# ZUMA-23: A Global, Phase 3, Randomized Controlled Study of Axicabtagene Ciloleucel Versus Standard-of-Care as First-Line Therapy in Patients With High-Risk Large B-Cell Lymphoma

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# Disclosures

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# Background

- The nearly 40% of patients with LBCL who relapse or are refractory after current first-line SOC regimens, such as R-CHOP and DA-EPOCH-R, have poor prognoses[1]
- High IPI score and the HGBL subtype of LBCL are associated with shorter PFS and OS[2,3]
  - Strategies to improve outcomes with first-line therapy in these patients have been largely unsuccessful; therefore, therapeutic options with different mechanisms of action are needed

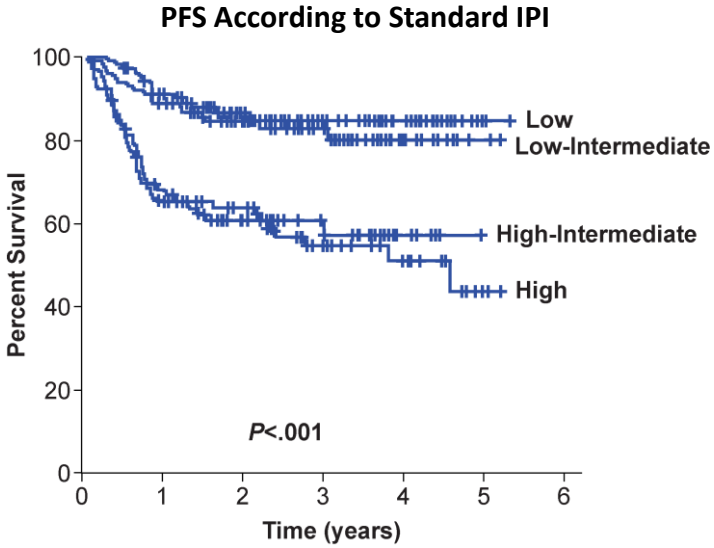


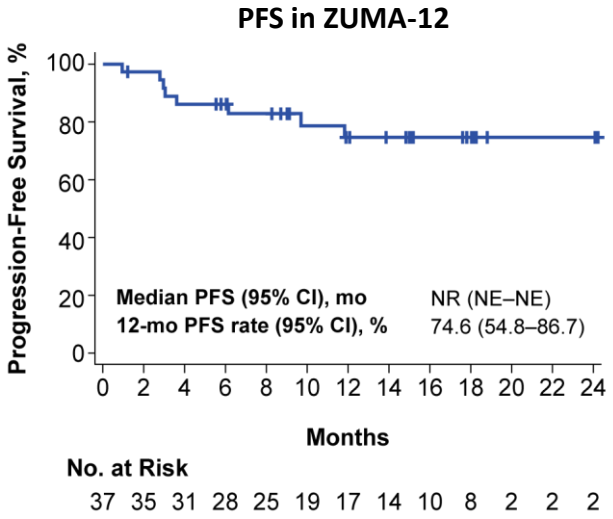

Figure adapted with permission from Sehn LH, et al. *Blood.* 2007;109:1857-1861.

1. Nastoupil LJ and Bartlett NL. *J Clin Oncol.* 2023;41:903-913. 2. Olszewski AJ, et al. *Blood.* 2022;140:943-954. 3. Sehn LH, et al. *Blood.* 2007;109:1857-1861.

DA-EPOCH-R, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; HGBL, high-grade B-cell lymphoma; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; OS, overall survival; PFS, progression-free survival; R-CHOP, rituximab + cyclophosphamide, doxorubicin, vincristine, and prednisone; SOC, standard-of-care.

# Background (Cont'd)

- Axi-cel is an autologous anti-CD19 CAR T-cell therapy approved to treat patients with R/R LBCL after demonstrating significant clinical benefit as second-line (ZUMA-7) and third-line and higher (ZUMA-1) therapy[1-4]
- The Phase 2 ZUMA-12 study assessed axi-cel as part of first-line therapy in patients with high-risk LBCL who were PET+ after 2 cycles of CIT[5]
  - Axi-cel showed a CR rate of 78% (89% ORR)
  - Responses were ongoing in 73% of patients after a median follow-up of 15.9 months
  - No new safety signals were reported in the first-line treatment setting
- ZUMA-23 is the first Phase 3, randomized controlled study conducted in any cancer to evaluate CAR T-cell therapy as a first-line regimen and will assess axi-cel versus SOC in patients with high-risk LBCL

