Novartis Kymriah® demonstrates strong responses in high-risk patients with relapsed or refractory follicular lymphoma in extended study follow-up

Dec 11, 2021

- Complete and overall response rates and durability of response were well maintained across majority of high-risk subgroups with a significant unmet need1
- Median follow-up of approximately 17 months from the ELARA study showed a 67% one-year progression-free survival (PFS) rate in patients with r/r FL; for those who had a complete response, 12-month PFS was 86%1
- Remarkable safety profile remained consistent with initial analysis; no high-grade cytokine release syndrome was reported within eight weeks post-infusion and no new safety signals were identified1

EAST HANOVER, N.J., Dec. 11, 2021 /PRNewswire/ -- Novartis announced Kymriah® (tisagenlecleucel) demonstrated strong efficacy in high-risk patients with relapsed or refractory (r/r) follicular lymphoma (FL) based on a subgroup analysis from an approximately 17-month median follow-up of the pivotal Phase II ELARA study[1]. These results were presented in an oral session at the 63rd American Society of Hematology Annual Meeting & Exposition (ASH) (Abstract #131).

In the subgroup analysis, results showed high rates of durable responses were induced by Kymriah in patients for the majority of high-risk disease subgroups, who typically have a poor prognosis. Complete response rate (CRR), overall response rate (ORR), and durability of response (DOR) were maintained in most patients in the high-risk subgroups, with the exception of those in three of the nine subgroups analyzed: those with progression-of-disease within two years (POD24), high total metabolic tumor volume (TMTV) and patients who had received five or more prior lines of therapy[1].

"It's truly exciting to see that after treatment with Kymriah in patients with difficult-to-treat, high-risk follicular lymphoma, patients are experiencing long-lasting responses with a low risk of severe adverse events," said Catherine Thieblemont, MD, PhD, Professor of Hematology in the Paris VII- University, France and Head of the Hemato-Oncology Unit of St-Louis Hospital in Paris.

High and durable responses were seen in the overall population of the ELARA study in which 94 patients were evaluable for efficacy with a median follow-up of approximately 17 months. The CRR was 69% (95% CI, 60-78), ORR was 86% (95% CI, 78-92), 12-month progression-free survival (PFS) was 67% (95% CI, 56-76) and nine-month DOR was 76% (95% CI, 65-84). For patients who had a complete response (CR), 12-month PFS was 86% (95% CI, 74-92) and the estimated DOR rate was 87% (95% CI, 75-93). In the safety analysis (n=97), the safety profile of Kymriah continued to reflect the remarkable results seen in earlier ELARA analyses. Within eight weeks of infusion, 48% of patients experienced cytokine release syndrome (CRS), with no patients experiencing CRS of grade 3 or higher as defined by the Lee scale, 37% had neurological events (3% were greater than or equal to grade 3) and there were no treatment-related deaths[1].

A separate analysis of hospitalization and intensive care unit patterns for patients treated in the inpatient and outpatient settings in the ELARA trial suggest Kymriah may reduce healthcare resource utilization for patients with r/r FL treated in the outpatient setting (Abstract #3533). Among patients treated in the outpatient setting (n=17), 35% did not require hospitalization during the first two months of the post-infusion period; those who did had a lower median average length of stay than the patients infused in an inpatient setting (4 days [n=17] vs 12 days [n=80]). Additionally, the mean hospitalization costs in the post-infusion period were substantially lower in the outpatient versus inpatient setting[2].

"The ability to administer Kymriah, a potentially definitive treatment, in the outpatient setting may reduce the burden of therapy for patients and their care teams," said Jeff Legos, Executive Vice President, Global Head of Oncology & Hematology Development, Novartis. "The breadth of follicular lymphoma data presented at this year's ASH demonstrate the potential for Kymriah to provide transformative results and a positive impact on health systems overall."

Novartis is committed to bringing the benefits of Kymriah to more patients with advanced blood cancers worldwide, with regulatory submissions for follicular lymphoma in the US and EU complete in October 2021. If approved in this indication, Novartis will look to confirm these results of the ELARA trial and related analyses in the real-world setting.

