



## Kite Announces Long-term Data From ZUMA-1 Showing Approximately Half of Refractory Large B-cell Lymphoma Patients Were Alive Three Years After Yescarta Treatment

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**-- 47 Percent of Refractory Large B-cell Lymphoma Patients in ZUMA-1 Pivotal Phase 2 Cohorts Were Alive Three Years after a Single Infusion of Yescarta --**

**-- Separate Cohort Finds Earlier Steroid Use May Reduce Risk of Severe Cytokine Release Syndrome and Neurologic Events --**

ORLANDO, Fla.--(BUSINESS WIRE)--Dec. 7, 2019-- Kite, a Gilead Company (Nasdaq: GILD), today announced new data from the ZUMA-1 trial of Yescarta® (axicabtagene ciloleuce) in adult patients with refractory large B-cell lymphoma. These results included updated overall survival data from the pivotal phase 2 study after three years following a single infusion of Yescarta, as well as an analysis from a separate safety management cohort of patients receiving early steroid intervention for cytokine release syndrome (CRS) and neurologic events. The data were presented today at the 61<sup>st</sup> American Society of Hematology (ASH) Annual Meeting & Exposition, in Orlando from December 7–10, 2019.

With a minimum follow-up of three years after a single infusion of Yescarta (median follow-up of 39.1 months), approximately half (n=47/101; 47 percent) of patients with refractory large B-cell lymphoma in ZUMA-1 pivotal phase 2 cohorts were alive, and the median overall survival (OS) was 25.8 months. These updated three-year survival data were presented as part of a ZUMA-1 analysis evaluating mechanism of secondary treatment failure following treatment with Yescarta (Abstract #203).

"With approximately half of patients with refractory large B-cell lymphoma in our registrational trial alive three years following treatment with Yescarta, we are delivering towards our goal of potentially life-saving therapy for many patients who previously faced limited treatment options and a poor prognosis prior to the introduction of CAR T therapy," said Christi Shaw, Chief Executive Officer of Kite. "These results, coupled with an analysis that suggests a reduced risk of severe CRS and neurological events with earlier use of steroids, further support our ongoing leadership in cell therapy and commitment to patient care."

Yescarta was the first CAR T cell therapy to be approved by the U.S. Food and Drug Administration (FDA) 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, and high grade B-cell lymphoma and DLBCL arising from follicular lymphoma. Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma. The Yescarta U.S. Prescribing Information has a BOXED WARNING for the risks of CRS and neurologic toxicities, and Yescarta is approved with a risk evaluation and mitigation strategy (REMS) due to these risks; see below for Important Safety Information.

Updated results from a separate ZUMA-1 safety management study (Cohort 4) were also presented at the meeting (Abstract #243). In this analysis, patients with relapsed or refractory large B-cell lymphoma treated with Yescarta received earlier steroid intervention, beginning when patients experienced Grade 1 neurologic events or experienced Grade 1 CRS with no improvement after three days of supportive care. Patients could receive optional bridging chemotherapy prior to Yescarta infusion.

In the analysis, 41 patients had received Yescarta, with a median follow-up of 8.7 months; 73 percent of patients received corticosteroids and 76 percent received tocilizumab. Earlier steroid use appeared to decrease the percentage of patients with Grade ≥3 CRS (2 percent) and neurologic events (17 percent), each of which were numerically lower than rates in the registrational cohorts of ZUMA-1 (13 percent CRS, 31 percent neurologic events). There were no Grade 4 or 5 CRS or neurologic events and no Grade 5 AEs related to Yescarta in Cohort 4.

Objective response rate per investigator assessment was 73 percent in Cohort 4, with 51 percent of patients achieving a complete response. The median duration of response was 8.9 months. Fifty-four percent of patients in this cohort remained in an ongoing response with at least six months of follow-up after Yescarta infusion. Median OS in Cohort 4 has not been reached.

"Results from ZUMA-1 Cohort 4 demonstrate that early steroid intervention has the potential to reduce the rate of severe CRS and neurologic events while appearing to maintain comparably impressive efficacy for Yescarta to the pivotal ZUMA-1 study cohorts," said Max S. Topp, MD, ZUMA-1 Cohort 4 investigator and Professor and Head of Hematology, University Hospital of Wuerzburg, Germany. "Data from this cohort suggest this approach with earlier steroid use may further improve the benefit/risk profile of this CAR T therapy."

