

Novartis announces longer-term analyses from pivotal Kymriah® trials that showed durable responses are maintained in patients with advanced blood cancers

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- - In the updated analysis from ELIANA, Kymriah demonstrated an 82% remission rate within 3 months in pediatric patients with r/r ALL; relapse-free survival was 62% at 24 months, with median duration of remission still not reached(1)
- - The longer follow-up from the JULIET study in patients with r/r DLBCL reported 64% relapse-free probability and a 43% probability of overall survival at 18 months, with median duration of response still not reached(2)
- - The safety profiles observed in both longer-term analyses remained consistent with previously reported results, with no emergence of new safety signals
- - ASH presentations demonstrate the Novartis commitment to understanding the long-term potential of Kymriah in transforming the treatment of ALL and DLBCL

EAST HANOVER, N.J., Dec. 1, 2018 /PRNewswire/ -- Novartis today announced longer-term analyses of both ELIANA and JULIET, the pivotal clinical trials of Kymriah (tisagenlecleucel) in children and young adult patients with relapsed or refractory (r/r) acute lymphoblastic leukemia (ALL) and adult patients with r/r diffuse large B-cell lymphoma (DLBCL), respectively. In these analyses, Kymriah continued to demonstrate strong efficacy with durable responses and maintained a consistent and well-characterized safety profile. These data are being presented at the 60th American Society of Hematology (ASH) annual meeting. Additionally, today, the New England Journal of Medicine published online the 14-month results from JULIET, the study led by the Abramson Cancer Center at the University of Pennsylvania³.

"After bringing the first CAR-T cell therapy to patients, Novartis is committed to continue our pioneering efforts to reimagine the treatment paradigm for patients with aggressive blood cancer," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "These analyses underscore the longer-term durability of response with Kymriah and its consistent safety profile, reinforcing our belief in the potential for CAR-T cell therapy to extend the lives of patients with these advanced B-cell malignancies."

In the 24-month follow-up analysis of the ELIANA study in children and young adults with r/r B-cell ALL, Kymriah demonstrated deep and durable responses without subsequent therapy in a significant portion of patients in this population. Among 79 evaluable patients, who were followed for at least three months or discontinued earlier, 82% (95% confidence interval [CI], 72% - 90%) achieved complete response (CR) or CR with incomplete blood count recovery (CRi) within three months of infusion; and among these responding patients, 98% had negative minimal residual disease (MRD-). The relapse-free survival rate was 62% at 24 months; and the median duration of remission (mDOR) and median overall survival (mOS) remained unreached, signifying responses are deep and sustained, and further reinforcing the potential for Kymriah to be a definitive therapy for many patients. The probability of OS was 76% (95% CI, 65% - 85%) at 12 months and 66% (95% CI, 58% - 79%) at 24 months. The safety profile observed in this updated analysis was consistent with previously reported results, with no emergence of new safety signals. Grade 3/4 cytokine

release syndrome (CRS) – as defined by the rigorous Penn Grading Scale – occurred in 49% of patients. Within eight weeks of infusion, 13% of patients experienced grade 3 neurological events, with no grade 4 events or cerebral edema¹. These updated data will be presented in an oral session at the ASH annual meeting (Abstract # 895; Monday, December 3, 4:30 PM PST).

"Our group has devoted a great deal of attention to advancing treatment options for children and young adults with B-cell ALL. This two-year analysis is an exciting milestone for the field, as it is the longest follow-up data for a multicenter CAR-T cell trial for those patients who have failed to respond to other treatment options," said Stephan A. Grupp, MD, PhD, Director of the Cancer Immunotherapy Program and Section Chief of Cell Therapy and Transplant at Children's Hospital of Philadelphia, and a Professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania. "Seeing that the majority of responding patients from ELIANA are still in remission for this long after a one-time infusion further establishes Kymriah as a truly transformative treatment option."

