

# Updates in DLBCL MANAGEMENT—

The Role of Antibody Drug Therapeutics in Frontline and Later-Line Management



 

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### Updates in DLBCL Management—The Role of Antibody Drug Therapeutics in Frontline and Later-Line Management

#### **PROGRAM CHAIR & FACULTY PRESENTER**

Mehdi Hamadani, MD Chief of Hematologic Malignancies Endowed Professor and Associate Director of Clinical Research Medical College of Wisconsin Milwaukee, WI

#### **PROGRAM OVERVIEW**

This interactive educational activity aims to enhance the ability of hematologists/oncologists and the broader multidisciplinary oncology team with the latest insights into the evolving treatment landscape of relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). Expert-led discussion will explore the clinical significance of key biomarkers in guiding treatment decisions, the most recent safety and efficacy data on available therapies, and patient-specific factors influencing treatment choices. Additionally, the program will highlight strategies for recognizing and managing potential adverse events associated with current treatment options. Attendees will gain actionable knowledge to optimize care for patients with R/R DLBCL.

#### TARGET AUDIENCE

The proposed educational activities are specifically designed to meet the educational needs of academic and community medical hematologists/oncologists, as well as members of the multidisciplinary oncology team, such as oncology NPs/PAs, and oncology pharmacists.

#### LEARNING OBJECTIVES

Upon the completion of this program, attendees should be able to:

- Evaluate the role of specific biomarkers to inform clinical decisions in R/R DLBCL
- Summarize the efficacy and safety of specific therapies in R/R DLBCL and patient-specific factors informing choice of therapy in the setting of resistance to prior therapy
- Describe potential adverse events associated with available therapies for the management of R/R DLBCL

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	Biosciences, Byondis, Kite Pharma, and Daiichi Sankyo
Mahdi Hamadani	Speakers Bureau: AstraZeneca, ADC Therapeutics America, Inc., BeiGene, Kite
Pharma, and S Contracted Re and Astellas P	Pharma, and Sobi
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Updates in **DLBCL** MANAGEMENT—

The Role of Antibody Drug Therapeutics in Frontline and Later-Line Management

#### Program Agenda

#### Introduction

- Incidence and prevalence of diffuse large B-cell lymphoma (DLBCL)
- Challenges in management of DLBCL, with 25% to 40% of patients failing to respond to rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) or polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) and progressing to later-line forms of chemotherapy
- Review the role of antibody-drug conjugates in relapsed/refractory (R/R) disease, as well as bispecific and chimeric antigen receptor T-cell (CAR-T) therapies in the later-line setting

# Assessment and Treatment of DLBCL: Considering the Role of Antibody Therapeutics as Part of a Novel Treatment Paradigm

- Characterizing DLBCL
  - Relevance of immunohistochemistry and flow cytometry assessment
  - o Relevance of karyotype, translocations, and presence or absence of gene rearrangements
  - Assessment of multiple molecular markers
- DLBCL therapy and gaps in management therapies
  - Frontline options (eg, R-CHOP and Pola-R-CHOP in the POLARIX trial)
  - Later-line options including antibody drug conjugates, bispecific antibodies, and CAR-T therapy
  - Sequencing and selection of bispecific agents, antibody-drug conjugate therapy, and other antibody therapeutics for DLBCL in the management of resistance to previously used mechanisms (eg, anti-CD20 agents)
- Clinical data informing use of specific treatment options in the relapsed/refractory setting of DLBCL, including safety and efficacy data
  - Antibody-drug conjugates (eg, brentuximab vedotin, polatuzumab vedotin, loncastuximab tesirine)
  - Bispecific antibodies (eg, glofitamab, epcoritamab)
  - Other antibodies (eg, tafasitamab)
  - Contrasting with CAR-T therapy (eg, axicabtagene ciloleucel, tisagenlecleucel, or lisocabtagene maraleucel)

#### Best Practices in Assessing Safety and Multidisciplinary Management in R/R DLBCL

- Discussing specific therapeutic options in the management of B-cell lymphomas
  - Recognizing and managing potential adverse events with antibody-drug conjugates, including blood dyscrasias and pneumonitis
  - Monitoring and management of adverse events associated with CAR-T therapy and bispecific antibodies, such as cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS)
  - o Best practices for discussing therapeutic options and multidisciplinary care