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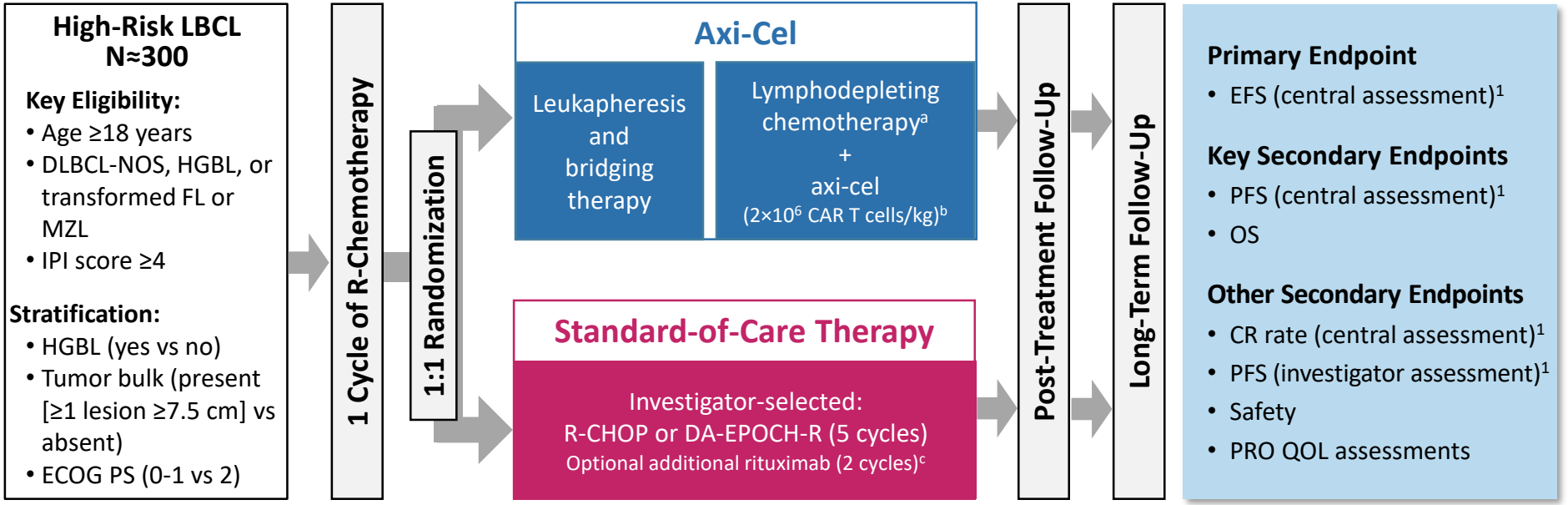
1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2022. 2. YESCARTA® (axicabtagene ciloleucel) [summary of product characteristics]. Amsterdam, The Netherlands: Kite Pharma EU; 2022. 3. Locke FL, et al. *N Engl J Med.* 2022;386:640-654. 4. Neelapu SS, et al. *N Engl J Med.* 2017;377:2531-2544. 5. Neelapu SS, et al. *Nat Med.* 2022;28:735-742.

Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CIT, chemoimmunotherapy; CR, complete response; LBCL, large B-cell lymphoma; mo, month; NE, not estimable; NR, not reached; ORR, objective response rate; PET, positron emission tomography; PFS, progression-free survival; R/R, relapsed/refractory; SOC, standard-of-care.

# ZUMA-23 Phase 3 Study Design




1. Cheson BD, et al. *J Clin Oncol.* 2014;32:3059-3068.

[a] Lymphodepleting chemotherapy will consist of cyclophosphamide (500 mg/m$^2$/day) and fludarabine (30 mg/m$^2$/day), received Days –5 through –3 before receiving axi-cel. [b] Prophylactic corticosteroids may be administered after axi-cel infusion per investigator discretion. [c] If standard of care per local clinical practice, patients may also receive 2 additional cycles of rituximab monotherapy.

Axi-cel, axicabtagene ciloleucel; CR, complete response; DA-EPOCH-R, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; FL, follicular lymphoma; HGBL, high-grade B-cell lymphoma; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; MZL, marginal zone lymphoma; NOS, not otherwise specified; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcomes; R-chemotherapy, rituximab plus chemotherapy; R-CHOP, rituximab + cyclophosphamide, doxorubicin, vincristine, and prednisone; QOL, quality of life.

