FOR ADULTS WITH RELAPSED/REFRACTORY (R/R)
FOLLICULAR LYMPHOMA (FL) AFTER ≥2 LINES OF SYSTEMIC THERAPY[1]

A close look at a potential YESCARTA® patient with FL

While information below is not from an actual patient and does not encompass all characteristics for YESCARTA eligibility, this profile is one example of the range of patients who may be candidates for YESCARTA.

Relapsed stage IIIA FL

AGE: 67 years

MEDICAL HISTORY:

- Relapsed FL
- ECOG PS of 0; Ann Arbor stage IIIA; high-risk FLIPI
- High tumor burden based on GELF criteria
  - Normal function of heart, lungs, liver, and kidneys

TWO PRIOR THERAPIES:

- R-bendamustine: Relapsed following 1 year, 11 months in CR
- O-CHOP: Relapsed following 4 months in CR

Is your patient's disease progressing quickly (≤24 months of remission)?
How high is their tumor burden or FLIPI score? Identify high-risk patients for YESCARTA.

CR=complete remission; ECOG PS=Eastern Cooperative Oncology Group performance status; FLIPI=Follicular Lymphoma International Prognostic Index; GELF=Groupe d'Etude des Lymphomes Folliculaires; O-CHOP=obinutuzumab, cyclophosphamide, doxorubicin, prednisolone, vincristine; R=rituximab.

INDICATION

YESCARTA® is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (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).

IMPORTANT SAFETY INFORMATION

BOXED WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITIES

- **Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving YESCARTA. Do not administer YESCARTA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.**
- **Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving YESCARTA, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with YESCARTA. Provide supportive care and/or corticosteroids as needed.**
- **YESCARTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA and TECARTUS REMS Program.**

Please see additional Important Safety Information throughout and full Prescribing Information, including BOXED WARNING and Medication Guide.

YESCARTA®
(axicabtagene ciloleucel) Suspension for IV infusion

IMPORTANT SAFETY INFORMATION

CYTOKINE RELEASE SYNDROME (CRS)

CRS, including fatal or life-threatening reactions, occurred. CRS occurred in 90% (379/422) of patients with non-Hodgkin lymphoma (NHL), including ≥ Grade 3 in 9%. CRS occurred in 93% (256/276) of patients with large B-cell lymphoma (LBCL), including ≥ Grade 3 in 9%. Among patients with LBCL who died after receiving YESCARTA, 4 had ongoing CRS events at the time of death. For patients with LBCL in ZUMA-1, the median time to onset of CRS was 2 days following infusion (range: 1-12 days) and the median duration was 7 days (range: 2-58 days). For patients with LBCL in ZUMA-7, the median time to onset of CRS was 3 days following infusion (range: 1-10 days) and the median duration was 7 days (range: 2-43 days). CRS occurred in 84% (123/146) of patients with indolent non-Hodgkin lymphoma (iNHL) in ZUMA-5, including ≥ Grade 3 in 8%. Among patients with iNHL who died after receiving YESCARTA, 1 patient had an ongoing CRS event at the time of death. The median time to onset of CRS was 4 days (range: 1-20 days) and median duration was 6 days (range: 1-27 days) for patients with iNHL.

Key manifestations of CRS (≥ 10%) in all patients combined included fever (85%), hypotension (40%), tachycardia (32%), chills (22%), hypoxia (20%), headache (15%), and fatigue (12%). Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), renal insufficiency, cardiac failure, respiratory failure, cardiac arrest, capillary leak syndrome, multi-organ failure, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome.