#### Conclusions

- Opportunities and best practices for the use of novel therapeutic combinations in DLBCL to overcome resistance to prior therapy
- Key takeaways

# Updates in DLBCL Management— The Role of Antibody Drug Therapeutics in Frontline and Later-Line Management

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### **Disclosures**

- Dr Hamadani discloses the following
  - Consulting fees: AlloVir, Autolus Therpeutics, Byondis, Caribou Biosciences, CRISPR Therapeutics, Daiichi Sankyo, Forte Biosciences, Genmab, Kite Pharma
  - Speakers Bureau: ADC Therapeutics, AstraZeneca, BeiGene, Kite Pharma, Sobi
  - Contracted research: ADC Therapeutics, Astellas Pharma, Spectrum Pharmaceuticals
- During this lecture the use of medications for both US Food and Drug Administration (FDA)approved and non-FDA-approved indications may be discussed
- All relevant financial relationships have been mitigated

This activity is supported by educational grants from ADC Therapeutics America, Inc., Genentech, a member of the Roche group, and Pfizer, Inc.

## **Learning Objectives**

- Evaluate the role of specific biomarkers to inform clinical decisions in relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL)
- Summarize the efficacy and safety of specific therapies in R/R DLBCL and patient-specific factors informing choice of therapy in the setting of resistance to prior therapy
- Describe potential adverse events associated with available therapies for the management of R/R DLBCL



CNS = central nervous system; LDH = lactate dehydrogenase; NHL = non-Hodgkin lymphoma.

Abramson JS, Shipp MA. Blood. 2005;106:1164-1174. Armitage JO, Weisenburger DD. J Clin Oncol. 1998;16:2780-2795. Eyre TA, et al. Lancet Oncol. 2022;23:e416-e426. National Cancer Institute (NCI). Cancer stat facts: NHL–DLBCL (https://seer.cancer.gov/statfacts/html/dlbcl.html). Accessed 3/11/2025.



Coiffier B, et al. N Engl J Med. 2002;346:235-242. Coiffier B, et al. Blood. 2010;116:2040-2045. Pescovitz MD. Am J Transplantat. 2006,6:859-866.

Unsuccessful Phase 3 Trials Trying to Improve Outcomes for DLBCL



ABC = activated B-cell (subtype); COO = cell of origin; DASL = whole-genome cDNA-mediated annealing, selection, extension, and ligation (assay); G-CHOP = obinutuzumab + CHOP; HR = hazard ratio; IHC = immunohistochemistry; NS = not significant; R = rituximab; R2CHOP = lenalidomide + R-CHOP; R-ABCVP = R + doxorubicin, bleomycin, cyclophosphamide, vindesine, prednisone.

Bartlett NJ, et al. J Clin Oncol. 2019;37:1790-1799. Crump M, et al. Blood. 2013;122:371. Cunningham D, et al. J Clin Oncol. 2011;29(suppl 15):8000. Davies A, et al. Lancet Oncol. 2019;20:649-662. Habermann TM, et al. J Clin Oncol. 2006;24:3121-3127. Jaeger U, et al. Haematologica. 2015;100:955-963. Lamy T, et al. Blood. 2018;131:174-181. Lowry L, et al. Radiother Oncol. 2011;29:8004. 2019;20:649-662. Habermann TM, et al. J Clin Oncol. 2006;24:3121-3127. Jaeger U, et al. Haematologica. 2015;95:963. Lamy T, et al. Blood. 2018;131:174-181. Lowry L, et al. Radiother Oncol. 2011;20:869-2. Nowakowski GS, et al. J Clin Oncol. 2021;39:1317-1328. Récher G, et al. Lancet. 2011;378:1856-868. Lamy T, et al. Blood. 2020;13:71. Stiff PJ, et al. J Clin Oncol. 2011;29:8001. Thieblemont C, et al. Blood. 2020;136(suppl 1):16-17. Witzig TE, et al. An Oncol. 2018;29:707-714. Yourse A, et al. J Clin Oncol. 2019;37:1285-1295.