About follicular lymphoma

Follicular lymphoma (FL), the second most common form of non-Hodgkin lymphoma (NHL), is an indolent lymphoma, and represents approximately 22% of NHL cases[3,4]. It is often an unrelenting malignancy with a relapsing and remitting pattern[5,6]. Throughout the lifetime of a patient with relapsing FL, he or she may be exposed to a median of five lines of prior treatment, with an upper range of 13 lines[7,8]. Although patients in third or later line treatment for FL have multiple systemic therapies available, the efficacy of these regimens drops off rapidly in later lines[5]. Additionally, because of this relapsing and remitting pattern, patients who are refractory to treatment or relapse may exhaust available treatment options[5].

About the ELARA trial

ELARA is a Phase II, single-arm, multicenter, open-label trial investigating the efficacy and safety of Kymriah in adult patients with r/r FL after at least two prior therapies. This international trial has enrolled patients from over 30 sites in 12 countries worldwide. The primary endpoint is complete response rate (CRR) based on best response by central review (Lugano 2014 criteria). Patients evaluable for efficacy had measurable disease at infusion and more than six months of follow-up from infusion or discontinued early. After infusion, disease assessments were performed every three months. In a high-risk subgroup analysis, patients evaluated included those with prior hematopoietic stem cell transplant, double-refractory disease, high Follicular Lymphoma International Prognostic Index at study entry, high lactate dehydrogenase at baseline, high C-reactive protein prior to infusion, radiological bulky disease, progression-of-disease within two years (POD24), high total metabolic tumor volume (TMTV), and patients who had received five or more prior lines of therapy[1]. Secondary endpoints include overall response rate, duration of response, progression-free survival, overall survival and safety. Primary analysis data announced at ASCO 2021 showed Kymriah led to responses for the majority of patients treated, with 66% achieving a complete response (95% CI, 56-75). The overall response rate was 86% (95% CI, 78-92)[9]. Importantly, no patients in ELARA trial experienced grade 3 or higher cytokine release syndrome related to Kymriah within the first 8 weeks following infusion, the most common side effect associated with CAR-T therapy[9].

About Novartis commitment to Oncology Cell Therapy

Novartis has a mission to reimagine medicine by bringing curative cell therapies to patients worldwide. Novartis has a deep CAR-T pipeline and ongoing investment in manufacturing and supply chain process improvements. With active research underway to broaden the impact of cell and gene therapy in oncology, Novartis is going deeper in hematological malignancies, reaching patients with other cancer types and evaluating next-generation CAR-T cell therapies that focus on new targets and utilize new technologies.

Novartis was the first pharmaceutical company to significantly invest in pioneering CAR-T research and initiate global CAR-T trials. Kymriah, the first approved CAR-T cell therapy, developed in collaboration with the Perelman School of Medicine at the University of Pennsylvania, is the foundation of Novartis' commitment to CAR-T cell therapy.

Kymriah is currently approved for use in at least one indication in 30 countries and at more than 350 certified treatment centers, with the ambition for further expansion to help fulfill the ultimate goal of bringing CAR-T cell therapy to every patient in need.

Novartis has a global CAR-T manufacturing footprint that includes both Novartis-owned and contract manufacturing sites. This comprehensive, integrated footprint strengthens the flexibility, resilience and sustainability of the Novartis manufacturing and supply chain.

US FDA approved indications for Kymriah

Kymriah® (tisagenlecleucel) is a CD19-directed genetically modified autologous T cell immunotherapy, which is indicated for:

- The treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.
- The treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma (FL). Limitations of Use: Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

Kymriah® (tisagenlecleucel) 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 the 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 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, weak, or short of breath, 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 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 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. No information is 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, tissues, sperm, oocytes, and other cells after receiving KYMRIAH.

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

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 15,000 people in the United States. For more information, please visit https://www.novartis.us.

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