The impact of tocilizumab and/or corticosteroids on the incidence and severity of CRS was assessed in 2 subsequent cohorts of LBCL patients in ZUMA-1. Among patients who received tocilizumab and/or corticosteroids for ongoing Grade 1 events, CRS occurred in 93% (38/41), including 2% (1/41) with Grade 3 CRS; no patients experienced a Grade 4 or 5 event. The median time to onset of CRS was 2 days (range: 1-8 days) and the median duration of CRS was 7 days (range: 2-16 days). Prophylactic treatment with corticosteroids was administered to a cohort of 39 patients for 3 days beginning on the day of infusion of YESCARTA. Thirty-one of the 39 patients (79%) developed CRS and were managed with tocilizumab and/or therapeutic doses of corticosteroids with no patients developing ≥ Grade 3 CRS. The median time to onset of CRS was 5 days (range: 1-15 days) and the median duration of CRS was 4 days (range: 1-10 days). Although there is no known mechanistic explanation, consider the risk and benefits of prophylactic corticosteroids in the context of pre-existing comorbidities for the individual patient and the potential for the risk of Grade 4 and prolonged neurologic toxicities.

Ensure that 2 doses of tocilizumab are available prior to YESCARTA infusion. Monitor patients for signs and symptoms of CRS at least daily for 7 days at the certified healthcare facility, and for 4 weeks thereafter. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time. At the first sign of CRS, institute treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids as indicated.

NEUROLOGIC TOXICITIES

Neurologic toxicities (including immune effector cell-associated neurotoxicity syndrome) that were fatal or life-threatening occurred. Neurologic toxicities occurred in 78% (330/422) of patients with NHL receiving YESCARTA, including ≥ Grade 3 in 25%. Neurologic toxicities occurred in 87% (94/108) of patients with LBCL in ZUMA-1, including ≥ Grade 3 in 31% and in 74% (124/168) of patients in ZUMA-7 including ≥ Grade 3 in 25%. The median time to onset was 4 days (range: 1-43 days) and the median duration was 17 days for patients with LBCL in ZUMA-1. The median time to onset for neurologic toxicity was 5 days (range: 1-133 days) and median duration was 15 days in patients with LBCL in ZUMA-7. Neurologic toxicities occurred in 77% (112/146) of patients with iNHL, including ≥ Grade 3 in 21%. The median time to onset was 6 days (range: 1-79 days) and the median duration was 16 days. Ninety-eight percent of all neurologic toxicities in patients with LBCL and 99% of all neurologic toxicities in patients with iNHL occurred within the first 8 weeks of YESCARTA infusion. Neurologic toxicities occurred within the first 7 days of infusion for 87% of affected patients with LBCL and 74% of affected patients with iNHL.

The most common neurologic toxicities (≥ 10%) in all patients combined included encephalopathy (50%), headache (43%), tremor (29%), dizziness (21%), aphasia (17%), delirium (15%), and insomnia (10%). Prolonged encephalopathy lasting up to 173 days was noted. Serious events, including aphasia, leukoencephalopathy, dysarthria, lethargy, and seizures occurred. Fatal and serious cases of cerebral edema and encephalopathy, including late-onset encephalopathy, have occurred.

The impact of tocilizumab and/or corticosteroids on the incidence and severity of neurologic toxicities was assessed in 2 subsequent cohorts of LBCL patients in ZUMA-1. Among patients who received corticosteroids at the onset of Grade 1 toxicities, neurologic toxicities occurred in 78% (32/41) and 20% (8/41) had Grade 3 neurologic toxicities; no patients experienced a Grade 4 or 5 event. The median time to onset of neurologic toxicities was 6 days (range: 1-93 days) with a median duration of 8 days (range: 1-144 days). Prophylactic treatment with corticosteroids was administered to a cohort of 39 patients for 3 days beginning on the day of infusion of YESCARTA. Of those patients, 85% (33/39) developed neurologic toxicities; 8% (3/39) developed Grade 3, and 5% (2/39) developed Grade 4 neurologic toxicities. The median time to onset of neurologic toxicities was 6 days (range: 1-274 days) with a median duration of 12 days (range: 1-107 days). Prophylactic corticosteroids for management of CRS and neurologic toxicities may result in higher grade of neurologic toxicities or prolongation of neurologic toxicities, delay the onset and decrease the duration of CRS.

Monitor patients for signs and symptoms of neurologic toxicities at least daily for 7 days at the certified healthcare facility, and for 4 weeks thereafter, and treat promptly.