Tilly H, et al. N Engl J Med. 2022;386:351-363. Polatuzumab vedotin (Polivy<sup>®</sup>). Prescribing information (PI) 2023 (www.gene.com/download/pdf/polivy\_prescribing.pdf). Modified from Creative Biolabs. ADC development for NHL (www.creative-biolabs.com/adc/adc-development-for-nhl.htm). URLs accessed 3/17/2025.

## **POLARIX—Primary Endpoint: PFS**

### Pola-R-CHP significantly improved PFS vs R-CHOP



Tilly H, et al. N Engl J Med. 2022;386:351-363.



Modified from National Comprehensive Cancer Network (NCCN) guidelines for B-cell lymphoma, V3.2023 (www.nccn.org/professionals/physician\_gls/pdf/b-cell.pdf). Accessed 3/17/2025.



ORR = overall response rate. Gisselbrecht C, et al. J Clin Oncol. 2010;28:4184-4190.

\*Tisa-cel is not FDA approved as

second-line treatment for DLBCL.



auto-HCT = autologous hematopoietic cell transplantation; axi-cel = axicabtagene ciloleucel; HDT = high-dose chemotherapy; sAAIPI = second-line/secondary AAIPI.

Locke FL, et al. N Engl J Med. 2022;386:640-654 and supplement. Bishop MR, et al. N Engl J Med. 2022;386:629-639. Kamdar M, et al. Lancet. 2022;399:2294-2308.

## EFS in Randomized Trials of CAR-T vs SoC as Second-Line Therapy Primary Refractory or Early Relapsed DLBCL



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# US Retrospective Analysis of Patients for Whom CAR-T Therapy Failed (n = 284)

#### From time of progression post-CAR-T

\*Median follow-up for surviving patients: <u>15.9 months</u> (range: 2.6–36.9)

Median OS for all patients with PD: 5.5 months
Median OS for patients who received salvage: 9.0 months



Zurko JC, et al. *Blood Adv*. 2023;7(12):2657-2669.

## New and Emerging Bispecific Antibodies in Non-Hodgkin Lymphomas



Odronextamab is an investigational therapy for the management of NHL.

BsAb = bispecific antibody; Fc = crystallizable fragment; FL = follicular lymphoma; Fab = fragment antigen binding; IV = intravenous; LC = liquid chromatography; SC = subcutaneous. 1. Hutchings M, et al. Lancet. 2021;398:1157-1169. 2. Budde LE, et al. J Clin Oncol. 2022;40:481-491. 3. Hosseini I, et al. NPJ Syst Biol Appl. 2020;6:28. 4. Minson A, Dickinson M. Leuk Lymphome. 2021;62:3098-3108. 5. Zhu M, et al. Clin Transl Sci. 2022;15:954-966. 6. Smith EJ, et al. Sci Rep. 2015;5:17943.

## **Approved Bispecifics in Lymphoma: Administration Schedules**

Bispecific	Route	Schedule	Duration
Glofitamab	IV	Weekly C1, every 3 weeks	12 cycles
Mosunetuzumab	IV	Weekly C1, every 3 weeks	8 cycles if complete response (CR); 17 cycles if partial response (PR)
Epcoritamab	SC	Weekly C1 to C3, every 2 weeks C4 to C9, every 4 weeks C ≥10	Until PD

C = Cycle; IV = intravenous; PD = progressive disease; SC = subcutaneous.

Glofitamab-gxbm (COLUMVI "). Prescribing information (PI) 2023 (https://www.columvi.com/). Mosunetuzumab-axgb (Lunsumio "). PI 2024 (https://www.lunsumio.com/). Epcoritamab-bysp (Epkinly®) PI 2024 (https://www.epkinly.com/). URLs accessed 3/17/2025.

