JADPRO Clinical Case Series

Bispecific Antibodies in DLBCL: Navigating the Evolving Treatment Landscape

SUPPORTED BY

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PRESENTER

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Program Agenda

- Overview of diffuse large B-cell lymphoma (DLBCL)
- Bispecific antibody therapy in third-line DLBCL
- EPCORE-NHL-1 and NP30179 pivotal clinical trial data
- Epcoritamab patient case studies
- Future directions

Diffuse Large B-cell Lymphoma: Background

- DLBCL accounts for 30%-40% of newly diagnosed cases of non-Hodgkin lymphoma (NHL)
- Initial R-CHOP treatment cures ~60% of cases
  - ~10%-15% are resistant to R-CHOP
  - 20%-25% relapse after R-CHOP
- Outcomes in relapsed/refractory (R/R) DLBCL are historically poor, but have improved in the era of cellular immunotherapy

Sehn LH et al. Blood, 2015;125:22-32.
R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone.

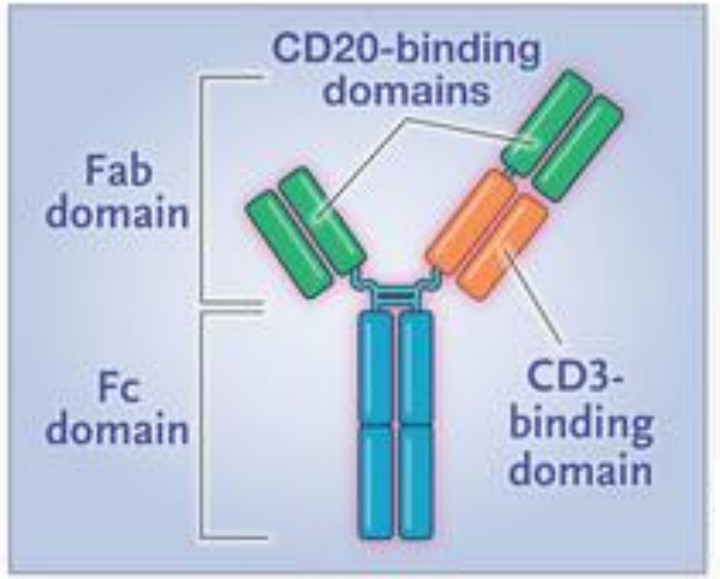
Evolving Treatment Landscape of R/R DLBCL

- CAR-T therapy is highly effective for a subset of patients
  - Now SOC in the second-line setting for early treatment failure or transplant ineligible
  - CAR-T can be safely administered in patients of advanced age and with comorbidities
- Bispecific antibodies are highly active in R/R DLBCL
  - Approved in third line
  - Being explored in all lines of therapy
- Non-cellular therapy treatments
  - Polatuzumab vedotin + bendamustine/rituximab
  - Tafasitamab + lenalidomide
  - Loncastuximab
  - Selinexor

SOC, standard of care.

CD20/CD3 Bispecific Antibodies in R/R DLBCL

- NCCN treatment recommendation for third-line therapy and beyond
- Bind to CD3 on T cells and CD20 on B cells, and induce T-cell mediated killing of lymphoma B cells
- CD20 is commonly expressed in B-cell malignancies like DLBCL
- “Off-the-shelf therapy”
- Administered subcutaneously or intravenously



Dickinson MJ, et al. N Engl J Med. 2022;387:2220-2231.

Clinical Trial Data (EPCORE-NHL-1 & NP30179)

Bispecific Antibody	Median Prior LOT (range)	ORR	CR	Median DoCR (mo) (95% CI)	Median PFS (mo) (95% CI)	Adverse Events					
						CRS		ICANS		Neutropenia	
						Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3
Glofitamab n = 154 aNHL × maximum 12 cycles	**3** (2-7)	51.6%	39.4%	Not reached (16.8-NE)	**4.9** (3.4-8.1)	59%	3.9%	5.2%	2.6%	11%	26.6%
Epcoritamab n = 157 LBCL treatment until PD or unacceptable toxicity	**3** (2-11)	63%	39%	Not reached	**4.4** (3.0-7.9)	47.1%	2.5%	5.7%	0.6%	7%	21%

Table courtesy of Dr. Peter Riedell.
Thieblemont C, et al. J Clin Oncol, 2023;41:2238-2247. Dickinson MJ, et al. N Engl J Med. 2022;387:2220-2231.
CRS, cytokine release syndrome; DoCR, duration of complete response; ICANS, immune effector cell-associated neurotoxicity syndrome; LOT, lines of therapy; mo, months; PD, progressive disease; PFS, progression-free survival.