IMPORTANT SAFETY INFORMATION

REMS

Because of the risk of CRS and neurologic toxicities, YESCARTA is available only through a restricted program called the YESCARTA and TECARTUS REMS Program which requires that: Healthcare facilities that dispense and administer YESCARTA must be enrolled and comply with the REMS requirements and must have on-site, immediate access to a minimum of 2 doses of tocilizumab for each patient for infusion within 2 hours after YESCARTA infusion, if needed for treatment of CRS. Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer YESCARTA are trained about the management of CRS and neurologic toxicities. Further information is available at www.YescartaTecartusREMS.com or 1-844-454-KITE (5483).

HYPERSENSITIVITY REACTIONS

Allergic reactions, including serious hypersensitivity reactions or anaphylaxis, may occur with the infusion of YESCARTA.

SERIOUS INFECTIONS

Severe or life-threatening infections occurred. Infections (all grades) occurred in 45% of patients with NHL. ≥ Grade 3 infections occurred in 17% of patients, including ≥ Grade 3 infections with an unspecified pathogen in 12%, bacterial infections in 5%, viral infections in 3%, and fungal infections in 1%. YESCARTA should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after infusion and treat appropriately. Administer prophylactic antimicrobials according to local guidelines.

Febrile neutropenia was observed in 36% of patients with NHL and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated.

In immunosuppressed patients, including those who have received YESCARTA, life-threatening and fatal opportunistic infections including disseminated fungal infections (e.g., candida sepsis and aspergillus infections) and viral reactivation (e.g., human herpes virus-6 [HHV-6] encephalitis and JC virus progressive multifocal leukoencephalopathy [PML]) have been reported. The possibility of HHV-6 encephalitis and PML should be considered in immunosuppressed patients with neurologic events and appropriate diagnostic evaluations should be performed.

Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, has occurred in patients treated with drugs directed against B cells, including YESCARTA. Perform screening for HBV, HCV, and HIV and management in accordance with clinical guidelines before collection of cells for manufacturing.

PROLONGED CYTOPENIAS

Patients may exhibit cytopenias for several weeks following lymphodepleting chemotherapy and YESCARTA infusion. ≥ Grade 3 cytopenias not resolved by Day 30 following YESCARTA infusion occurred in 39% of all patients with NHL and included neutropenia (33%), thrombocytopenia (13%), and anemia (8%). Monitor blood counts after infusion.

HYPOGAMMAGLOBULINEMIA

B-cell aplasia and hypogammaglobulinemia can occur. Hypogammaglobulinemia was reported as an adverse reaction in 14% of all patients with NHL. Monitor immunoglobulin levels after treatment and manage using infection precautions, antibiotic prophylaxis, and immunoglobulin replacement. The safety of immunization with live viral vaccines during or following YESCARTA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during YESCARTA treatment, and until immune recovery following treatment.

SECONDARY MALIGNANCIES

Secondary malignancies may develop. Monitor life-long for secondary malignancies. In the event that one occurs, contact Kite at 1-844-454-KITE (5483) to obtain instructions on patient samples to collect for testing.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Due to the potential for neurologic events, including altered mental status or seizures, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks following YESCARTA infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

Please see additional Important Safety Information throughout.

References: 1. YESCARTA® (axicabtagene ciloleucel). Prescribing information. Kite Pharma, Inc; 2022. **2.** Data on file [1]. Kite Pharma, Inc; 2022. **3.** Data on file [2]. Kite Pharma, Inc; 2022. **4.** Data on file [3]. Kite Pharma, Inc; 2022. **5.** Neelapu SS, Chavez JC, Sehgal AR, et al. Long-term follow-up analysis of ZUMA-5: a phase 2 study of axicabtagene ciloleucel (axi-cel) in patients with relapsed/refractory indolent non-Hodgkin lymphoma. Presented at: 63rd ASH Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. Abstract 93. **6.** 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 (suppl). doi:10.1016/S1470-2045(21)00591-X **7.** Data on file [4]. Kite Pharma, Inc; 2022. **8.** Data on file. Kite Pharma, Inc; 2020.

