cytopenia events were reported from June 17, 2022[2]–May 17, 2024**
  - Two new fatal AEs were reported[b]: COVID-19 and acute myeloid leukemia
  - Three new infections were reported[b]: rhinitis (Grade 2), pneumonia (Grade 2), and infected skin ulcer (Grade 1)

n (%)	N=154[b]
AE	152 (98.7)
Grade ≥3 AE	102 (66.2)
SAE	76 (49.4)
Grade 5 (fatal) AE	11 (7.1)
AE leading to treatment discontinuation	14 (9.1)
AE leading to glofitamab dose modification/interruption	30 (19.5)

Most patients did not experience new AEs since the previous analysis[1]

All AEs and SAEs were recorded for ≤90 days after the last dose of study treatment or until the initiation of another systemic anti-cancer therapy, whichever came first. After this period, AEs, SAEs and deaths were only reported if believed to be related to prior treatment with the study drug. [a]By ASTCT Grade; [b]Previous CCOD. [c]All events have an onset prior to the previous CCOD and have been included due to database updates; [d]Safety-evaluable population (all treated patients; one patient enrolled in the intention-to-treat population did not receive any study drug and was excluded from the safety-evaluable population). AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CCOD, data cut-off date; CRS, cytokine release syndrome; ICANS, immune effector cell associated neurotoxicity syndrome; SAE, serious adverse event.

1. Dickinson MJ, et al. N Engl J Med 2022;387:2220–31;
2. Dickinson M, et al. ICML 2023;Oral095.

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Take Home Points:

Glofitamab is an approved CD20xCD3 bispecific Ab with sustained responses in 3L R/R DLBCL

After more than 3 years of follow-up, –An estimated 77.2% of patients with a CR at EOT were alive 24 months later

Safety profile remains manageable and consistent with previous analyses

SkyGlo : Phase III Glofi+RCHP-Pola vs RCHP-Pola in untreated LBCL with ≥2 IPI ongoing and open at CU

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Updated Clinical Results

A Multicenter, Open-Label, Phase 3 Study of Tabelecleucel for Solid Organ or Allogeneic Hematopoietic Cell Transplant Recipients with Epstein–Barr Virus-Driven Post Transplant Lymphoproliferative Disease after Failure of Rituximab or Rituximab Plus Chemotherapy

Armin Ghobadi[1], Robert Baiocchi[2], Amer M. Beitinjaneh[3], Sridhar Chaganti[4], Sylvain Choquet[5], Daan Dierickx[6], Rajani Dinavahi[7], Xinyuan Duan[7], Laurence Gamelin[7], Kris Michael Mahadeo[8], Aditi Mehta[9], Sarah Nikiforow[10], Ran Reshef[11], Roberta Valenti[12], Sandrine Roye[13], Jean-Claude Vedovato[12], and Susan E Prockop[14]

[1]Division of Oncology, Washington University School of Medicine, St. Louis, MO; [2]James Comprehensive Cancer Center, The Ohio State University, Columbus, OH; [3]Division of Transplantation and Cellular Therapy, University of Miami Hospital and Clinics, Sylvester Comprehensive Cancer Center, Miami, FL; [4]Centre for Clinical Haematology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [5]Hôpital Pitié-Salpêtrière, AP-HP, Paris, France; [6]University Hospitals Leuven, Leuven, Belgium; [7]Atara Biotherapeutics, Thousand Oaks, CA; [8]Pediatric Transplant and Cellular Therapy, Duke University, Durham, NC; [9]Atara Biotherapeutics, South San Francisco, CA; [10]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; [11]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY; [12]Pierre Fabre Laboratories, Boulogne Billancourt, France; [13]Institut de Recherche Pierre Fabre, Pierre Fabre Laboratories, Toulouse, France; [14]Stem Cell Transplant Program, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA

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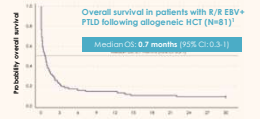
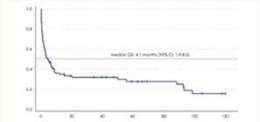
Unmet need for effective treatment for R/R EBV+ PTLD