Treatment Considerations

Epcoritamab

- Administered subcutaneously
- 28-day cycle
- Premedication: Cycle 1: steroid, antipyretic, antihistamine; Cycles 2+ with prior grade 2-3 cytokine release syndrome [CRS]), steroid if CRS with prior dose
- Step-up dosing with Cycle 1
  - 0.16 mg (Day 1)
  - 0.8 mg (Day 8)
  - 48 mg, full dose (Day 15)
- Admit Cycle 1, Day 15 for 24-hour observation
- Weekly dosing Cycles 1-3, every-other week Cycles 4-9, monthly Cycles 10+
- Continue until progression or intolerance

Epcoritamab prescribing information.

Glofitamab

- Administered intravenously
- 21-day cycle
- Premedication: Cycles 1-3: steroid, antipyretic, antihistamine; Cycles 4+: antipyretic, antihistamine, steroid if CRS with prior dose
- Step-up dosing
  - Obinutuzumab 1,000 mg (Day 1)
  - 2.5 mg (Day 8)
  - 10 mg (Day 15)
- Cycles 2+ 30 mg every 3 weeks (4-hour infusion), Cycles 3-12 (2-hour infusion)
- All patients, admit Cycle 1, Day 8. Admit Day 15 if any prior CRS
- Continue for a maximum of 12 cycles or until progression or intolerance

Glofitamab prescribing information.

Case Study 1: Epcoritamab for the Management of R/R DLBCL

- EV is a 76-year-old woman with a history of R/R DLBCL arising from follicular lymphoma (FL)
- ECOG 1
- Medical history: Hypertension, atrial fibrillation, deep vein thrombosis
  - On lisinopril and apixaban
- 6 prior lines of therapy including CAR T-cell therapy
  - Most recent treatment w/ tafasitamab/lenalidomide → Progressive disease
- Baseline platelet count 90,000 (grade 1 thrombocytopenia)
  - Bone marrow biopsy prior to treatment w/ no evidence of DLBCL or FL
- Treatment with epcoritamab recommended

EV Treatment Course

- Began Cycle 1 step-up dosing with premedications
- Admitted for observation on Cycle 1, Day 15
- Grade 1 CRS with a fever of 38.5°C on Day 15
  - Treated with antipyretics and intravenous fluids with symptom resolution
  - Infectious work-up negative
  - No further CRS and no ICANS
- PET imaging s/p 2 cycles of treatment consistent with a partial response, treatment continued
- Imaging s/p 4 cycles of treatment demonstrated a deepened response and was consistent with a complete response
- EV is tolerating therapy well and will continue unless progression or unacceptable toxicity

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; s/p, status post.

Polling Question: Case 1

Would you recommend a bispecific antibody to your patient with relapsed DLBCL who has a history of CRS and ICANS and for whom CAR T-cell therapy previously failed?

A. Yes **35%**

B. No **0%**

C. It depends on the patient and the severity of the toxicity **52%**

D. I would consider an alternate therapy approved for relapsed/refractory DLBCL **13%**

Case Study 2: Epcoritamab R/R DLBCL after CAR T-cell Therapy Failure

- KB is a 54-year-old man with history of primary refractory DLBCL
- ECOG 0
- Medical history: Hypertension and former tobacco use
- 5 prior lines of therapy
- Relapsed ~5 months after lisocabtagene maraleucel CAR T-cell therapy
  - Cervical lymph node biopsy consistent with recurrent DLBCL (CD10+, CD20+, CD5-)
  - No B symptoms
- Treatment with epcoritamab recommended

KB Treatment Course

- Began Cycle 1 with step-up dosing and premedications
- Admitted for observation on Cycle 1, Day 15
- No CRS or ICANS
- Grade 3 neutropenia
- Absolute neutrophil count (ANC) of 650 on Day 16
  - Afebrile, no signs or symptoms of infection
  - 300 µg of G-CSF x1
  - Antibacterial and antifungal prophylaxis
  - Resolved by Day 22
    - ANC 1,600; antibacterial and antifungal meds discontinued
- PET imaging s/p 2 cycles c/w a CR, which was maintained on repeat imaging s/p cycle 4
- Continuing on therapy given evidence of efficacy and tolerability (G1 fatigue and anemia)

Polling Question: Case 2

When educating patients who are receiving first- or second-line therapies do you mention potential later-line therapies, or do you wait until the patient's disease has progressed?

