Yescarta® (axicabtagene ciloleucel)
Use in Hepatitis C Virus (HCV) infection

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The full indication, important safety information, and boxed warnings for cytokine release syndrome, neurologic toxicities and secondary hematological malignancies are available at:
https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi

Relevant Prescribing Information[1]

Per the YESCARTA US Prescribing Information (USPI), perform screening for HBV, HCV, and HIV and management in accordance with clinical guidelines before collection of cells for manufacturing.

Clinical Studies

ZUMA-1, ZUMA-5, and ZUMA-7 Studies

ZUMA-1 was a phase 1/2 multicenter, single-arm, open-label study which evaluated the safety and efficacy of YESCARTA in patients with chemorefractory diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), or transformed follicular lymphoma (TFL).[2,3]

In the ZUMA-1 study, patients with a known history of infection with hepatitis C virus (anti-HCV positive) were ineligible to enroll in the study.[4] Patients with a history of hepatitis C were permitted if the viral load was undetectable per quantitative polymerase chain reaction (PCR) and/or nucleic acid testing.[4]

ZUMA-5 is a multicenter, single arm, Phase 2 study to evaluate the efficacy of YESCARTA in patients with relapsed/refractory (r/r) indolent Non-Hodgkin Lymphoma (iNHL), including follicular lymphoma (FL, Grades 1-3a) and marginal zone lymphoma (MZL, nodal or extranodal).[5,6] In the ZUMA-5 study, patients with a known history acute or chronic active hepatitis C infection were excluded from this study. History of hepatitis C is permitted if, the viral load is undetectable per Infectious Disease Society of America (IDSA) guidelines or applicable country guidelines.[6]

The ZUMA-7 study is an international, multicenter, randomized, phase 3 trial comparing YESCARTA with standard care as second-line treatment in patients with early relapsed (≤ 12 months) or refractory large B-cell lymphoma (LBCL).[7] Patients with a known history of infection with hepatitis C virus (anti-HCV positive) were excluded from this study. If there is

a positive history of treated hepatitis C, the viral load must be undetectable per quantitative PCR and/or nucleic acid testing.[8]

Therefore, there are no clinical trial data available on the use of YESCARTA in patients with detectable viral loads of HCV infection.

Real-World Evidence

Strati, et al. report a case of a 60-year-old patient, treated with YESCARTA for r/r DLBCL after 2 prior lines of therapy. This patient had a long-lasting history of chronic hepatitis C that was unresponsive to interferon or ribavirin therapy. At the time of evaluation, the patient's HCV ribonucleic acid (RNA) was 15.1 million IU/mL and alanine aminotransferase (ALT) was 70 U/L. The patient achieved complete response (CR) 1 month after infusion (ongoing at 6 months) and experienced treatment complications by Grade 3 cytokine release syndrome (CRS) and Grade 3 chimeric antigen receptor (CAR)-related encephalopathy syndrome (CRES), reversible with anti-IL-6 therapy. No significant increase in HCV RNA or ALT/bilirubin levels were observed. No fulminant hepatitis was observed, and no concomitant liver cirrhosis was detected.[10] Additional information from this case series can be found using the links provided in the citation details below.[9]

It is at the discretion of the treating physician on whether to prescribe YESCARTA in patients with active or a prior history of hepatitis C infection.

References

1. YESCARTA® (axicabtagene ciloleucel) [US Prescribing Information]. Santa Monica, CA: Kite Pharma, Inc. 2024
2. Locke FL, Neelapu SS, Bartlett NL, et al. Primary Results from ZUMA-1: A Pivotal Trial of Axicabtagene Ciloleucel (Axi- cel; KTE-C19) in Patients With Refractory Aggressive Non-Hodgkin Lymphoma (NHL). Presented at: American Association of Cancer Research Annual Meeting. April 1-5, 2017; Washington, DC; Abstract CT019.
3. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. *N Engl J Med*. 2017;377(26):2531-2544. DOI: 10.1056/NEJMoa1707447
4. [Redacted Protocol]. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. *N Engl J Med*. 2017. DOI: 10.1056/NEJMoa1707447
5. 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
6. [Supplementary Appendix] 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
7. Locke FL, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma. N Engl J Med. 2022;386(7):640-654. DOI: 10.1056/NEJMoa2116133
8. [Supplementary Appendix] Locke FL, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma. N Engl J Med. 2022;386(7):640-654. DOI: 10.1056/NEJMoa2116133
9. Strati P, Nastoupil LJ, Fayad LE, Samaniego F, Adkins S, Neelapu SS. Safety of CAR T-Cell Therapy in Patients with B-Cell Lymphoma and Chronic Hepatitis B or C Virus Infection. *Blood*. 2019;133(26):2800-2802. DOI: 10.1182/blood.2019000888

Abbreviations

ALT=alanine aminotransferase
CAR=chimeric antigen receptor
CR=complete response
CRES= CAR-related encephalopathy syndrome
CRS=cytokine release syndrome
DLBCL=diffuse large B-cell lymphoma
FL=follicular lymphoma
HBsAg=hepatitis B surface antigen
HBV=hepatitis B virus
HCV=hepatitis C virus
HIV=human immunodeficiency virus
IDSA=Infectious Disease Society of America
iNHL=indolent Non-Hodgkin Lymphoma
LBCL= large B-cell lymphoma
MZL=marginal zone lymphoma
PCR=polymerase chain reaction
PET-CT= Positron emission tomography-computed tomography
PMBCL=primary mediastinal B-cell lymphoma
r/r=relapsed/refractory
TFL=transformed follicular 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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