- Initial treatments for EBV+ PTLD include reduction in immunosuppression (RIS) and anti-CD20 antibody ± chemotherapy (CT),[1,4] but response rates are variable
- The reported median survival rates—0.7 months for allogeneic HCT and 4.1 months for SOT—in patients with EBV+ PTLD who did not respond to rituximab ± CT highlight a critical and urgent unmet need in this patient population[5-8]





1. Dierickx D, Habermann TM. *N Engl J Med* 2018;378:549–62; 2. Al-Mansour Z, *et al. Curr Hematol Malig Rep* 2013;8:173–80; 3. Dierickx D, *et al. Curr Opin Oncol* 2022;34:413–21; 4. Mucha K, *et al. Nephrol Dial Transplant* 2010;25:2689–98; 5. Trappe RU, *et al. J Clin Oncol* 2017;35:536–43; 6. Socié G, *et al. Bone Marrow Transplant.* 2024;59:32–8; 7. Sanz J, *et al. Blood* 2020;136(Suppl 1):1454; 8. Dhanireddy V, *et al. Blood* 2021;138(Suppl 1):2328.

CT, chemotherapy; EBV+, Epstein-Barr virus-positive; HCT, hematopoietic cell transplant; OS, overall survival; PTLD, post-transplant lymphoproliferative disease; RIS, reduction in immunosuppression; R/R, relapsed/refractory; SOT, solid organ transplant

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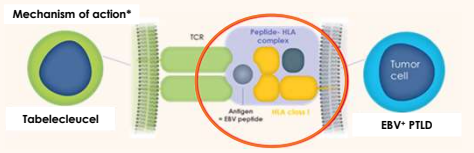
Tabelecleucel is a novel treatment for R/R EBV+ PTLD

- Tabelecleucel is an off-the-shelf, non-genetically modified, allogeneic, EBV-specific T-cell immunotherapy that targets and eliminates EBV-infected cells in an HLA-restricted manner



Manufacturing
Derived from unrelated third-party healthy donors and cryo-preserved in a bio-bank adapted to cover multiple HLA profiles

Product selection
Based on the characterization of HLA restriction and donor: recipient compatibility

Administration
No lymphodepletion or pre-medication, 1-hour post-injection monitoring, can be administered both in inpatient and outpatient settings

*Tabelecleucel is a polyclonal T cell population enriched for the recognition of EBV antigens, with variable CD8+/CD4+ ratio.
EBV, Epstein-Barr virus; EBV+, Epstein-Barr virus-positive; HLA, human leukocyte antigen; PTLD, post-transplant lymphoproliferative disease;

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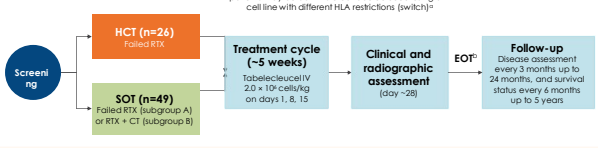
ALLELE Study Design

Patients receive additional treatment cycles until best response is achieved. In cases of non-response, patients may be administered tabelecleucel using a T-cell line with different HLA restrictions (switch)[a]



Key eligibility criteria:
- Prior allogeneic HCT or SOT
- Biopsy-proven EBV+ PTLD
- Previous RTX or RTX-CT[b] failure
- ECOG PS ≤3

Primary endpoint: ORR[c]

Key secondary endpoints:
- TTR and time to best response
- OS in responders vs non-responders

*Patients may receive up to 4 (in HCT group) or 2 (in SOT group) different HLA restrictions. [b]Evaluated by independent review. [c]Including R-CHOP. [d]Defined as any of the following: maximal response achieved; unacceptable toxicity; initiation of non-protocol therapy; or failure of up to 4 (in HCT group) or 2 (in SOT group) different HLA restrictions; CT, chemotherapy; EBV+, Epstein-Barr virus-positive; ECOG PS, Eastern Cooperative Oncology Group performance status; HCT, hematopoietic cell transplant; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; RTX, rituximab; SOT, solid organ transplant; TTR, time to response.

