For adults with relapsed/refractory (r/r) follicular lymphoma (FL) after ≥2 lines of systemic therapy

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 score 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.**

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.

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.

YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion

IMPORTANT SAFETY INFORMATION (continued)

CYTOKINE RELEASE SYNDROME (CRS), including fatal or life-threatening reactions, occurred. CRS occurred in 88% (224/254) of all patients with non-Hodgkin lymphoma (NHL), including Grade ≥3 in 10%. CRS occurred in 94% (101/108) of patients with large B-cell lymphoma (LBCL), including Grade ≥3 in 13%. Among patients with LBCL who died after receiving YESCARTA®, 4 had ongoing CRS events at the time of death. The median time to onset of CRS was 2 days (range: 1-12 days) and the median duration was 7 days (range: 2-58 days) for patients with LBCL. CRS occurred in 84% (123/146) of patients with indolent non-Hodgkin lymphoma (iNHL), including Grade ≥3 in 8% (11/146). 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 (80%), hypotension (38%), tachycardia (29%), hypoxia (21%), chills (21%), and headache (13%). Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, multi-organ failure and hemophagocytic lymphohistiocytosis/macrophage activation syndrome. In a subsequent cohort of LBCL patients, tocilizumab and/or corticosteroids were administered for ongoing Grade 1 events. CRS occurred in 93% (38/41) of these patients and 2% (1/41) had Grade 3 CRS, with no patients experiencing a Grade 4 or 5 event. The median time to onset of CRS was 2 days (range: 1 to 8 days) and the median duration of CRS was 7 days (range: 2 to 16 days). Key manifestations of CRS (>5%) included pyrexia, hypotension, chills, headache, nausea, tachycardia, C-reactive protein increased, fatigue, hypoxia, and vomiting. Ensure that 2 doses of tocilizumab are available prior to YESCARTA infusion. Following 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 that were fatal or life-threatening occurred. Neurologic toxicities occurred in 81% (206/254) of all patients with NHL receiving YESCARTA, including Grade ≥3 in 26%. Neurologic toxicities occurred in 87% (94/108) of patients with LBCL, including Grade ≥3 in 31%. The median time to onset was 4 days (range: 1-43 days) and the median duration was 17 days for patients with LBCL. 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 for patients with iNHL. 98% 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 89% of affected patients with LBCL and 74% of affected patients with iNHL. The most common neurologic toxicities (≥10%) in all patients combined included encephalopathy (53%), headache (45%), tremor (31%), dizziness (20%), delirium (16%), aphasia (15%), and insomnia (11%). Prolonged encephalopathy lasting up to 173 days was noted. Serious events, including leukoencephalopathy and seizures, as well as fatal and serious cases of cerebral edema, have occurred. In a subsequent cohort of LBCL patients who received corticosteroids at the onset of Grade 1 toxicities, neurologic toxicities occurred in 78% (32/41) of these patients and 20% (8/41) had Grade 3 neurologic toxicities with no patients experiencing 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). The most common neurologic toxicities were consistent with the overall LBCL population treated with YESCARTA. Following YESCARTA infusion, 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.

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 47% (119/254) of all patients with NHL. Grade ≥3 infections occurred in 19% of patients, Grade ≥3 infections with an unspecified pathogen occurred in 15%, bacterial infections in 5%, viral infections in 2%, 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 anti-microbials according to local guidelines. Febrile neutropenia was observed in 40% of all 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, can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV 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 30% of all patients with NHL and included neutropenia (22%), thrombocytopenia (13%), and anemia (5%). Monitor blood counts after infusion.

HYPOGAMMAGLOBULINEMIA and B-cell aplasia can occur. Hypogammaglobulinemia occurred in 17% 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 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; 2021. **2.** Ghione P, Patel A, Bobillo S, et al. A comparison of updated clinical outcomes from ZUMA-5 (axicabtagene ciloleucel) and the international SCHOLAR-5 external control cohort in relapsed/refractory follicular lymphoma (r/r FL). Abstract presented at: 2021 European Hematology Association Virtual Congress; June 12, 2021. **3.** A phase 2 multicenter study of axicabtagene ciloleucel in subjects with relapsed/refractory indolent non-Hodgkin lymphoma (ZUMA-5). Clinicaltrials.gov. Published April 7, 2017. Updated June 3, 2021. Accessed July 21, 2021. https://clinicaltrials.gov/ct2/show/NCT03105336. **4.** 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

FOR ADULTS WITH: ✓ R/R FL ✓ AFTER ≥2 LINES OF SYSTEMIC THERAPY

IMPRESSIVE REMISSION RATES AND DOR[1]

91% ORR*

60% CR†

Median DOR not estimable (n=74); 14.5-month median follow-up for DOR

Continued remission at 18 months **74%**

18-MONTH PFS[2]

A post hoc analysis evaluated PFS (n=86); mPFS not reached at 23.3-month median follow-up

69% PFS at 18 months

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

WELL-CHARACTERIZED SAFETY

- Most CRS and neurologic events in ZUMA-5 occurred early, were generally reversible, and were managed per established guidance[1,4]
- **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]

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 and alkylating agent. In total, 146 patients were treated with YESCARTA and included in the safety analysis; 81 patients with FL were evaluable for efficacy. Primary efficacy endpoint was ORR; select secondary endpoints included DOR, PFS, and safety.[1,3]

18-month data based on a post hoc analysis follow-up of 86 ≥3L patients from the ZUMA-5 study. Variables were balanced for patient characteristics and were successfully matched through propensity scoring (SMD<0.1); this included POD24, number of prior LOT, relapsed vs refractory, prior stem cell transplant, size of largest node, response to prior LOT, time since last therapy, and age.[2]

*Per the International Working Group Lugano Classification (Cheson 2014), as assessed by the independent review committee.

†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.

FOR A CHANCE AT A **COMPLETELY MEANINGFUL RESPONSE**, FIND A TREATMENT CENTER AT: yescartahcp.com/centers

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS: The most common non-laboratory adverse reactions (incidence ≥20%) in patients with iNHL 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.

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

3L=third line; CAR T=chimeric antigen receptor T cell; CRS=cytokine release syndrome; DOR=duration of response; LOT=lines of therapy; mPFS=median progression-free survival; ORR=objective response rate; PFS=progression-free survival; PI=Prescribing Information; POD24=progression of disease within 2 years; SMD=standardized mean difference.

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