KYMRIAH AND YESCARTA

FDA approves the first cell-based gene therapies in the United States.

Background

In 2017, the U.S. Food and Drug Administration (FDA) approved the first new cell-based gene therapies known as "CAR-T." Kymriah (tisagenlecleucel-T) and Yescarta (axicabtagene ciloleucel) were both approved to treat different forms of cancer.

What are cell-based gene therapies?

Cell-based gene therapy is a type of immunotherapy that collects and uses patients' own immune cells to treat their cancer.[1] There are different forms of cellular therapies with CAR-T being one of them. CAR-T therapy is a customized treatment that requires drawing blood from patients and separating out the T-cells (a type of white blood cell). The T-cells are genetically engineered to produce receptors on their surface called chimeric antigen receptors, or CARs. The CARs direct the T-cells to target and kill tumor cells. Once the cells are modified, they are infused back into the patient to target and kill the cancer cells.

What two CAR-T therapies were recently approved?

On August 30, 2017, Kymriah, manufactured by Novartis, was approved for the treatment of patients up to 25 years of age with acute lymphoblastic leukemia (ALL) who are not responding to treatment or in second or later relapse.[2] Following Kymriah, on October 18, 2017, Yescarta, manufactured by Kite, a Gilead Company, was approved to treat adult patients with diffuse large B-cell lymphoma (DLBCL) who have not responded to or who have relapsed after at least two other kinds of treatment.[3]

What types of cancer are Kymriah and Yescarta indicated for?

Kymriah treats acute lymphoblastic leukemia (ALL), a cancer of the bone marrow and blood, in which the body makes abnormal lymphocytes (a type of white blood cell). The disease progresses quickly and is the most common childhood cancer in the United States.[4] The National Cancer Institute estimates that approximately 3,100 patients aged 20 and younger are diagnosed with ALL each year.[5]

Kymriah is approved for use in pediatric and young adult patients with B-cell ALL, the most common form, and is intended for patients whose cancer has not responded to or has returned after initial treatment, which occurs in an estimated 15%–20% of patients.[6] In a clinical trial of 63 patients with ALL who received Kymriah, there was an overall 83% remission rate within three months of treatment.[7]

Yescarta is indicated for diffuse large B-cell lymphoma (DLBCL), the most common type of non-Hodgkin lymphoma (NHL) in adults.[3] NHLs are cancers that begin in certain cells of the immune system and can be either fast-growing (aggressive) or slow-growing. Approximately 72,000 new cases of NHL are diagnosed in the United States each year, and DLBCL represents approximately one in three newly diagnosed cases.[3]

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In a clinical trial of 100 patients with relapsed or refractory DLBCL who received Yescarta, there was an overall 51% remission rate within the first six months of treatment.[3]

How are Kymriah and Yescarta administered?

Both Kymriah and Yescarta are infused cellular therapy products (CAR-T) that are administered intravenously one time, as a single course of treatment.[1,3] The administration may occur in either an outpatient or inpatient setting. There are several steps involved in the process leading up to the administration. First, the patient's T-cells are collected through a procedure known as leukapheresis. The T-cells are sent to a facility where the cells are genetically modified and expanded. Prior to receiving Kymriah or Yescarta, a short course of chemotherapy is administered. This preparation cycle, from collecting the T-cells until the administration of Kymriah or Yescarta takes approximately 22 days.

What safety issues are associated with the use of Kymriah and Yescarta?

Treatment with either Kymriah or Yescarta has the potential to cause severe side effects.[7,8] Both drugs carry a boxed warning for two serious safety risks: 1) cytokine release syndrome, a systemic immune system response to the activation and production of CAR-T cells causing high fever and flu-like symptoms, and 2) neurological events which can be life threatening. Other severe side effects of the two CAR-T therapies include serious infections, low blood pressure (hypotension), acute kidney injury, fever and decreased oxygen (hypoxia). Most symptoms appear within one to 22 days following infusion of the drug. There may be an increased risk of infections for a prolonged period of time. In clinical studies, a significant percentage of those receiving Kymriah or Yescarta experienced serious side effects that resulted in inpatient admissions, including intensive care stays.

Both Kymriah and Yescarta are limited distribution drugs (LDD) and are available through a Risk Evaluation and Mitigation Strategy (REMS) program. LDD are medications used to treat conditions affecting only a small number of patients that meet special requirements. Because of this, the manufacturer may choose to limit the distribution of a drug to only a few pharmacies or as recommended by the FDA. This type of restricted distribution helps the manufacturer keep track of the inventory of the drug, educate the dispensing pharmacists about the required necessary monitoring, and ensure that any risks associated with the medication are minimized.

What is the total cost of treatment for Kymriah and Yescarta?

The wholesale acquisition cost (WAC) for one treatment of Kymriah is $475,000 and $373,000 for one treatment of Yescarta.[9,10] It is important to note that this is just the cost for the drug. There will be additional costs associated with the drug administration and, in some cases, costs for an inpatient admission due to serious side effects of the CAR-T treatment. Based on the risk and incidence of serious side effects reported in the clinical studies and the potential for a hospital admission to manage these side effects, the total cost of a single course of treatment with Kymriah or Yescarta may be in the range of $500,000 to $750,000.[10,11]

How are Kymriah and Yescarta covered?

Kymriah and Yescarta are covered under standard medical benefit plans and are subject to a medical necessity review. Cigna covers Kymriah as medically necessary 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. Cigna covers Yescarta as medically necessary for the treatment of adults with large B-cell lymphoma that has relapsed or has not responded to two or more standard treatments.

Cigna performs medical necessity reviews for both Kymriah and Yescarta through a dedicated team that consists of specialized transplant case managers and medical directors that have knowledge in handling genetic therapies. Customers authorized to receive these therapies are assigned to a case manager who will coordinate care.

How many people are candidates for Kymriah and Yescarta?

According to information provided by Novartis, there may be approximately 600 patients per year in the United States who are candidates for Kymriah, half of whom have commercial insurance coverage.[10] Based on a claim analysis of individuals with a diagnosis of ALL across our commercial book of business, we estimate there may be 40–60 Cigna customers per year who are candidates for Kymriah. This equates to a prevalence rate of approximately one customer receiving Kymriah per 275,000 customers.[12]

According to information provided by Kite, there may be approximately 7,400 patients per year in the United States who are candidates for Yescarta, half of whom have commercial insurance coverage.[11] Based on a claim analysis of individuals with a diagnosis of DLBCL across our commercial book of business, we estimate there may be 300–400 Cigna customers per year who are candidates for Yescarta. This equates to a prevalence rate of approximately one customer receiving Yescarta per 40,000 customers.[12]

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