YESCARTA®
(axicabtagene ciloleucel) Suspension for IV infusion

Choose YESCARTA® for patients with R/R FL

YESCARTA is a CAR T therapy given as a single infusion[1]

FOR ADULTS WITH:

- R/R FL
- After ≥2 lines of systemic therapy

Primary efficacy analysis (n=81)[1]*

91% ORR
60% CR†

~36-month follow-up (N=127)[2-4‡]

38.6 months median DOR
(number of responders=119; 95% CI, 29.0-NE)[§]
Median follow-up of 34.9 months

76% OS rate at 36 months
(95% CI, 66.9-82.2)
mOS was NE
Median follow-up of 41.6 months

DOR and OS data are descriptive and should be carefully interpreted in light of the single-arm design. OS data are not included in the YESCARTA PI.

ZUMA-5 was a phase 2, single-arm, open-label, multicenter trial evaluating the efficacy and safety of a single infusion of YESCARTA in adult patients with R/R FL who had received ≥2 prior lines of therapy, including a combination of anti-CD20 monoclonal antibody and alkylating agent. In total, 146 patients were treated with YESCARTA and included in the safety analysis. The primary efficacy endpoint was ORR; select secondary endpoints included DOR, PFS, OS, and safety.[1,5]
DOR and OS were secondary endpoints in the phase 2, single-arm, open-label ZUMA-5 study. The primary efficacy analysis included in the YESCARTA PI was performed using the inferential analysis set, which includes the first 81 of 120 patients enrolled with at least 9 months of follow-up from the date of first response. The ~36-month follow-up data were evaluated using the full analysis set of ZUMA-5, which includes 127 patients with FL enrolled in the trial. Three of these patients did not receive YESCARTA. ORR (CR + PR) at 36 months was 94% (119/127). In the PI, mDOR (n=74) was not estimable at a 14.5-month median follow-up for DOR. The rate of continued remission at 18 months was 74%. ~36-month data and investigator-assessed data are not in the PI and should be carefully interpreted in light of the single-arm design.[1,2,5-7]

DOR is measured from the date of first objective response to the date of progression or death from any cause.[1]
OS is defined as the time from the date of leukapheresis to the date of death from any cause.[4]

*Per the International Working Group Lugano classification (Cheson 2014), as assessed by the independent review committee.[1]
†CR required documentation of a negative bone marrow biopsy after treatment in patients who did not have a negative bone marrow biopsy between their most recent disease progression prior to ZUMA-5 and initiation of lymphodepleting chemotherapy.[1]
‡KM estimate.[3,4]
§Per the International Working Group Lugano classification (Cheson 2014), as assessed by the investigator.[3]

Well-characterized safety

- **Most CRS and neurologic toxicities in ZUMA-5 occurred early, were generally reversible, and were managed per established guidance[1,8]**
- **CRS—Grade ≥3 incidence: 8%; overall incidence: 84%; median time to onset: 4 days (range: 1 to 20 days); median duration: 6 days (range: 1 to 27 days)[1]**
- **Neurologic toxicities—Grade ≥3 incidence: 21%; overall incidence: 77%; occurrence within first 7 days of infusion: 74%; median time to onset: 6 days (range: 1 to 79 days); median duration: 16 days[1]**

Find a treatment center to consult with a specialist: yescartahcp.com/centers

CAR T=chimeric antigen receptor T cell; CD20=cluster of differentiation 20; CI=confidence interval; CR=complete remission; CRS=cytokine release syndrome; DOR=duration of response; FL=follicular lymphoma; KM=Kaplan-Meier; mDOR=median duration of response; mOS=median overall survival; NE=not estimable; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; PI=Prescribing Information; PR=partial remission; R/R=relapsed/refractory.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS
The most common non-laboratory adverse reactions (incidence ≥ 20%) in patients with iNHL in ZUMA-5 included fever, CRS, hypotension, encephalopathy, fatigue, headache, infections with pathogen unspecified, tachycardia, febrile neutropenia, musculoskeletal pain, nausea, tremor, chills, diarrhea, constipation, decreased appetite, cough, vomiting, hypoxia, arrhythmia, and dizziness.

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