Yescarta® (axicabtagene ciloleucel [axi-cel]) Use in Patients with Human Immunodeficiency Virus (HIV)

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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]

According to the YESCARTA US Prescribing Information (USPI), there are no contraindications to YESCARTA.[1]

Perform screening for Hepatitis B virus (HBV), Hepatitis C virus (HCV), and Human Immunodeficiency Virus (HIV) and management in accordance with clinical guidelines before collection of cells for manufacturing.[1]

Available Data

Kite Clinical Trial Data: ZUMA-1, ZUMA-5, and ZUMA-7 Studies

ZUMA-1 is 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, or transformed follicular lymphoma (FL).[2]

ZUMA-5 is a multicenter, single arm, phase 2 study to evaluate the safety and efficacy of Yescarta in patients with relapsed/refractory indolent non-Hodgkin lymphoma (iNHL), including FL (Grades 1-3a) and marginal zone lymphoma (MZL, nodal or extranodal).[3]

ZUMA-7 is a multicenter, open-label, randomized, phase 3 study to assess the safety and efficacy of Yescarta versus standard care as second-line treatment in patients with early relapsed (≤ 12 months from first-line treatment) or refractory large B-cell lymphoma (LBCL).[4]

In the ZUMA-1, ZUMA-5, and ZUMA-7 studies, patients with a known history of HIV infection were ineligible for inclusion.[5-7] There are no clinical trial data available on the use of Yescarta in patients with HIV infection.

Real World Evidence

A literature search identified a registry study and several case reports discussing the use of Yescarta in a limited number of patients with HIV-associated non-Hodgkin lymphoma (NHL), including LBCL and FL.

In a collaboration between the AIDS Malignancy Consortium (AMS) and the Center for International Blood and Marrow Transplant Research (CIBMTR), Barta et al. describes patient and treatment characteristics and outcomes for patients with HIV treated with CD19-directed CAR T cells.[8] The interim analysis (data cutoff: 07/11/2022) includes data from 21 patients across 13 centers, with 95% (n=20) who received axi-cel and 5% (n=1) who received brexucabtagene autoleucel. All patients had NHL (n=1 follicular lymphoma, n=1 mantle cell lymphoma, n=19 large B cell lymphoma). The median pre-CAR-T CD4 count was 228 cells/mm^3 (range 0-252). The HIV viral load pre-CAR-T was available for 10 patients, with 8 patients having a viral load of <100 copies/mL (median 21 copies/mL, range 0-$10x10^6$). Cytokine release syndrome (CRS) occurred in 9 (69%) patients and immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in 3 patients (23%), with 2 experiencing Grade 3 ICANS and 1 experiencing Grade 4 ICANS. All cases of CRS and ICANS resolved after a median of 4 (1-13) days and 5 (4-8) days, respectively. With a median follow-up of 6 months, overall survival at 3 and 6 months was 83% (95% CI, 58-98) and 64% (95% CI, 35-89), respectively. Of the 4 patients who died, 3 died of disease progression, and 1 of a bacterial infection 6 months after CAR T cell infusion.

Yuen et al. describes the outcomes of a bi-institutional retrospective study of 14 patients with DLBCL and secondary CNS involvement, three of which had underlying controlled HIV with non-Epstein-Barr virus (EBV) and were treated with axi-cel.[9] Additionally, two of the three patients with HIV had active CNS disease. After a median follow-up of 5.9 months, an objective response was not achieved for patients with HIV, and severe neurotoxicity occurred in one of the three patients. All three patients with HIV-DLBCL died from disease progression, with deaths on Day 32, Day 94, and Day 157 following axi-cel infusion.

A retrospective analysis conducted by Abbasi et al. describes outcomes of ten patients with DLBCL that underwent Yescarta therapy.[10] Within this cohort, one patient had HIV and was on anti-retroviral therapy with an undetectable HIV viral load and a CD4 count of 127 cells/µL prior to Yescarta infusion. This patient achieved a complete response at 3 months, as assessed by PET/CT. According to the authors, the patient with HIV infection did not have significant toxicities.

Abramson et al. describes the outcomes of two patients on anti-retroviral therapy with HIV-associated DLBCL treated with Yescarta.[11] Prior to Yescarta infusion, the first patient had a detectable HIV viral load of 67 copies/mL and a CD4 count of 52 cells/mm^3, and the second patient had an undetectable HIV viral load and a CD4 count of 127 cells/mm^3. Both patients received dose-reduced lymphodepleting chemotherapy in the context of HIV and baseline cytopenias, and both patients achieved complete remission. The first patient developed Grade 2 CRS and Grade 3 neurologic toxicity, and the second patient had no CRS or neurologic toxicity.

Allred et al. describes the outcomes of one patient with HIV-associated DLBCL treated with Yescarta.[12] Prior to Yescarta infusion, the patient was on anti-retroviral therapy with an undetectable HIV viral load and a CD4 count of 170 cells/µL. At one month, the patient achieved a partial remission; the total metabolic tumor volume was 26.3 cm^3 after CAR-T compared to 129.7 cm^3 prior to CAR-T. Repeat surveillance PET/CT at 2 months post-infusion demonstrated evidence of disease progression in the right leg and numerous

subcutaneous, cutaneous and intramuscular lesions. The patient also developed Grade 1 CRS and Grade 2 ICANS post-infusion.

Of note, the AMS in collaboration with the National Cancer Institute and Memorial Sloan Kettering Cancer Center, is conducting a phase 1 trial to demonstrate the safety and feasibility of axicabtagene ciloleucel for relapsed/refractory HIV-associated aggressive B-cell non-Hodgkin lymphoma in participants with well-controlled HIV.[13] For more information on this clinical trial (NCT05077527), please access the following ClinicalTrials.gov hyperlink: https://clinicaltrials.gov/ct2/show/NCT05077527.

It is at the discretion of the treating physician on whether to prescribe Yescarta in patients with a known history of HIV.

References

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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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