A. I provide a potential roadmap for future therapies when initiating first-line therapy **38%**

B. I will mention later-line therapies once disease has progressed past first-line **25%**

C. I try to focus on each line of therapy as it happens **25%**

D. I will discuss later-line therapies in the first-line if the patient asks for information **12%**

Case Study 3: Managing Side Effects Associated with Bispecific Antibody Therapy

- CB is a 63-year-old woman with a history of relapsed high grade B-cell lymphoma
- ECOG 1
- Medical history: Insulin-dependent diabetes mellitus (well-controlled), hypertension, obesity
- 2 prior lines of therapy
- Treatment with epcoritamab recommended

CB Treatment Course

- Began Cycle 1 with step-up dosing and premedications
- Antiviral and PJP prophylaxis
- Grade 1 injection site reactions
  - Managed with as-needed topical steroid for pruritis, no associated pain
- Admitted for observation on Cycle 1, Day 15; developed CRS ~12 hours post-dose (hospitalized for 36 hours)
- Grade 2 CRS (fever 39°C and hypotension)
  - Antipyretics and intravenous fluids
  - 1 dose of tocilizumab with symptom resolution and no recurrent CRS
  - Infectious work-up negative
- Uncontrolled glucose levels r/t steroids with Cycle 1
  - Required temporary increase in basal insulin dose and sliding scale insulin
  - Returned to baseline insulin dosing by Cycle 3
- No ICANS or grade 3/4 toxicities
- Now on monthly dosing schedule with continued clinical benefit and tolerance

Polling Question: Case 3

If your patient developed steroid-induced hyperglycemia during treatment requiring medication, how would you approach managing this new issue?

A. Refer to endocrinology **0%**

B. Collaborate with the primary care physician **14%**

C. Manage in your oncology clinic **21%**

D. Combination strategy **64%**

Clinical Pearls

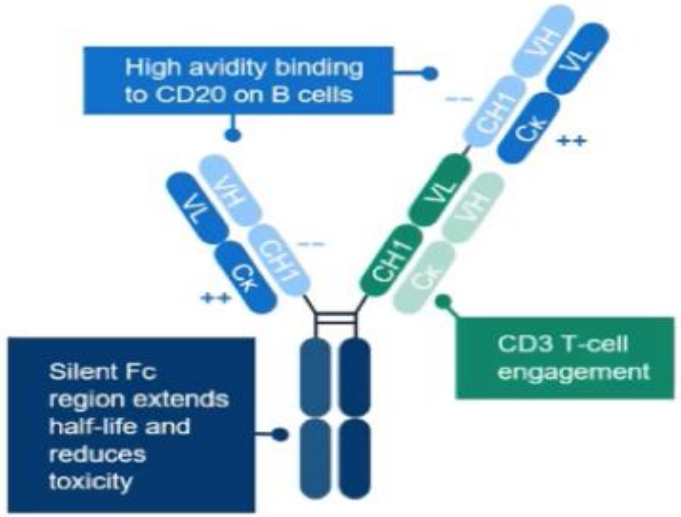
- Bispecific antibodies are effective in patients who have failed multiple lines of therapy and can be safely given to elderly patients with comorbidities
- Bispecific antibody therapy is an effective treatment strategy for relapsed/refractory DLBCL, even after CAR T-cell therapy failure
- Bispecific antibodies have a manageable side-effect profile

The Future of Bispecific Antibody Therapy

- **Unanswered Questions**
  - What agents are best to combine with bispecific antibodies?
  - What is the optimal duration of therapy?
  - Mechanisms of resistance/relapse to bispecific antibody therapy?
  - Sequencing of therapy?
- **Clinical Trials**
  - R-CHOP vs. R-CHOP + epcoritamab
  - Glofitamab + Pola-R-CHP
  - Second line: bispecific + platinum-based salvage therapy
  - Mosunetuzumab consolidation after autologous stem cell transplant in R/R DLBCL

Epcoritamab

Glofitamab



Pola-R-CHP, polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone.

Q & A

Please type your questions for Jacklyn Gideon into the **question box**.

Thank You