Epcoritamab: CD3 x CD20 Bispecific Antibody (SC administration)

- Epcoritamab: CD3 × CD20 bispecific antibody (humanized mouse IgG1-based)
- Induces T-cell activation by binding to CD3 on T cells and CD20 on malignant B cells
- Promotes immunologic synapse between bound cells, resulting in apoptosis of B cells
- Binds to a distinct epitope on CD20 differently from epitopes of rituximab or obinutuzumab
- Retains activity in the presence of CD20 monoclonal antibodies (mAbs)



 $\label{eq:product} \mbox{Epcoritamab} \mbox{ is FDA-approved for refractory/relapsed} \ (\mbox{R/R}) \ \mbox{DLBCL}.$ 

Hutchings M, et al. Blood. 2020;136(suppl 1):402. Engelberts P.J, et al. EBioMedicine. 2020;52:102625. Chiu C, et al. European Hematology Association (EHA) 2020: Poster EP1330. Hutchings M, et al. Lancet. 2021;398:1157-1169.



ICANS = Immune effector cell-associated neurotoxicity syndrome. Thieblemont C, et al. J Clin Oncol. 2022;41:2238-2247.

**EPCORE NHL-1: Favorable Long-Term Outcomes Among Complete Responders** 



Kaplan-Meier estimates are shown.

<sup>a</sup> Based on COVID-19-adjusted sensitivity analyses, which censored deaths due to COVID-19.

COVID-19 = coronavirus disease 2019; LBCL = large B-cell lymphoma

Karrini Y, et al. American Society of Clinical Oncology (ASCO) 2024; Poster 7039 (https://meetings.asco.org/abstracts-presentations/232717). Kaimi Y, et al. Society of Hernatologic Oncology (SOHO) 2024; Poster ABCL-191. URLs accessed 3/17/2025.

#### Glofitamab: Bispecific Antibody Targeting CD20 and CD3 in 2:1 Ratio Glofitamab is CD3/CD20 bispecific antibody for DLBCL Humanized mouse IgG1-based antibody Unique 2:1 molecular configuration allows Glofitamab "double binding" to CD20 (highlighted in High avidity binding blue zones) to CD20 on B cells Advantages of 2:1 design - Associated with superior potency under experimental conditions as compared with 1:1 binding bispecific agents CD3 T-cell engagement - Allows concomitant treatment with Silent Fc region anti-CD20 antibodies-pre-dosing extends half-life and reduces toxicity Glofitamab is FDA-approved for R/R DLBCL. Dickinson M, et al. N Engl J Med. 2022;387:2220-2231; Hutchings M, et al. J Clin Oncol. 2021;39:1959-1970.

## Glofitamab Monotherapy at RP2D Induces Durable Complete Responses

Heavily pretreated, highly refractory population

Pivotal phase 2 results presented at ASCO 2022

- DLBCL NOS, HGBCL, trFL or PMBCL; ≥2 prior therapies
- Glofitamab 2.5/10/30 mg (N = 155)
- Efficacy
  - CR rate: 39.4% (61/155)
  - ORR: 51.6% (80/155)

Received FDA approval on June 15, 2023, for R/R DLBCL after 2 prior therapy lines



Clinical cutoff date: March 14, 2022. \*Time from the initial occurrence of a CR until PD or death due to any cause, whichever occurs first. CCDD = clinical cutoff date; CI = confidence Interval; CRS = cytokine release syndrome; DCR = duration of complete response; IRC = Independent review committee; PD = progressive disease; PMBCL = primary mediastinal large B-cell lymphoma; RP2D = recommended phase 2 dose; trFL = transformed follicular lymphoma. Dickinson M, et al. ASC0 2022; Abstract/500. Dickinson M, et al. N Engl J Med. 2022; 387:2220-2231.

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#### **Response Rates and DoCR: Update Follow-Up ASH 2023 DoCR by IRC** All R/R Prior DLBCL/trFL CAR-T patients 100 (N = 155)<sup>3</sup> (N = 132)1+‡ (N = 52)<sup>+</sup> All patients (N = 62) R/R DLBCL/trFL (N = 58) 26 (50) 80 (52) 74 (56) 80 55% Prior CAR-T (N = 19) Probability (%) ORR, n (%) [95% Cl] Censored [43.5-59.7] [47.2-64.7] [35.8-64.2] 60 19 (37) 62 (40) 58 (44) CR rate, n (%) [95% CI] 40 [32.2-48.2] [35.3-52.8] [23.6-51.0] 26.9 28.3 22.0 Median DoCR, months 20 (95% CI) (19.8-NR) (19.8-NR) (6.7-NR) 0 55.0 56.2 33.1 3 . 12 . 15 . 18 21 24-month DoCR, % Ó 6 24 27 30 33 36 39 (95% CI) (41.1 - 68.8)(41.9 - 70.4)(7.2 - 59.0)Time (months) 28 23 13 29.6 23.0 29.6 Median CR follow-up, 27 34 22 17 12 months (range) (0 - 39)(0 - 39)(0 - 33)13 10 11 10 Ongoing CRs, n/N (%) 34/62 (55) 32/58 (55) 10/19 (53)