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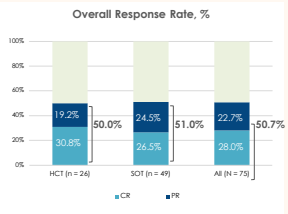
Primary Endpoint: ORR

	HCT (n = 26)	SOT (n = 49)	All (N = 75)
Responders, n (%)[a]	13 (50.0)	25 (51.0)	38 (50.7)
[95% CI]	[29.9, 70.1]	[36.3, 65.6]	[38.9, 62.4]
Before 1st restriction switch	12 (46.2)	20 (40.8)	32 (42.7)
[95% CI]	[26.6, 66.6]	[27.0, 55.8]	[31.3, 54.6]
Median (range) time, months 13	n =	n = 25	n = 38
TTRz	1.0 (0.6–9.0)	2.0 (0.7–4.7)	1.1 (0.6–9.0)
Time to best response	1.0 (0.6–9.0)	2.1 (0.7–7.3)	1.6 (0.6–9.0)
Estimated DOR, median (95% CI), months[b]	19.0 (1.5, NE)	NE (6.8, NE)	23.0 (12.1, NE)



- The ORR (complete response [CR] + partial response [PR]) in all patients was **50.7%** (n = 38/75), with a best overall response of CR in 21 patients (**28.0%**) or PR in 17 (**22.7%**)
- Median time to response in all patients was **1.1 months**

Data cutoff date: Oct 9, 2023
[a]Response assessed per Lugano classification with LYRIC modification by IORA. [b]Estimated by the Kaplan-Meier method.
CI, confidence interval; CR, complete response; DOR, duration of response; HCT, hematopoietic cell transplant; IORA, independent oncologic response adjudication; NE, not estimable; PR = partial response; TTRz, time to response.

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Safety Outcomes

	HCT (n = 26)	SOT (n = 49)	All (N = 75)
TESAEs, n (%)			
Any	17 (65.4)	30 (61.2)	47 (62.7)
Treatment-related[a]	2 (7.7)	4 (8.2)	6 (8.0)
Treatment-related fatal	0	0	0
Treatment Emergent Identified and Potential Risks including AESI by SOC, n (%)			
Tumor flare reaction	0	0	0
Infusion-related reaction	0	0	0
Cytokine release syndrome	0	0	0
Transmissi on of infectious disease	0	0	0
Graft-vs-host disease	2 (7.7)	0	2 (2.7)
Bone marrow/organ rejection	0	3 (6.1)	3 (4.0)
ICANS	0	0	0
Immunogenicity[b]	0	0	0

- Most treatment-emergent serious adverse events (TESAEs) were not treatment related
- None of the fatal TESAEs were related to tabelecleucel
- **No cases of tabelecleucel-related graft-vs-host disease or organ rejection were reported**

Data cutoff date: Oct 9, 2023
Fatal TESAEs were disease progression (n = 7), multiple organ dysfunction syndrome (n = 2), respiratory failure (n = 1), COVID-19 (n=1), acute respiratory distress (n=1), pneumococcal sepsis (n=1), shock (n=1).
[a]Treatment-related TESAEs were diarrhea, hypoxia (grade 3), pyrexia (n =1 each), and 1 patient with grade 3 hypotension, pyrexia, rash, grade 4 rash erythematous, and tachycardia. [b]47 subjects had pan anti-HLA antibody testing completed, 38 of which were evaluable (18 in target population) for anti-HLA antibody assessment
AESI, adverse event of special interest; HCT, hematopoietic cell transplant; ICANS, immune effector cell-associated neurotoxicity syndrome; SOT, solid organ transplant; TESAE, treatment-emergent serious adverse event.

