

Kymriah™ (tisagenlecleucel) in children and young adults with B-cell ALL that is refractory or relapsed at least twice

FACT SHEET

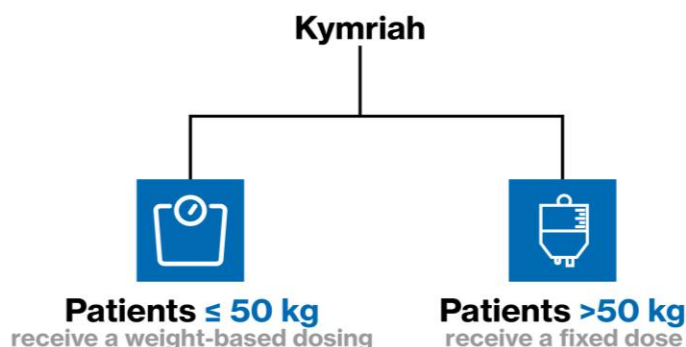
Kymriah (pronounced: Kim-RYE-ah) is the first FDA-approved CAR-T cell therapy available in the US

Product Description

Kymriah™ (tisagenlecleucel) suspension for intravenous infusion, formerly CTL019, is a CD-19 directed genetically modified autologous T cell immunotherapy 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.

Kymriah is a type of treatment called chimeric antigen receptor T cell (CAR-T) therapy, which uses the patient's own T cells to fight cancer.

Kymriah is a one-time treatment with a dose range based on patient weight.



About Kymriah

Manufacturing Kymriah involves extracting T cells from a patient's own blood through a specialized blood filtration system called leukapheresis, which is done intravenously. The T cells are then sent to the Novartis manufacturing facility and genetically reprogrammed to recognize cancer cells and other cells expressing a specific antigen. After the CAR-T cells undergo expansion and strict quality testing, they are shipped to the treatment center and infused back into the patient.

Kymriah uses the 4-1BB costimulatory domain in its chimeric antigen receptor to enhance cellular expansion and persistence.

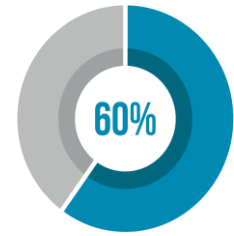
Kymriah is manufactured for each individual patient at the Novartis Morris Plains, New Jersey facility, which has manufactured CAR-T cells for more than 250 patients in global clinical trials. Novartis has a reproducible, flexible and validated manufacturing process which builds on years of global clinical trial experience.

During Kymriah manufacturing, Novartis uses a cryopreserved leukapheresis process that supports treatment of patients in clinical trials from around the world. Cryopreserved leukapheresis gives physicians the flexibility to schedule apheresis at a time that is in the best interest of their patients.

About ALL

- ALL is a cancer of the lymphocytes, a type of white blood cell of the body's immune system¹. People with ALL have an overabundance of these cells, which build up and crowd out the bone marrow, preventing it from producing normal blood-forming cells like red blood cells and platelets¹. This deficiency causes the main symptoms of ALL, which are anemia and bleeding¹.
- The ALL patient journey is long, complex and emotional, not only for patients but also their families and caregivers.
- There has been an urgent need for new treatment options for patients with relapsed or refractory B-cell ALL, whose prognosis is poor. Patients often must undergo multiple treatments, including chemotherapy, radiation, targeted therapy or stem cell transplant, yet less than 10% of patients survive five years^{3,4}.

~5,000 cases of ALL are diagnosed annually



occur in patients less than 20 years of age²

Development

In 2012, Novartis and the University of Pennsylvania (Penn) entered into a global collaboration to further research, develop and commercialize CAR-T cell therapies, including Kymriah, for the investigational treatment of cancers. Children's Hospital of Philadelphia (CHOP) was the first institution to investigate Kymriah in the treatment of pediatric patients and led a single site trial.

Novartis Commitment

Novartis is a leader in next-generation immuno-oncology (IO). Novartis is at the forefront of investigational immunocellular therapy and was the first pharma company to significantly invest in CAR-T research, work with pioneers in CAR-T and initiate global CAR-T trials. Novartis is committed to helping eligible patients have access to Kymriah.

To address the unique aspects of the therapy, Novartis has developed various patient access programs to support safe and timely access for patients. Novartis is also providing traditional support to patients by helping them navigate insurance coverage, and by providing financial assistance for those who are uninsured or underinsured.

Important Safety information

The full prescribing information, including Boxed WARNING, for Kymriah can be found at: <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/kymriah.pdf>

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 high fever, difficulty breathing, 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 health care 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 health care 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 health care provider will do blood tests to check all of their blood cell counts after treatment with Kymriah. Patients should be advised to tell their health care 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 health care provider about their treatment with Kymriah before receiving a live virus vaccine.

After treatment with Kymriah, patients will be monitored life-long by their health care provider, as they may develop secondary cancers or recurrence of their leukemia.

Patients should not drive, operate heavy machinery, or do other dangerous activities for 8 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, and dizziness/lightheadedness. However, these are not all of the possible side effects of Kymriah. Patients should talk to their health care provider for medical advice about side effects.

Prior to a female patient starting treatment with Kymriah, their health care 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. If either sex partner has received Kymriah, patients should talk to their health care provider about birth control and pregnancy.

Patients should tell their health care 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.

References:

1. National Cancer Institute, "Childhood Acute Lymphoblastic Leukemia Treatment (PDQ®) – Patient Version." https://www.cancer.gov/types/leukemia/patient/child-all-treatment-pdq#link/_1. Accessed August 4, 2017
2. National Cancer Institute. SEER Cancer Stat Facts: Acute Lymphocytic. Bethesda, MD, <http://seer.cancer.gov/statfacts/html/aly1.html>. Accessed May 2017.
3. Leukemia & Lymphoma Society, "Acute Lymphoblastic Leukemia." <https://www.lls.org/leukemia/acute-lymphoblastic-leukemia/treatment/relapsed-and-refractory>. Accessed August 4, 2017.
4. Ronson, A., Tvito, A., Rowe, JM., "Treatment of Relapsed/Refractory Acute Lymphoblastic Leukemia in Adults." *Current Oncology Reports*, 2016 Jun;18(6):39. <https://www.ncbi.nlm.nih.gov/pubmed/27207612>. Accessed August 4, 2017.