Median time on study: 32.1 months (range: 0-43)

With 32 months median follow-up, glofitamab showed high response rates and durable remissions across subgroups.

\*Intent-to-treat population (DLBCL, trFL, HGBCL, and PMBCL). †Patients in this subgroup had similar baseline characteristics to the overall population. ‡Primary efficacy population reported in the glofitamab USPI, all patients received at least 1 dose of glofitamab

ASH = American Society of Hematology; CI = confidence interval; NE = not estimable; NR = not reached; USPI = United States prescribing information.

1. Hutchings M, et al. American Society of Hematology 2023.; Abstract 433. 2. Glofittamab-gram (Columvi<sup>11</sup>). Pl 2023 (https://www.gene.com/download/pdf/columvi\_prescribing.pdf). Accessed 3/17/2025.



FOT = end-of-treatment

Hutchings M, et al. American Society of Hematology 2023; Abstract 433.

	N/diseas <u>e</u>	Grade 1 to 4 CRS	Grade ≥3 CRS	Grade 1 to 4 neurotoxicity	Grade ≥3 neurotoxicity
Glofitamab	N = 155/ DLBCL	63%	3% (Grade ≥2 12%)	8%	3%
/losunetuzumab*	N = 90/FL	44%	2%	5%	1%
Epcoritamab	N = 157/ LBCL	49.7%	2.5%	6.4%	0.6%

Dickinson M, et al. N Engl J Med. 2022;387(24):2220-2231. Budde LE, et al. Lancet Oncol. 2022;23(8):1055-1065. Thieblemont C, et al. J Clin Oncol. 2022;41(12):2238-2247.

Potential Adverse Events Considerations: Bispecific Antibodies

- Cytopenias are frequent and manageable; rates of neutropenic fevers are not high
- Infectious disease prophylaxis (eg, pneumocystis jirovecii pneumonia [PJP] prophylaxis, antivirals) and monitoring immunoglobulin levels are important supportive care considerations
- Important to recognize the unique adverse event (AE) profile of bispecific antibodies
  - Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are potential AEs associated with CAR-T therapy and bispecific T-cell engagers

Lee DW, et al. Blood. 2014;124(2):188-195. NCCN guidelines for B-cell lymphoma, V3.2023 (www.nccn.org/professionals/physician\_gis/pdf/b-cell.pdf). Accessed 2/24/2024. Hutchings M, et al. Blood. 2020;136(suppl 1):45-46. Hutchings M, et al. Lancet. 2021;398:1157-1691. Bannerji R, et al. ASH 2020; Abstract 400. Engelberts PJ, et al. EBioMedicine. 2020;52:10262.



Duell J, et al. Haematologica. 2021;106:2417-2426.

# Real-World Evidence of Tafasitamab-Lenalidomide's Activity in HGBCL and Post CAR-T



TLOC study		
DHL/THL	n = 27	
ORR	18%	
CR rate	15%	

Response to tafasitamab/lenalidomide according to CAR-T response			
DoR after CAR-TI	≥6 months (n = 11)	<6 months (n = 15)	
ORR	36%	7%	
CR	36%	7%	

DHL = double-hit lymphoma: THL = triple-hit lymphoma.

Qualis D, et al. Blood. 2022;140(suppl 1):787-789. Qualis D, et al. Blood. 2023;142(26):2327-2331. Qualis D, et al. American Society of Hematology (ASH) 2022; Abstract 323. TLOC unpublished data, courtesy Dr. David Qualis.



