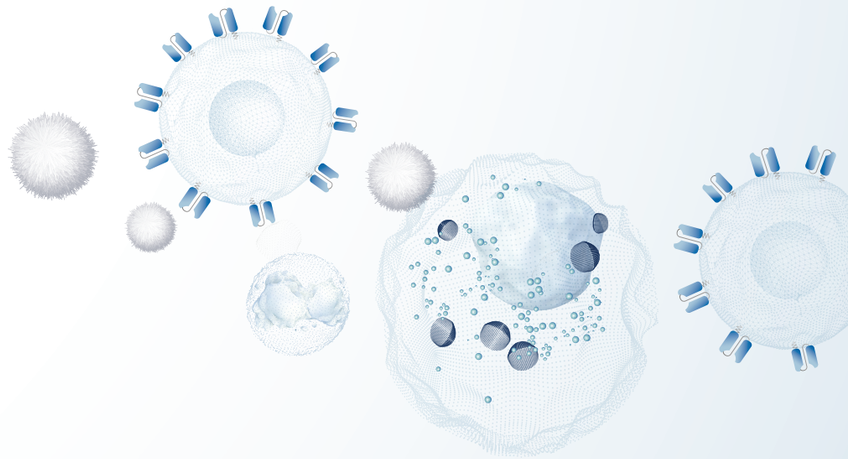
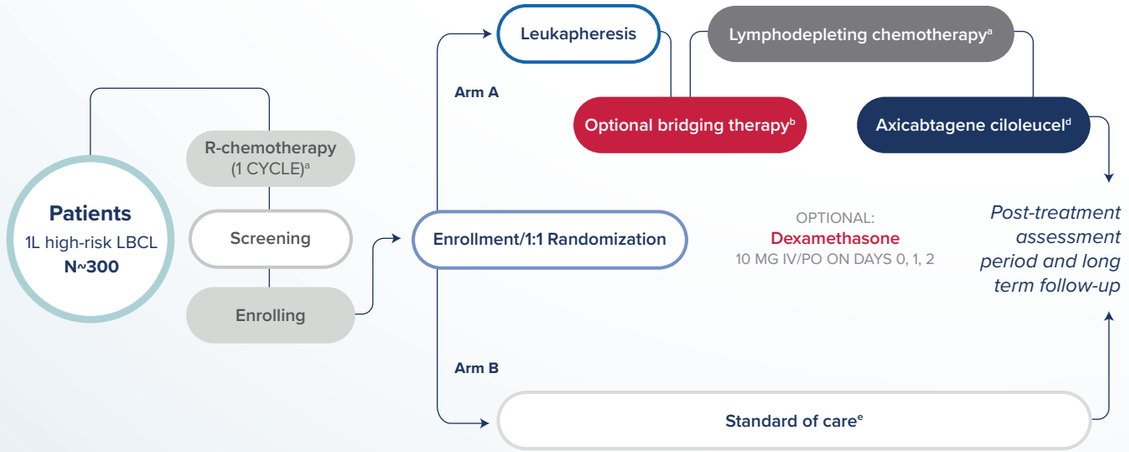
ClinicalTrials.gov Identifier: NCT05605899 • EudraCT Identifier: 2022-501489-24-00

ZUMA-23: An Adaptive Phase 3, Randomized, Open-Label, Multicenter Study to Compare the Efficacy and Safety of Axicabtagene Ciloleucel versus Standard of Care Therapy as First-Line Therapy in Participants with High-Risk Large B-Cell Lymphoma



Study Design[1-3]



[a]Participants will receive the investigator's choice of either R-CHOP or DA-EPOCH-R for a total of 6 cycles (21-day cycle).
[b]Bridging therapy with R-CHOP or DA-EPOCH-R will be administered during the cell manufacturing period.

1L, first line; DA-EPOCH-R, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; LBCL, large B-cell lymphoma; IV, intravenous; PO, by mouth; R-CHOP, Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone.

Endpoints[1-3]

Primary Endpoint

- EFS

Key Secondary Endpoints

- PFS
- OS

Secondary Endpoints

- CR rate
- AEs, SAEs, deaths and changes in safety laboratory values
- PROs/QOL

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AEs, adverse events; CR, complete response; EFS, event-free survival; OS, overall survival; PFS, progression-free survival; PROs, patient-reported outcomes; QoL, quality of life; SAEs, serious adverse events.

The safety and efficacy of these investigational agents have not been established, and they have not received marketing authorization in this setting. There is no guarantee that these investigational agents and/or uses will receive Health Authority approval and/or become commercially available.

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Key Eligibility Criteria[1-3,a]

Key Inclusion Criteria

- 18 Years and older
- Histologically confirmed LBCL based on 2016 WHO classification by local pathology lab assessment, including the following:
  - DLBCL, NOS
  - HGBL (including HGBL with MYC and BCL2 and/or BCL6 rearrangements (DHL/THL) based on FISH analysis, and HGBL-NOS
  - Note: Transformed DLBCL from follicular lymphoma or from marginal zone lymphoma is eligible if no prior treatment with anthracycline-containing regimen
- High-risk disease defined as an IPI score of 4 or 5 at initial diagnosis
- Ann Arbor Stage III or IV disease
- Have received only 1 cycle of R-chemotherapy
- Adequate bone marrow, renal, hepatic, pulmonary, and cardiac function
- Females of childbearing potential must have a negative serum or urine pregnancy test

Key Exclusion Criteria

- The following WHO 2016 subcategories by local assessment
  - T-cell/histiocyte-rich LBCL
  - Primary DLBCL of the CNS
  - Primary mediastinal (thymic) LBCL
  - B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma
  - Burkitt lymphoma
- Presence of malignant cells detected in the CSF, brain metastases, or a history of CNS involvement of lymphoma
- Presence of cardiac lymphoma involvement
- Any prior treatment for LBCL other than the 1 cycle of R-chemotherapy
- Patients positive for HIV
  - Note: Patients with a history of HIV and taking appropriate anti-HIV medications, with an undetectable viral load by PCR and a CD4 count >200 cells/µL are eligible to enroll

[a]Other protocol defined Inclusion/Exclusion criteria may apply.

BCL2/BCL6, B-cell lymphoma 2/6; CNS, central nervous system; CSF, cerebrospinal fluid; DHL, double-hit lymphoma; DLBCL, diffuse large B-cell lymphoma; FISH, fluorescence in situ hybridization; HGBL, high-grade B-cell lymphoma; HIV, human immunodeficiency virus; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; MYC, Master Regulator of Cell Cycle Entry and Proliferative Metabolism; NOS, not otherwise specified; PCR, polymerase chain reaction; THL,triple-hit lymphoma; WHO, World Health Organization.

Key Eligibility Criteria (cont'd)

Key Exclusion Criteria (cont'd)

- Patients with a history of acute or chronic active hepatitis B or C infection
  - Note: Patients with a history of treated hepatitis B or C infection and undetectable viral load are eligible to enroll
- Medical conditions likely to interfere with assessment of safety or efficacy of study treatment. Please refer to protocol for further details
- History of clinically significant cardiac disease within 12 months before enrollment
- History of any medical condition requiring maintenance systemic immunosuppression/systemic disease modifying agents within the last 2 years

References

1. Clinicaltrials.gov website. Accessed February 27, 2024. https://clinicaltrials.gov/ct2/study/NCT05605899
2. Data on file. Kite Pharma, Inc. 2022.
3. Clinicaltrialsregister.eu website.

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