The 19-month analysis from the JULIET study of Kymriah in adult patients with r/r DLBCL showed prolonged durability of response in patients (n=99) who had previously been through multiple rounds of chemotherapy and unsuccessful stem cell transplants. The overall response rate (ORR) after a median of 19 months of follow-up was 54% (95% CI, 43% - 64%; CR, 40%; partial response [PR], 13%) among patients who were followed for at least 3 months or discontinued earlier. The mDOR was not reached at the time of analysis indicating most responders were still experiencing a response at the time of analysis; and the relapse-free probability, which was 66% (95% CI, 51%-78%) at 6 months, remained consistent at 64% (95% CI, 48%-76%) between 12-month and 18-month analyses. Further, 54% (15/28) of patients who had achieved a PR converted to CR. Median OS for all infused patients was 11.1 months (95% CI, 6.6 months-NE) and not reached (95% CI, 21 months-NE) for patients in CR. The OS probability was 48% (95% CI, 38%-57%) at 12 months and 43% (95%CI, 33%-53%) at 18 months (max follow-up, 29 months). Analyses of ORR, DOR and OS data showed consistent results across all patient subgroups, regardless of relapsed/refractory status, age and high-risk cytogenetics.

The safety profile observed in the 19-month follow-up from JULIET continued to be consistent with previous reports and no deaths occurred due to causes other than disease progression in this longer-term follow up analysis. Within eight weeks of infusion with Kymriah, Grade 3/4 CRS, as defined by the Penn Grading Scale, was reported in 23% of patients. CRS management was conducted per the Penn CRS management algorithm, which is specific to Kymriah. Tocilizumab and steroids were used in 16% and 11% of patients, respectively, to treat CRS. Eleven percent of patients had Grade 3/4 neurologic adverse events, which were managed with supportive care².

The updated JULIET data will be presented today in a poster at the ASH annual meeting (Abstract #1684; Saturday, December 1, 6:15 PM PST).

"Before CAR-T cell therapy, achieving and maintaining a prolonged complete response in adult patients with relapsed or refractory DLBCL was incredibly rare, but now we are seeing Kymriah result in durable complete responses more than a year and a half after infusion⁴," said lead author of the updated JULIET analysis, Stephen J. Schuster, MD, the Robert and Margarita Louis-Dreyfus Professor in Chronic Lymphocytic Leukemia and Lymphoma Clinical Care and Research in the University of Pennsylvania's (Penn) Perelman School of Medicine and director of the Lymphoma Program at the Abramson Cancer Center. "For physicians treating this patient population, duration of response and a consistent safety profile are incredibly important data points, and the findings from this updated analysis further instill confidence in the continuing potential of Kymriah in the treatment of these patients."

Kymriah is approved in the US, the EU, Canada and Switzerland for children and young adults with relapsed

or refractory ALL and in adult patients with relapsed or refractory DLBCL, making it the only CAR-T cell therapy approved for two distinct indications and delivering the transformative potential for durable responses for patients who relapse or don't respond to initial therapies and for whom the outlook is poor. Patients do not need to be in complete remission to receive Kymriah and no donor is required.

About the ELIANA Trial

ELIANA is the first pediatric global CAR-T cell therapy registration trial, examining patients in 25 centers in 11 countries across the US, Canada, Australia, Japan and the EU, including: Austria, Belgium, France, Germany, Italy, Norway and Spain, demonstrating effective distribution of Kymriah across four continents using a global supply chain. In 2012, Novartis and Penn entered into a global collaboration to further research, develop and commercialize CAR-T cell therapies, including Kymriah, for the investigational treatment of cancers.

About the JULIET Trial

JULIET is the first multi-center global registration study for Kymriah in adult patients with r/r DLBCL. JULIET, led by researchers at the University of Pennsylvania, is the largest and only registration study examining a CAR-T cell therapy in DLBCL, enrolling patients from 27 sites in 10 countries across the US, Canada, Australia, Japan and Europe, including Austria, France, Germany, Italy, Norway and the Netherlands.