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Take Home Points:

Tabelecleucel has promising efficacy in refractory PTLD

ORR 50.7% in all patients (best overall response: CR in 28%; PR in 22.7%) and was well tolerated

Median DOR 23.0 months

Tabelecleucel is approved in Europe and is planned for FDA review in 2025

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Abstract #569 Pembrolizumab maintenance instead of transplant for patients with rel/ref HL in CR after pembro-GVD

Alison Moskowitz, Gunjan Shah, Nivetha Ganesan, Helen Hancock, Theresa Davey, Tiffany Chang, Brittney Munayirji, Monifa Douglas, Alayna M. Santarosa, Alexander Boardman, Philip Caron, Kevin David, Zachary Epstein-Peterson, Lorenzo Falchi, Paola Ghione, Andrew Intlekofer, Paul Hamlin, Steven Horwitz, William Johnson, Anita Kumar, Jennifer Lue, Efrat Luttwak, Ariela Noy, Colette Owens, Maria Palomba, Gilles Salles, Raphael E. Steiner, Robert Stuver, Pallawi Torka, Santosha Vardhana, Andrew Zelenetz, Joachim Yahalom, Ahmet Dogan, Heiko Schoder, Craig H. Moskowitz

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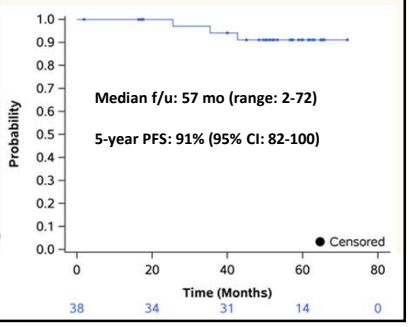
Phase II study of 2nd-line pembro-GVD → ASCT

- 39 pts (38 evaluable; 1 with composite lymphoma)
- ORR: 100%
- CR: 95% (92% after 2 cycles)
- 36 transplanted (2 opted out)
- 1 relapse, 2 deaths (unrelated)



Updated from Moskowitz AJ, et al. JCO 2021
Data cut off: 9/20/2024

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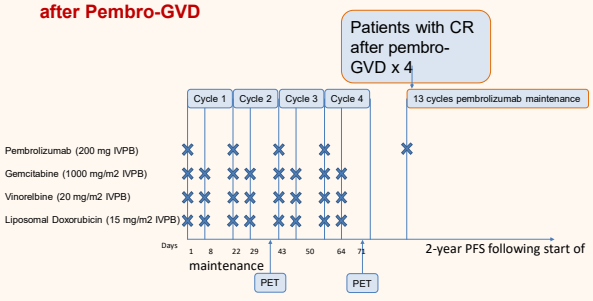
Pembro Maintenance Instead of Transplant for pts in CR after Pembro-GVD



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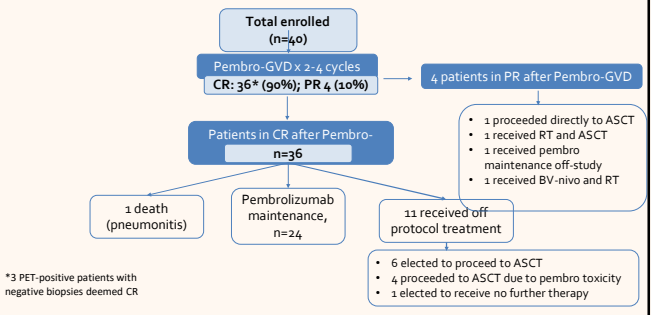
Pembro Maintenance Instead of Transplant for pts in CR after Pembro-GVD



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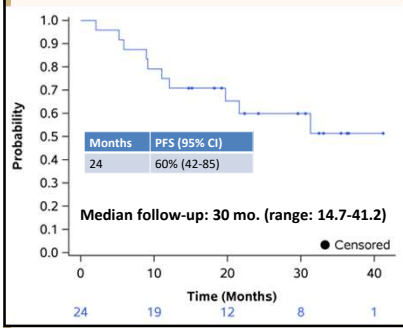
Pembro Maintenance Instead of Transplant for pts in CR after Pembro-GVD



10 relapses:
- 4 pts during pembro maintenance
- 3 pts within 6 months of last pembro
- 3 pts beyond 6 months of last pembro

