Yescarta® (axicabtagene ciloleucel, axi-cel)
Cessation of Prior Therapies in ZUMA-5

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Summary

Cessation of Therapies Prior to Leukapheresis

Prior systemic therapy:

- In the ZUMA-5 study, at least two weeks or five half-lives, whichever is shorter, must have elapsed since any prior systemic therapy and enrollment/leukapheresis, except for systemic inhibitory/stimulatory immune checkpoint therapy.[1] At least three half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy and enrollment/leukapheresis (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists).[1]

Prior corticosteroid (≥5 mg/day of prednisone or equivalent) or immunosuppressive therapy:

- Must be avoided for seven days prior to enrollment/leukapheresis and five days prior to YESCARTA administration.[1]

Cessation of Bridging Therapy Prior to Conditioning Chemotherapy and Yescarta Infusion

- In the ZUMA-5 study, bridging therapy was allowed.[2] Bridging therapy must be administered after enrollment/leukapheresis and completed at least five days prior to Yescarta administration.[1]
- In the ZUMA-5 study, a new baseline positron emission tomography-computed tomography (PET-CT) was performed for patients who received bridging therapy between enrollment/leukapheresis and start of lymphodepleting chemotherapy.[1]

Cessation of Vaccines Prior to Conditioning Chemotherapy and Yescarta Infusion

Per the Yescarta US Prescribing Information (USPI), vaccination with live virus vaccines is not recommended for at least six weeks prior to the start of lymphodepleting chemotherapy, during Yescarta treatment, and until immune recovery following treatment with Yescarta.[2]

Prescribing Information[2]

YESCARTA is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

- Adult patients with large B-cell lymphoma (LBCL) that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy.
- Adult patients with relapsed or refractory LBCL after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma (HGBCL), and DLBCL arising from follicular lymphoma (FL).

Limitations of Use: YESCARTA is not indicated for the treatment of patients with primary central nervous system lymphoma.

- Adult patients with relapsed or refractory FL after two or more lines of systemic therapy. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Vaccination with live virus vaccines is not recommended for at least six weeks prior to the start of lymphodepleting chemotherapy, during YESCARTA treatment, and until immune recovery following treatment with YESCARTA.

YESCARTA should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after YESCARTA infusion and treat appropriately. Administer prophylactic antimicrobials according to local guidelines.

Study Background

ZUMA-5 Study Design[1]

ZUMA-5 (NCT03105336) was a phase 2 open-label, multicenter, single-arm study that assessed the safety and efficacy of Yescarta for the treatment of patients with relapsed/refractory non-Hodgkin lymphoma (iNHL), including FL (Grades 1-3a) and marginal zone lymphoma (MZL, nodal or extranodal).[1] Key eligibility criteria included adult patients who had 2 or more lines of therapy that must have included an anti-CD20 monoclonal antibody combined with an alkylating agent.[1] In the study, patients must have had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0-1 and adequate hematologic (absolute lymphocyte count [ALC] ≥100/µL, absolute neutrophil count [ANC] ≥1000/µL, and a platelet count ≥75,000/µL), renal, hepatic, and cardiac function. If patients showed signs and symptoms of an active infection, they were not allowed to receive treatment until the infection resolved.[1]

Cessation of Prior Therapies

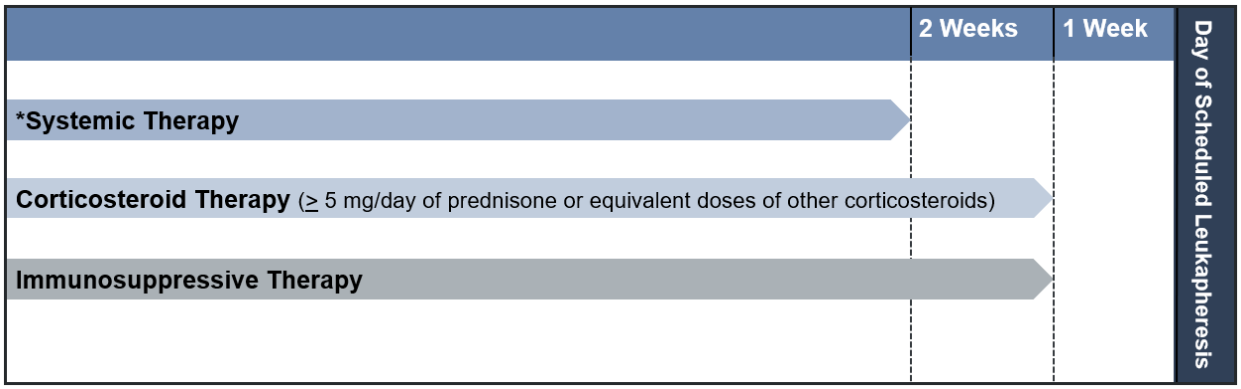
Suggested Timing of Current or Previous Therapies Prior to Leukapheresis:

The following information taken from the ZUMA-5 study protocol provides suggested washout periods prior to the scheduled date of **leukapheresis**.