### U.S. Important Safety Information for Yescarta

#### 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.**

**CYTOKINE RELEASE SYNDROME (CRS):** CRS occurred in 94% of patients, including 13% with ≥ 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 infusion of Yescarta<sup>®</sup>. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for 4 weeks after infusion. 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 occurred in 87% of patients. Ninety-eight percent of all neurologic toxicities occurred within the first 8 weeks, with a median time to onset of 4 days (range: 1-43 days) and a median duration of 17 days. Grade 3 or higher occurred in 31% of patients. The most common neurologic toxicities included encephalopathy (57%), headache (44%), tremor (31%), dizziness (21%), aphasia (18%), delirium (17%), insomnia (9%) and anxiety (9%). Prolonged encephalopathy lasting up to 173 days was noted. Serious events including leukoencephalopathy and seizures occurred with Yescarta<sup>®</sup>. Fatal and serious cases of cerebral edema have occurred in patients treated with Yescarta<sup>®</sup>. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of neurologic toxicities. Monitor patients for signs or symptoms of neurologic toxicities for 4 weeks after infusion and treat promptly.

**YESCARTA<sup>®</sup> REMS:** Because of the risk of CRS and neurologic toxicities, Yescarta<sup>®</sup> is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Yescarta<sup>®</sup> REMS. The required components of the Yescarta<sup>®</sup> REMS are: Healthcare facilities that dispense and administer Yescarta<sup>®</sup> must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of 2 doses of tocilizumab are available for each patient for infusion within 2 hours after Yescarta<sup>®</sup> infusion, if needed for treatment of CRS. Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense or administer Yescarta<sup>®</sup> are trained about the management of CRS and neurologic toxicities. Further information is available at [www.YESCARTAREMS.com](http://www.YESCARTAREMS.com) or 1-844-454-KITE (5483).

**HYPERSENSITIVITY REACTIONS:** Allergic reactions may occur. Serious hypersensitivity reactions including anaphylaxis may be due to dimethyl sulfoxide (DMSO) or residual gentamicin in Yescarta<sup>®</sup>.

**SERIOUS INFECTIONS:** Severe or life-threatening infections occurred. Infections (all grades) occurred in 38% of patients, and in 23% with  $\geq$  Grade 3. Grade 3 or higher infections with an unspecified pathogen occurred in 16% of patients, bacterial infections in 9%, and viral infections in 4%. Yescarta<sup>®</sup> should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after Yescarta<sup>®</sup> infusion and treat appropriately. Administer prophylactic anti-microbials according to local guidelines. Febrile neutropenia was observed in 36% of patients 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. 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<sup>®</sup> infusion. Grade 3 or higher cytopenias not resolved by Day 30 following Yescarta<sup>®</sup> infusion occurred in 28% of patients and included thrombocytopenia (18%), neutropenia (15%), and anemia (3%). Monitor blood counts after Yescarta<sup>®</sup> infusion.

**HYPOGAMMAGLOBULINEMIA:** B-cell aplasia and hypogammaglobulinemia 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<sup>®</sup> 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<sup>®</sup> treatment, and until immune recovery following treatment.

**SECONDARY MALIGNANCIES:** Patients may develop secondary malignancies. Monitor life-long for secondary malignancies. In the event that a secondary malignancy 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<sup>®</sup> 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 adverse reactions (incidence  $\geq$  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.

#### About Kite

Kite, a Gilead Company, is a biopharmaceutical company based in Santa Monica, California. Kite is engaged in the development of innovative cancer immunotherapies. The company is focused on chimeric antigen receptor and T cell receptor engineered cell therapies. For more information on Kite, please visit [www.kitepharma.com](http://www.kitepharma.com).

#### About Gilead Sciences

Gilead Sciences, Inc. is a research-based biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet medical need. The company strives to transform and simplify care for people with life-threatening illnesses around the world. Gilead has operations in more than 35 countries worldwide, with headquarters in Foster City, California. For more information on Gilead Sciences, please visit the company's website at [www.gilead.com](http://www.gilead.com).

#### Forward-Looking Statement

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the possibility of unfavorable results from other ongoing and additional clinical trials involving Yescarta. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead and Kite, and Gilead and Kite assume no obligation to update any such forward-looking statements.

U.S. Prescribing Information for Yescarta, including **BOXED WARNING**, is available at [www.kitepharma.com](http://www.kitepharma.com) and [www.gilead.com](http://www.gilead.com).

Yescarta is a registered trademark of Gilead Sciences, Inc., or its related companies.

For more information on Kite, please visit the company's website at [www.kitepharma.com](http://www.kitepharma.com) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000. Follow Kite on social media on Twitter ([@KitePharma](https://twitter.com/KitePharma)) and [LinkedIn](https://www.linkedin.com/company/kitepharma).

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