Study findings were previously presented as a poster at the International Conference on Malignant Lymphoma (ICML) Virtual Congress, June 18–22, 2021. 1. Crump M, et al. Blood. 2017;130:1800-1808. 2. Gisselbrecht C, et al. Br J Heematol. 2018;182:633-643. 3. Zammarchi F, et al. Blood. 2018;131:1094-1105. 4. Calmi PF, et al. Lancet Oncol. 2021;22:790-800. 5. Calmi PF, et al. ASH 2020; Abstract 1183. 6. Calmi PF, et al. ASCO 2021; Abstract 7546.

Overall Response Rate and Long-Term Responses Observed in the All-Treated Population



Data cutoff: September 15, 2022.

The median duration of follow-up was 7.8 months (range, 0.3–42.6 months) in the all-treated population and 35.0 months (range, 4.4–42.6 months) in patients with a CR. <sup>a</sup>Event-free is defined as no progressive disease or death starting from Day 1, Cycle 1 of Lonca treatment. **CR = complete response; Lonca = loncastuximab tesirine-lpyi; ORR = overall response rate.** 

CR = complete response; Lonca = ioncastuximab tesinne-ipy; ORR = overall response rate. Calmi PF, et al. *Haematologica*. 2023. (https://doi.org/10.3324/haematol.2023.283459). Accessed 3/17/2025.



CR = complete response; DOR = duration of response

N = 187

**CD19 status** 

**Prior CAR-T** Yes (N = 112)

<4

Age >75 years

4+

Yes

No

No

Positive

Negative

Caimi PF, et al. Haematologica. 2023. (https://doi.org/10.3324/haematol.2023.283459). Accessed 3/17/2025.



## **Real-World Data for Loncastuximab**

Avers E. et al. ASH 2023; Abstract 312, Zelikson V et al. Haematologica, 2025;110;706-714.

20

0

0

0

1

#### **ECHELON-3: Study Design** Multicenter, double-blind, placebo-controlled, randomized phase 3 trial Stratified by CD30 status (≥1% vs <1%), cell of origin (GCB vs non-GCB), prior CAR-T therapy (yes vs no), prior SCT (yes vs no) BV 1.2 mg/kg Q3W + rituximab 375 mg/m<sup>2</sup> IV Q3W Patients with R/R DLBCL\* after ≥2 lines + lenalidomide 20 mg PO QD of systematic therapy (no prior BV or lenalidomide), ineligible for/PD after (n = 112) HSCT or CAR-T treatment, ECOG-PS ≤2, FDG-avid measurable disease, and no Placebo + rituximab 375 mg/m<sup>2</sup> IV Q3W active cerebral/meningeal disease or + lenalidomide 20 mg PO QD grade $\geq 2$ peripheral neuropathy (n = 118)(N = 230)\*Including but not limited to transformed DLBCL, high-grade DH/TH lymphoma, DLBCL-NOS. Primary endpoint: OS in ITT population Key secondary endpoints: PFS and ORR by investigator in ITT population, CR and DoR by investigator, OS in patients with CD30+ disease, safety/tolerability

FDG = fluorodeoxyglucose; ITT = Intention-to-treat; PO = by mouth; Q3W = every 3 weeks; QD = every day. Klm JA, et al. ASCO 2024; Abstract LBA7005. NCT04404283 (https://clinicaltrials.gov/study/NCT04404283?tab=history&e=37). Accessed 3/17/2025.

#### BV + Len + R Placebo + Len + R **0S** n = 112 n = 118 Median OS, months 13.8 8.5 HR (95% CI) 0.629 (0.445-0.891) Р .0085 Median follow-up, months 18.9 15.5 PFS n = 112 n = 118 Median PFS, months 4.2 2.6 HR (95% CI) 0.527 (0.380-0.729) Р <.0001 Median follow-up, months 11.1 8.8





OS prespecified efficacy boundary was crossed at interim analysis

 Median duration of treatment: 3.6 months (BV) vs 2.0 months (placebo)
 BV = brentuximab vedotin; ITT = intention-to-treat; Len = lenalidomide; OS = overall survival; PFS = progression-free survival; R = rituximab.
 Kim JA, et al. ASCO 2024; Abstract LBA7005.