# Key Inclusion Criteria and Exclusion Criteria

| Key Inclusion Criteria | Key Exclusion Criteria |
|---|---|
| • Age ≥18 years<br>• Histologically confirmed LBCL, based on WHO 2016 classification[1] by local assessment, including the following:<br>– DLBCL-NOS<br>– HGBL (*MYC* + *BCL2*/*BCL6* rearrangements and NOS)<br>– Note: Transformed DLBCL from FL or MZL is eligible if there was no prior treatment with anthracycline-containing regimen<br>• High-risk disease defined as an IPI score of 4-5 at initial diagnosis<br>• Have received only 1 cycle of R-chemotherapy<br>• Adequate bone marrow, renal, hepatic, pulmonary, and cardiac function | • The following WHO 2016[1] subcategories by local assessment:<br>– T-cell/histiocyte-rich LBCL<br>– Primary DLBCL of the CNS<br>– PMBCL<br>– B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical HL<br>– Burkitt lymphoma<br>• Presence of detectable CSF-malignant cells, brain metastases, or a history of CNS involvement of lymphoma<br>• Presence of CNS disorder; history of stroke, transient ischemic attack, or PRES <12 months prior to enrollment<br>• History of acute or chronic active hepatitis B or C infection unless the viral load is undetectable by PCR and/or nucleic acid testing<br>• HIV-positive unless taking appropriate anti-HIV medications, with an undetectable viral load by PCR and with a CD4 count >200 cells/µL |

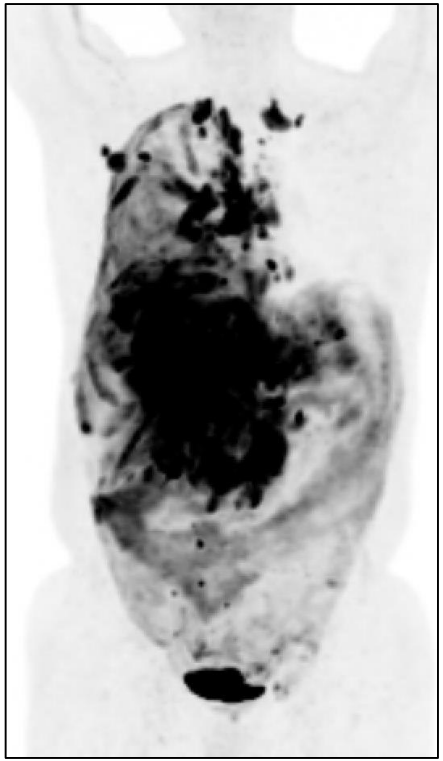
1. Swerdlow SH, et al. *Blood*. 2016;127:2375-2390.

CNS, central nervous system; CSF, cerebrospinal fluid; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBL, high-grade B-cell lymphoma; HL, Hodgkin lymphoma; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; MZL, marginal zone lymphoma; NOS, not otherwise specified; PCR, polymerase chain reaction; PMBCL, primary mediastinal (thymic) B-cell lymphoma; PRES, posterior reversible encephalopathy syndrome; R-chemotherapy, rituximab plus chemotherapy; WHO, World Health Organization.

# Clinical Vignette

- Patients with IPI 4 or 5 are often quite sick
- The first cycle of R-chemotherapy prior to trial enrollment will allow sick patients to participate

- Patient 1
  - 63-year-old male with HGBL (*MYC* and *BCL6* rearrangements)
  - IPI 5: ECOG PS 3, LDH 2× ULN, >2 extranodal sites, and stage IV disease

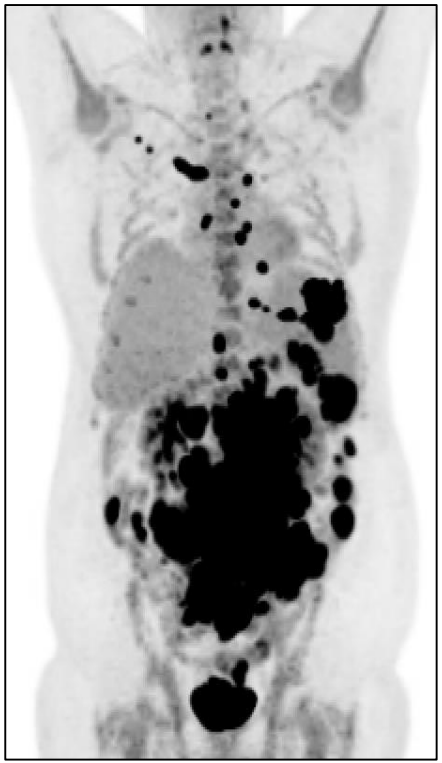


ECOG PS, Eastern Cooperative Oncology Group performance status; HGBL, high-grade B-cell lymphoma; IPI, International Prognostic Index; LDH, lactate dehydrogenase; ULN, upper limit of normal.