- **At least two weeks or five half-lives, whichever is shorter, between any systemic therapy, including chemotherapy, and the scheduled date of enrollment/leukapheresis.**[1]
  - Exception: at least three half-lives between any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy and the scheduled date of enrollment/leukapheresis (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1 BB agonists).[1]
- At least one week between any prior corticosteroid therapy (at a pharmacologic dose) and the scheduled date of enrollment/leukapheresis and five days prior to Yescarta infusion.[1]
- At least one week between any immunosuppressive therapy and the scheduled date of enrollment/leukapheresis and five days prior to Yescarta infusion.[1]
- In ZUMA-5, toxicities due to prior therapy must have been stable and recovered to ≤ Grade 1 (except for clinical non-significant toxicities such as alopecia) before proceeding to enrollment/leukapheresis.[1]

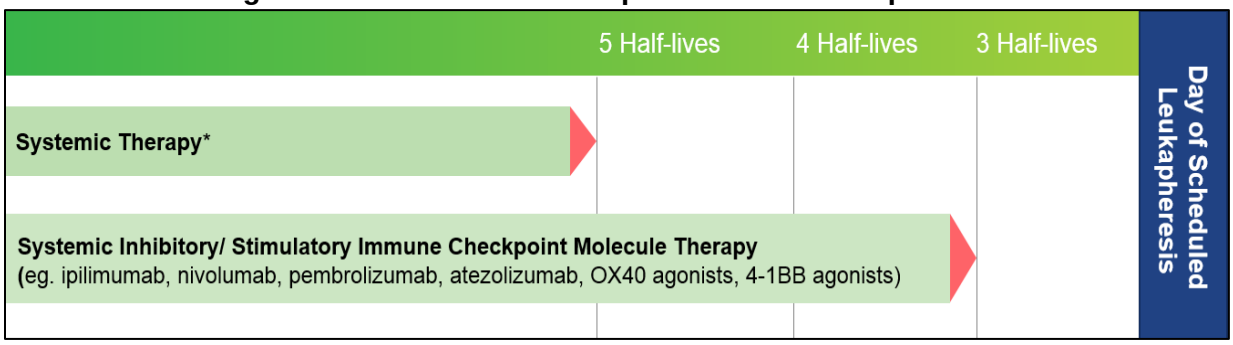
The suggested timing on cessation of current or previous therapies prior to enrollment/leukapheresis in ZUMA-5 is further illustrated in Figures 1 and 2.

Figure 1. Cessation of Therapies Prior to Leukapheresis[1]



*In ZUMA-5, at least two weeks or five half-lives, whichever is shorter, must have elapsed since any prior systemic therapy (except for systemic inhibitory/stimulatory immune checkpoint molecule therapy [see Figure 2 below])

Figure 2. Cessation of Therapies Prior to Leukapheresis[1]



*In ZUMA-5, at least two weeks or five half-lives, whichever is shorter, must have elapsed since any prior systemic therapy (see Figure 1 above)

Suggested Timing of Bridging Therapy Prior to Lymphodepleting Therapy and Yescarta Infusion:

The following information taken from the ZUMA-5 study protocol provides suggested washout periods prior to the scheduled start date of **lymphodepleting chemotherapy** and **Yescarta infusion**.

The use of bridging therapy after leukapheresis and before lymphodepleting chemotherapy is at the discretion of the treating physician. As stated in the USPI, while the patient awaits the product, additional chemotherapy (not the lymphodepletion) may be necessary and may increase the risk of adverse events during the pre-infusion period.[2]

The ZUMA-5 protocol permitted the use of bridging therapy that was at the discretion of the treating physician.[3] In the ZUMA-5 study, when bridging therapy was given between the last PET-CT and conditioning chemotherapy, the baseline PET-CT scan was repeated.[1,3] Additionally, bridging therapy was administered to six patients in the ZUMA-5 study.[3]

References

1. Supplement to: Jacobson CA, Chavez JC, Sehgal AR, et al. Axicabtagene ciloleucel in relapsed or refractory indolent non- Hodgkin lymphoma (ZUMA-5): a single-arm, multicentre, phase 2 trial. *Lancet Oncol*. 2021;published online Dec 8. doi: 10.1016/S1470-2045(21)00591-X
2. YESCARTA® (axicabtagene ciloleucel) [US Prescribing Information]. Santa Monica, CA: Kite Pharma, Inc. 2023.
3. Jacobson CA, Chavez JC, Sehgal AR, et al. Axicabtagene ciloleucel in relapsed or refractory indolent non-Hodgkin lymphoma (ZUMA-5): a single-arm, multicentre, phase 2 trial. *Lancet Oncol*. 2022;23(1):91-103. doi: 10.1016/S1470-2045(21)00591-X

Abbreviations

ALC=absolute lymphocyte count
ANC=absolute neutrophil count
DLBCL=diffuse large B-cell lymphoma
ECOG PS=Eastern Cooperative Oncology Group performance status
FL=follicular lymphoma
HGBCL= high grade B-cell lymphoma
iNHL=relapsed/refractory non Hodgkin lymphoma
LBCL=large B-cell lymphoma
MZL=marginal zone lymphoma
NOS= not otherwise specified
PET/CT=positron emission tomography/computed tomography
PMBCL= primary mediastinal large B-cell lymphoma
USPI= US Prescribing Information

Product Label

For the full indication, important safety information, and Boxed Warning(s), please refer to the YESCARTA® (axicabtagene ciloleucel) US Prescribing Information available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi.pdf.

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉ MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or www.accessdata.fda.gov/scripts/medwatch

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