CAR T therapy for adult patients with relapsed/refractory large B-cell lymphoma after ≥2 lines of systemic therapy:

YES, a range of patients with r/r LBCL may be eligible 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 large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitation of Use: Yescarta® is not indicated for the treatment of patients with primary central nervous system lymphoma.

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® REMS.

Please see additional Important Safety Information inside.
TIME IS OF THE ESSENCE—KNOW WHEN TO CONSIDER YESCARTA® CAR T THERAPY

CHEMO-REFRACTORY

Refractory stage II E DLBCL
**AGE:** 50 years
**MEDICAL HISTORY:**
- Extramedullary disease present (localized)
- Activated B-cell-like subtype
- Refractory to front-line therapy with 6 cycles of R-CHOP and second-line DHAP
- ECOG score 1

PATIENT IS READY FOR SOMETHING DIFFERENT THAN CHEMOTHERAPY

CHEMO-NONRESPONSIVE (TRANSPLANT INTENDED)

Stage III DLBCL, unable to transplant due to inadequate response to second-line therapy
**AGE:** 58 years
**MEDICAL HISTORY:**
- Progressed after achieving complete response with R-CHOP
- Underwent induction chemotherapy (R-ICE) to prepare for transplant, but did not respond
- ECOG score 1

PATIENT HAS A STRONG WILLINGNESS TO TREAT AGGRESSIVELY

IMPORTANT SAFETY INFORMATION (continued)

**CYTOKINE RELEASE SYNDROME** (CRS) occurred in 94% of patients, with 13% ≥ Grade 3. Among patients who died after receiving YESCARTA, 4 had ongoing CRS at death. The median time to onset was 2 days (range: 1-12 days) and median duration was 7 days (range: 2-58 days). Key manifestations include fever (78%), hypotension (41%), tachycardia (28%), hypoxia (22%), and chills (20%). 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, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome. 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.

**SAFETY PROFILE**
- **CRS:** Grade ≥3 incidence, 13%; overall incidence, 94%
- **Neurologic toxicities:** Grade ≥3 incidence, 31%; overall incidence, 87%
- At the 2-year follow-up, no new serious adverse events, and no new onset of CRS or neurological events, have been reported related to YESCARTA.

*ZUMA-1 was a phase 2, open-label, single-arm, multicenter pivotal trial in 101 adults with r/r LBCL. For FDA approval, efficacy was established on the basis of complete remission rate and DOR, as determined by an independent review committee.*

**IMPORTANT SAFETY INFORMATION (continued)**

**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 28% of patients and included thrombocytopenia (18%), neutropenia (19%), and anemia (13%). Monitor blood counts after infusion.

**HYPOGAMMAGLOBULINEMIA** and B-cell aplasia can occur. Hypogammaglobulinemia occurred in 15% of patients. 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.

Please see additional Important Safety Information throughout inside spread.
IMPORTANT SAFETY INFORMATION (continued)

CYTOKINE RELEASE SYNDROME
CRS occurred in 6% of patients, with 11% in 2-Grade 3. Among patients who died after receiving YESCARTA, 4 died owing to CRS or death. The median time to onset was 2.8 days (range: 1-10 days) and median duration was 7 days (range: 2-58 days). Key manifestations include fever (78%), hypotension (41%), tachycardia (28%), hypoxia (22%), and chills (39%). Serious events including leukoencephalopathy and seizures, as well as fatal encephalopathy lasting up to 173 days were noted. 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.

NEUROLOGIC TOXICITIES
Leukoencephalopathy occurred in 87% of patients, 19% of which occurred within the first 7 weeks, with a median time of onset of 4 days (range: 1–4 days) and a median duration of 17 days. Headache occurred in 44% of patients. Tremors (31%), dizziness (21%), aphasia (18%), delirium (17%), insomnia (9%), and anxiety (9%) occurred. Monitor life-long for secondary malignancies. In the event that one occurs, contact Kite at 1-844-454-KITE (5483). For additional information on neurologic toxicities visit YESCARTA.com/nci.

HYPOGAMMAGLOBULINEMIA
Hypogammaglobulinemia occurred in 15% of patients. 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.

CHEMO-INSENSITIVE (TRANSPLANT INELIGIBLE)

Stage III DLBCL
AGE: ≥ 50 years
MEDICAL HISTORY:
- Extramedullary disease
- Partial response to prior chemotherapy
- Relapsed within 3 months after first-line chemotherapy
- Progressed after second-line chemotherapy
- Relapsed following achy leukemia response
- Re-escalation with R-ICE but only achieved stable disease
- Relapsed after second-line chemotherapy

Other available options
- R-CHOP, consolidation (TRANSPLANT INTENDED)
- R-ICE
- R-DHAP
- R-ICE, consolidation (TRANSPLANT INELIGIBLE)
- R/PMBC

TIME IS OF THE ESSENCE—KNOW WHEN TO CONSIDER YESCARTA® CAR T THERAPY

When treating r/ LBCL,

HYPERSENSITIVITY REACTIONS:
- Allergic reactions, including serious hypersensitivity reactions or anaphylaxis, may occur with YESCARTA.

References:
Perform screening for HBV, HCV, and HIV in accordance with local guidelines. Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving YESCARTA.

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.

ADVERSE REACTIONS: The most common (incidence ≥ 20%) include CRS, fever, hypotension, encephalopathy, tachycardia, fatigue, headache, decreased appetite, chills, diarrhea, febrile neutropenia, infections-pathogen unspecified, nausea, hypoxia, tremor, cough, vomiting, dizziness, constipation, and cardiac arrhythmias.

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