9 pts proceeded to transplant following:
- BV/benda (n=1)
- BV-ICE (n=1)
- ICE (n=1)
- BV/nivo, ICE, RT (n=2)
- Pembro-GVD (n=2)
- Pembro-GVD, ICE (n=1)

1 pt not transplanted due to comorbidities
- receiving palliative pembro plus gemcitabine, achieved CR

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Take Home Points:

Pembro-GVD x 4 → pembro maintenance may allow a subset of pts to be cured without transplant

Patients who relapse during or after maintenance can successfully be salvaged with third-line therapy and autologous stem cell transplant

Patients with stage IV disease are more likely to require transplant

Plan for phase II randomized, non-inferiority study evaluating transplant vs pembrolizumab maintenance for patients with rel/ref stage I-III HL in CR after pembro-GVD

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P1009

Fixed-Duration Acalabrutinib plus Venetoclax With or Without Obinutuzumab versus Chemoimmunotherapy for First-Line Treatment of Chronic Lymphocytic Leukemia: Interim Analysis of the Multicenter, Open-Label, Randomized, Phase 3 AMPLIFY Trial

Jennifer R. Brown, MD,[1] John F. Seymour, MD,[2] Wojciech Jurczak, MD,[3] Andrew Aw, MD,[4] Malgorzata Wach, MD,[5] Arpad Illes, MD,[6] Alessandra Tedeschi, MD,[7] Carolyn Owen, MD,[8] Alan Skarbnik, MD,[9] Daniel Lysak, MD,[10] Ki-Seong Eom,[11] Martin Šimković, MD,[12] Miguel Arturo Pavlovsky, MD,[13] Arnon Philip Kater, MD,[14] Barbara Eichhorst, MD,[15] Kara Miller, MS,[16] Veerendra Munugalavadla, PhD,[16] Ting Yu, MD,[16] Marianne de Borja, MS,[17] Paolo Ghia, MD[18,19]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Peter MacCallum Cancer Centre, Royal Melbourne Hospital, The University of Melbourne, Melbourne, VIC, Australia; [3]Maria Skłodowska-Curie National Institute of Oncology, Kraków, Poland; [4]University of Ottawa, Ottawa, Ontario, Canada; [5]Medical University of Lublin, Lublin, Poland; [6]University of Debrecen, Debrecen, Hungary; [7]ASST Grande Ospedale Metropolitano Niguarda, Niguarda Cancer Center, Milano, Italy; [8]University of Calgary and Foothills Medical Centre, Calgary, Canada; [9]Novant Health Cancer Institute, Charlotte, NC, USA; [10]Fakultní Nemocnice Plzen, Plsen, Czech Republic; [11]Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea; [12]Hradec Králové, University Hospital and Charles University in Prague, Hradec Kralove, Czech Republic; [13]FUNDALEU, Clinical Research Center, Buenos Aires, Argentina; [14]Amsterdam University Medical Center, Amsterdam, on behalf of HOVON, Netherlands; [15]University Hospital Cologne, Cologne, Germany; [16]AstraZeneca, South San Francisco, CA, USA; [17]AstraZeneca, Mississauga, ON, Canada; [18]Università Vita-Salute San Raffaele, Milano, Italy; [19]IRCCS Ospedale San Raffaele, Milano, Italy

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AMPLIFY Study Design

TN CLL (N=867)

Key inclusion criteria
- Age ≥18 years
- TN CLL requiring treatment per iwCLL 2018 criteria[1]
- Without del(17p) or *TP53*
- ECOG PS ≤2

Key exclusion criteria
- CIRS-Geriatric >6
- Significant cardiovascular disease

Stratification
- Age (>65 vs ≤65 years)
- IGHV mutational status
- Rai stage (≥3 vs <3)
- Geographic region

RANDOMIZE 1:1:1

AMPLIFY: randomized, multicenter, open-label, Ph 3 trial

- AV (14 cycles)
- AVO (14 cycles)
- FCR/BR[a] (6 cycles)

Crossover was not allowed

Primary endpoint: IRC-assessed PFS (AV vs FCR/BR)

