Kymriah™ (tisagenlecleucel) – New drug approval

- On August 30, 2017, the FDA announced the approval of Novartis' Kymriah (tisagenlecleucel), 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 the first therapy based on gene transfer approved by the FDA.
- ALL is a cancer of the bone marrow and blood, in which the body makes abnormal lymphocytes. The disease progresses quickly and is the most common childhood cancer in the U.S.
    - ALL can be of either T-cell or B-cell origin, with B-cell being the most common.
    - The National Cancer Institute estimates that approximately 3,100 patients ≤ 20 are diagnosed with ALL each year.
- Kymriah is a genetically-modified autologous T-cell immunotherapy. Each dose of Kymriah is a customized treatment created using an individual patient's own T-cells, a type of white blood cell known as a lymphocyte. The patient's T-cells are collected and sent to a manufacturing center where they are genetically modified to include a new gene that contains a chimeric antigen receptor (CAR) that directs the T-cells to target and kill leukemia cells that have a specific antigen (CD19) on the surface. Once the cells are modified, they are infused back into the patient to kill the cancer cells.
- The safety and efficacy of Kymriah were demonstrated in one single-arm trial involving 63 pediatric and young adult patients with relapsed or refractory B-cell precursor ALL.
    - Overall, 83% (95% CI: 71, 91; $p < 0.0001$) of patients achieved complete remission (CR) or CR with incomplete blood count recovery within three months of treatment.
    - In addition, no minimal residual disease – a blood marker that indicates potential relapse – was detected among responding patients. The median duration of remission was not reached.
- Kymriah carries a boxed warning regarding the risk of cytokine release syndrome (CRS) and neurological toxicities.
- Other warnings and precautions of Kymriah include Kymriah REMS to mitigate CRS and neurological toxicities, hypersensitivity reactions, serious infections, prolonged cytopenias, hypogammaglobulinemia, secondary malignancies, and effects on ability to drive and use machinery.
- The most common adverse reactions (> 20%) with Kymriah use were CRS, hypogammaglobulinemia, infections-pathogen unspecified, pyrexia, decreased appetite, headache, encephalopathy, hypotension, bleeding episodes, tachycardia, nausea, diarrhea, vomiting, viral infectious disorders, hypoxia, fatigue, acute kidney injury, and delirium.
- For patients ≤ 50 kg, the recommended dose of Kymriah is 0.2 to 0.5 x 10^6 CAR-positive viable T-cells per kg of body weight given intravenously (IV). For patients > 50 kg, the recommended dose is 0.1 to 2.5 x 10^8 CAR-positive viable T-cells (non-weight based dosing) given IV.
    - Kymriah is for autologous use only. Patient's identity must be verified prior to infusion.
    - Patients should be premedicated with acetaminophen and an H1 antihistamine.
    - Confirm availability of Actemra® (tocilizumab) prior to infusion.

Continued . . .

    - Thaw Kymriah prior to infusion.

- Kymriah will be shipped directly to the cell lab associated with the infusion center in a liquid nitrogen Dewar. The infusion bag must be stored in the vapor phase of liquid nitrogen (≤ minus120°C) in a temperature-monitored system.

- The wholesale acquisition cost of Kymriah is $475,000 per treatment.

- Kymriah will be available in 20 centers within a month and 35 centers afterwards. Kymriah will be available as a frozen suspension of genetically modified autologous T cells in one infusion bag labeled for the specific recipient.

OptumRx® specializes in the delivery, clinical management and affordability of prescription medications and consumer health products. We are an Optum® company — a leading provider of integrated health services. Learn more at **optum.com**.

All Optum® trademarks and logos are owned by Optum, Inc. All other brand or product names are trademarks or registered marks of their respective owners.

This document contains information that is considered proprietary to OptumRx and should not be reproduced without the express written consent of OptumRx.

RxNews® is published by the OptumRx Clinical Services Department.

©2017 Optum, Inc. All rights reserved.