## **ECHELON-3: Response**

All patients	BV + Len + R (n = 112)	Placebo + Len + R (n = 118)	Р
ORR, %	64.3	41.5	.0006
• CR	40.2	18.6	
With CD30-negative disease (<1%)	n = 76	n = 80	Р
ORR, %	60.5	37.5	.0063
• CR	40.8	15.0	
With CD30-positive disease (≥1%)	n = 36	n = 38	Р
ORR, %	72.2	50.0	.0602
▪ CR	38.9	26.3	

#### Median DoR

- All patients: 8.3 months (BV) vs 3.0 months (placebo)
- In patients who achieved a CR: 18.9 months (BV) vs not reached (placebo)
- Median time to CR onset: 1.58 months (BV) vs 1.61 months (placebo)

BV = brentuximab vedotin; CR = complete response; DoR = duration of response; Len = lenalidomide; ORR = overall response rate; R = rituximab. Kim JA, et al. ASCO 2024; Abstract LBA7005.

**Conclusions** 

- R-CHOP remains SoC treatment for patient with newly diagnosed DLBCL; however, Pola + CHP is also a standard option for patients with IPI score 2–5, advanced-stage
- Second-line therapies for patients who are ineligible for or decline transplant and CAR-T therapy include tafasitamab/lenalidomide, polatuzumab/BR, or other chemoimmunotherapy (ie, R-GemOx)
- Available third-line and later-line options for patients who are ineligible for or decline CAR-T therapy or those who have progressed on CAR-T therapy include bispecifics, tafasitamab/lenalidomide, polatuzumab/BR, loncastuximab tesirine, and selinexor
- CAR-T therapy has been approved as treatment of choice for DLBCL in third line and now in second line for patients with primary refractory disease and early relapse



Q&A



## Program Resources https://linktr.ee/DLBCLManagement

- 0 • • • • 0
- **CREATE** a free personalized office poster
- **REGISTER** for a variety of CME activities
- VIEW supplemental resources and animations

**Overview of Diffuse Large B-Cell Lymphoma Front-Line Therapy** 

Resource	Address
Bartlett NL, Wilson WH, Jung SH, et al. Dose-adjusted EPOCH-R compared with R-CHOP as frontline therapy for diffuse large B-cell lymphoma: Clinical outcomes of the phase III intergroup trial Alliance/CALGB 50303. <i>J Clin Oncol</i> . 2019;37:1790-1799.	https://ascopubs.org/doi/10.1200/JCO.18.01994
Coiffier B, Lepage E, Briere J, et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. <i>N Engl J</i> <i>Med.</i> 2002;346:235-242.	https://www.nejm.org/doi/10.1056/NEJMoa011795
Coiffier B, Thieblemont C, Van Den Neste E, et al. Long- term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: A study by the Groupe d'Etudes des Lymphomes de l'Adulte. <i>Blood</i> . 2010;116:2040-2045.	https://ashpublications.org/blood/article/116/12/2040 /27477/Long-term-outcome-of-patients-in-the-LNH- 98-5
Davies A, Cummin TE, Barrans S, et al. Gene-expression profiling of bortezomib added to standard chemoimmunotherapy for diffuse large B-cell lymphoma (REMoDL-B): An open-label, randomised, phase 3 trial. <i>Lancet Oncol</i> . 2019;20:649-662.	https://www.sciencedirect.com/science/article/pii/S14 70204518309355
Jaeger U, Trneny M, Melzer H, et al. Rituximab maintenance for patients with aggressive B-cell lymphoma in first remission: Results of the randomized NHL13 trial. <i>Haematologica</i> . 2015;100:955-963.	https://haematologica.org/article/view/7441
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Sehn LH, Martelli M, Trněný M, et al. A randomized, open-label, Phase III study of obinutuzumab or rituximab plus CHOP in patients with previously untreated diffuse large B-Cell lymphoma: Final analysis of GOYA. <i>J Hematol Oncol</i> . 2020;13:71.	https://jhoonline.biomedcentral.com/articles/10.1186/ s13045-020-00900-7
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Thieblemont C, Phillips T, Ghesquieres H, et al. Epcoritamab, a novel, subcutaneous CD3xCD20 bispecific T-cell-engaging antibody, in relapsed or refractory large B-cell lymphoma: Dose expansion in a phase I/II trial. <i>J Clin Oncol</i> . 2023;41:2238-2247.	https://ascopubs.org/doi/10.1200/JCO.22.01725