If primary endpoint met, secondary endpoints tested in fixed sequential hierarchy:
1) IRC-PFS (AVO vs FCR/BR)
2) uMRD (AV vs FCR/BR)
3) uMRD (AVO vs FCR/BR)
4) OS (AV vs FCR/BR)
5) OS (AVO vs FCR/BR)

NCT03836261. Data cutoff: April 30, 2024.
[a]FCR/BR administered in cycles 1 to 6.
A, acalabrutinib; AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CIRS-Geriatric, Cumulative Illness Rating Scale-Geriatric; CLL, chronic lymphocytic leukemia; ECOG PS, Eastern Cooperative Oncology Group performance status; FCR, fludarabine-cyclophosphamide-rituximab; IGHV, immunoglobulin heavy-chain variable region gene; IRC, independent review committee; iwCLL, International Working Group on CLL; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; TN, treatment-naive; uMRD, undetectable measurable residual disease.
[1]Hallek M, et al. Blood. 2018;131:2745-60.

Abstract #1009

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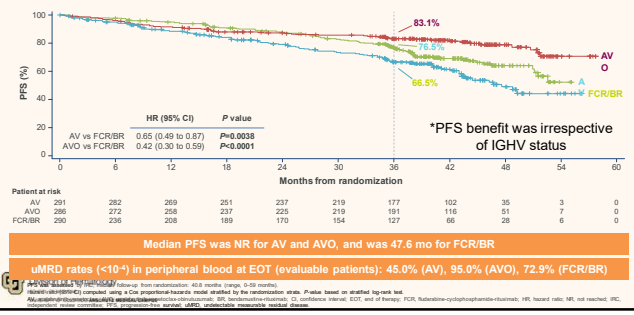
PFS Significantly Improved With AV and AVO vs FCR/BR

Abstract #1009



Median PFS was NR for AV and AVO, and was 47.6 mo for FCR/BR

uMRD rates (<10⁻⁴) in peripheral blood at EOT (evaluable patients): 45.0% (AV), 95.0% (AVO), 72.9% (FCR/BR)

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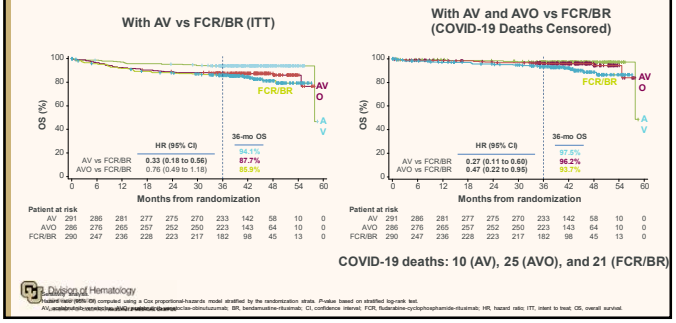
OS Benefit

Abstract #1009



COVID-19 deaths: 10 (AV), 25 (AVO), and 21 (FCR/BR)

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Safety Summary

Abstract #1009

	AV (n=291)	AVO (n=284)	FCR/BR (n=259)
Duration of exposure, median (range), mo	12.9 (1–18)	12.9 (0–18)	5.6 (1–11)
Summary of AEs			
Any AE	270 (92.8)	269 (94.7)	236 (91.1)
Any AE grade ≥3	156 (53.6)	197 (69.4)	157 (60.6)
Any serious AE	72 (24.7)	109 (38.4)	71 (27.4)
Serious AEs leading to death	10 (3.4)	17 (6.0)	9 (3.5)
AE leading to treatment discontinuation	23 (7.9)	57 (20.1)	28 (10.8)

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Take Home Points:

AMPLIFY - First phase 3 study of fixed-duration therapy with a combination of venetoclax and a second-generation BTKi in patients with TN CLL

- uMRD rates highest in the AVO arm
- AV and AVO had tolerable safety profiles, with low incidence of cardiac AEs typically associated with BTKis (ie, atrial fibrillation, hypertension)
- AVO had higher toxicity rates
- Will likely be the basis of submission for approval of AV+/- O

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Thank You!

Email manali.kamdar@cuanschutz.edu
X @mana1981

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