Kymriah® (tisagenlecleucel, formerly CTL019) US Important Safety information

Kymriah may cause side effects that are severe or life-threatening, such as Cytokine Release Syndrome (CRS) or Neurological Toxicities. Patients with CRS may experience symptoms including difficulty breathing, fever (100.4°F/38°C or higher), chills/shaking chills, severe nausea, vomiting and diarrhea, severe muscle or joint pain, very low blood pressure, or dizziness/lightheadedness. Patients may be admitted to the hospital for CRS and treated with other medications.

Patients with neurological toxicities may experience symptoms such as altered or decreased consciousness, headaches, delirium, confusion, agitation, anxiety, seizures, difficulty speaking and understanding, or loss of balance. Patients should be advised to call their healthcare provider or get emergency help right away if they experience any of these signs and symptoms of CRS or neurological toxicities.

Because of the risk of CRS and neurological toxicities, Kymriah is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called Kymriah REMS.

Serious allergic reactions, including anaphylaxis, may occur after Kymriah infusion. Kymriah can increase the risk of life-threatening infections that may lead to death. Patients should be advised to tell their healthcare provider right away if they develop fever, chills, or any signs or symptoms of an infection.

Patients may experience prolonged low blood cell counts (cytopenia), where one or more types of blood cells (red blood cells, white blood cells, or platelets) are decreased. The patient's healthcare provider will do blood tests to check all of their blood cell counts after treatment with Kymriah. Patients should be advised to tell their healthcare provider right away if they get a fever, are feeling tired, or have bruising or bleeding.

Patients may experience hypogammaglobulinemia, a condition in which the level of immunoglobulins (antibodies) in the blood is low and the risk of infection is increased. It is expected that patients may develop hypogammaglobulinemia with Kymriah, and may need to receive immunoglobulin replacement for an indefinite amount of time following treatment with Kymriah. Patients should tell their healthcare provider about their treatment with Kymriah before receiving a live virus vaccine.

After treatment with Kymriah, patients will be monitored lifelong by their healthcare provider, as they may develop secondary cancers or recurrence of their cancer.

Patients should not drive, operate heavy machinery, or do other dangerous activities for eight weeks after receiving Kymriah because the treatment can cause temporary memory and coordination problems, including sleepiness, confusion, weakness, dizziness, and seizures.

Some of the most common side effects of Kymriah are difficulty breathing, fever (100.4°F/38°C or higher), chills/shaking chills, confusion, severe nausea, vomiting and diarrhea, severe muscle or joint pain, very low blood pressure, dizziness/lightheadedness, and headache. However, these are not all of the possible side effects of Kymriah. Patients should talk to their healthcare provider for medical advice about side effects.

Prior to a female patient starting treatment with Kymriah, their healthcare provider may do a pregnancy test. There is no information available for Kymriah use in pregnant or breast-feeding women. Therefore, Kymriah is not recommended for women who are pregnant or breast feeding. Patients should talk to their healthcare provider about birth control and pregnancy.

Patients should tell their healthcare provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

After receiving Kymriah, patients should be advised that some commercial HIV tests may cause a false-positive test result. Patients should also be advised not to donate blood, organs, or tissues and cells for transplantation after receiving Kymriah.

Please see the full Prescribing Information for Kymriah, including Boxed WARNING, and Medication Guide at www.Kymriah.com

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References:

- Grupp S., et al. Updated Analysis of the Efficacy and Safety of Tisagenlecleucel in Pediatric and Young Adult Patients with Relapsed/Refractory (r/r) Acute Lymphoblastic Leukemia. 60th American Society of Hematology Annual Meeting and Exposition. Abstract #112599.
- Schuster S., et al. Sustained Disease Control for Adult Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma: An Updated Analysis of Juliet, a Global Pivotal Phase 2 Trial of Tisagenlecleucel, Acute Lymphoblastic Leukemia. 60th American Society of Hematology Annual Meeting and Exposition. Abstract #11525.
- Schuster S., et al. Tisagenlecleucel in Adult Relapsed/Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. December 2018.
- Van Den Neste E., et al. Outcome of patients with relapsed diffuse large B-cell lymphoma who fail second-line salvage regimens in the International CORAL study. Bone Marrow Transplant. January 2016.

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