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BULLETIN:

FDA APPROVES FIRST GENE THERAPY

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The FDA approved Novartis' Kymriah (tisagenlecleucel, CTL-019), a CD19 CAR T cell therapy – the first gene therapy approved in the U.S. – for B-cell precursor acute lymphoblastic leukemia (ALL) patients age ≤25 with disease that is refractory or in second/later relapse.

- Kymriah was given a boxed warning for cytokine release syndrome (CRS), and the FDA addressed that by, at the same time, granting expanded approval for Roche's Actemra (tocilizumab) as a treatment for T cell-induced CRS. The FDA noted that 69% of T cell-induced CRS had complete resolution of CRS within two weeks with one or two doses of Actemra.
- Novartis was approved with a risk evaluation and mitigation strategy (REMS), which requires that hospitals and their associated clinics using Kymriah be specially certified. That includes training to recognize and manage CRS and neurological events, protocols to ensure the drug is only given to patients after verifying that tocilizumab is available for immediate administration, and warning patients about the signs and symptoms of toxicity.
- Novartis must conduct a postmarketing observational study involving patients treated with Kymriah. The study is aimed at monitoring for the risk of secondary malignancies. It is supposed to be a prospective, multicenter, ≥1,000-patient study with 15-year follow-up. The FDA agreed to the timetable the company submitted: For the protocol to be submitted by September 8, 2017, study completion by December 31, 2037, and a final report submitted by December 31, 2038. Novartis also must submit annual reports on the status of the study.

FDA Commissioner Scott Gottlieb, MD, stressed the groundbreaking nature of this approval – the first gene therapy approved in the U.S. – predicting it would "change the face of medicine." He also noted that this is not the only gene therapy on the horizon because the FDA has granted more than 550 active investigational new drug (IND) applications related to gene therapy products, and there are 76 active INDs related to CAR T cell products.

FDA officials declined to discuss the cost of Kymriah. The Centers for Medicare and Medicaid Services (CMS) apparently are already working on the coverage issue, and FDA officials said CMS "will issue some documents later that will expand on what they intend to do."

Asked in what other conditions CAR T therapy looks most promising, an official said, "For right now, the other studies indicating CAR T to have the greatest promise are in hematologic malignancies, including adult forms of leukemia…and certain kinds of non-Hodgkin's lymphoma."

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