# Clinical Vignette (Cont'd)

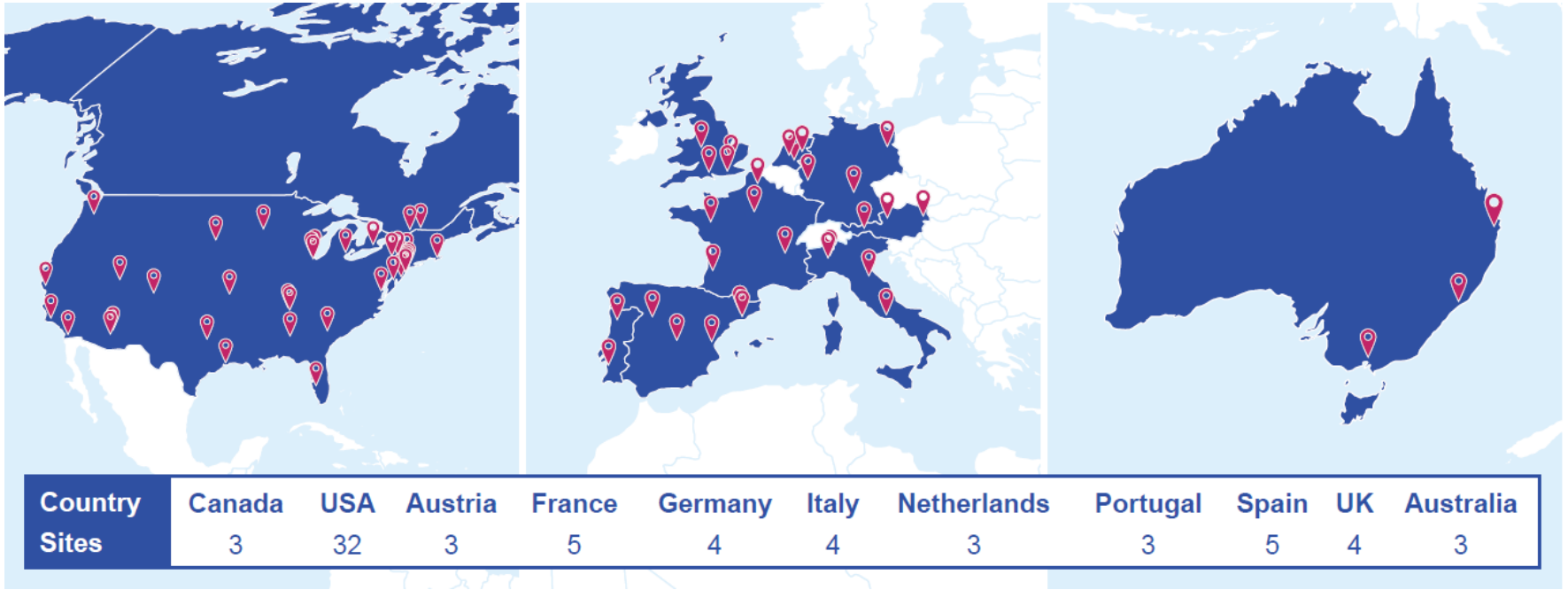
- Patients with IPI 4 or 5 are often quite sick
- The first cycle of R-chemotherapy prior to trial enrollment will allow sick patients to participate

- Patient 2
  - 48-year-old male with LBCL (GCB-like), Ki-67 proliferation index 100%
  - IPI 4: ECOG PS 2, LDH 3× ULN, >2 extranodal sites, and stage IV disease



ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; GBC, germinal center B-cell; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; ULN, upper limit of normal.

# ZUMA-23 Clinical Trial Sites



| Country | Canada | USA | Austria | France | Germany | Italy | Netherlands | Portugal | Spain | UK | Australia |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sites | 3 | 32 | 3 | 5 | 4 | 4 | 3 | 3 | 5 | 4 | 3 |

- This study is currently recruiting participants globally
- The study was funded by Kite and registered at ClinicalTrials.gov (NCT05605899)

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- These data were previously presented at the 2023 Annual Meeting of the American Society of Clinical Oncology[1]




1. Westin J, et al. ASCO 2023. Abstract TPS7578.