Tilly H, Morschhauser F, Sehn LH, et al. Polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma. <i>N Engl J Med</i> . 2022;386:351-363.	https://www.nejm.org/doi/10.1056/NEJMoa2115304
Witzig TE, Tobinai K, Rigacci L, et al. Adjuvant everolimus in high-risk diffuse large B-cell lymphoma: Final results from the PILLAR-2 randomized phase III trial. <i>Ann Oncol</i> . 2018;29:707-714.	https://www.annalsofoncology.org/article/S0923- 7534(19)35489-4/fulltext
Younes A, Sehn LH, Johnson P, et al. Randomized phase III trial of ibrutinib and rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone in non-germinal center B-cell diffuse large B-cell lymphoma. <i>J Clin Oncol</i> . 2019;37:1285-1295.	https://ascopubs.org/doi/10.1200/JCO.18.02403

## Treatment for Relapsed/Refractory Diffuse Large B-Cell Lymphoma

Resource	Address
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Bartlett NL, Hahn U, Kim WS, et al. Brentuximab vedotin combination for relapsed diffuse large B-cell lymphoma. <i>J Clin Oncol. 2025</i> ;43:1061-1072.	https://ascopubs.org/doi/10.1200/JCO-24-02242
Bishop MR, Dickinson M, Purtill D, et al. Second-line tisagenlecleucel or standard care in aggressive B-cell lymphoma. <i>N Engl J Med</i> . 2022;386:629-639.	https://www.nejm.org/doi/10.1056/NEJMoa2116596
Budde LE, Assouline S, Sehn LH, et al. Single-agent mosunetuzumab shows durable complete responses in patients with relapsed or refractory B-cell lymphomas: Phase I dose-escalation study. <i>J Clin Oncol</i> . 2022;40:481-491.	https://ascopubs.org/doi/10.1200/JCO.21.00931
Budde LE, Sehn LH, Matasar M, Schuster SJ, et al. Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study. <i>Lancet Oncol.</i> 2022:23:1055-1065.	https://www.sciencedirect.com/science/article/abs/pii /S1470204522003357
Caimi PF, Ai W, Alderuccio JP, et al. Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): A multicentre, open-label, single- arm, phase 2 trial. <i>Lancet Oncol.</i> 2021;22:790-800.	https://www.sciencedirect.com/science/article/abs/pii /S147020452100139X
Crump M, Neelapu SS, Farooq U, et al. Outcomes in refractory diffuse large B-cell lymphoma: Results from the international SCHOLAR-1 study. <i>Blood.</i> 2017;130:1800-1803.	https://ashpublications.org/blood/article/130/16/1800 /36474/Outcomes-in-refractory-diffuse-large-B-cell
Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B- cell lymphoma. <i>N Engl J Med.</i> 2022;387:2220-2231.	https://www.nejm.org/doi/10.1056/NEJMoa2206913

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Gisselbrecht C, Van Den Neste E. <i>Br J Haematol.</i> How I manage patients with relapsed/refractory diffuse large B cell lymphoma. <i>Br J Haematol.</i> 2018;182:633-643.	https://onlinelibrary.wiley.com/doi/10.1111/bjh.15412
Kamdar M, Solomon SR, Arnason J, et al. Lisocabtagene maraleucel versus standard of care with salvage chemotherapy followed by autologous stem cell transplantation as second-line treatment in patients with relapsed or refractory large B-cell lymphoma (TRANSFORM): Results from an interim analysis of an open-label, randomised, phase 3 trial. <i>Lancet</i> . 2022;399:2294-2308.	https://www.sciencedirect.com/science/article/abs/pii /S0140673622006626
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Zurko J, Nizamuddin I, Epperla N, et al. Peri-CAR-T practice patterns and survival predictors for all CAR-T patients and post-CAR-T failure in aggressive B-NHL. <i>Blood Adv.</i> 2023;7:2657-2669.	https://ashpublications.org/bloodadvances/article/7/1 2/2657/486571/Peri-CAR-T-practice-patterns-and- survival

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