Chimeric Antigen Receptor T-Cell Therapy
(CAR-T cell therapy)

The FDA approved a new type of immunotherapy medicine called CAR-T cell therapy on August 30, 2017. **Kymriah** (Tisagenlecleucel), the CAR-T cell therapy developed by the drug company Novartis, and the University of Pennsylvania, treats ALL, or acute lymphoblastic leukemia in kids and young adults. Though not yet approved to treat other Lymphomas, clinical trial results are promising.

In a healthy functioning immune system, white blood cells, or lymphocytes, protect the body against infection, identify invaders, and remove or destroy pathogens. Three types of lymphocytes work against cancer: B cells, T cells, and Natural killer cells. The function of healthy T cells is to search out and destroy invaders. However, in some cancers, the T cells become less effective, have low proliferation, or don’t recognize cancer as a foreign body. Immunotherapy uses a patient’s own immune cells to treat the cancer.

CAR-T cell therapy is a cancer treatment custom made for each patient. During an outpatient procedure the patient’s blood is collected and taken to a lab. The T cells are then filtered from the patient’s blood, a process known as leukapheresis, and then genetically engineered, or turbocharged, with a chimeric antigen receptor (CAR). Together this is now the CAR-T. The CAR-T proteins are programmed to recognize, target, and kill the cancer cells. Advances in the engineering of CAR-T cells have improved its ability to continue multiplying into hundreds of millions of copies of these cells after infusion into a patient. It essentially boosts the cancer killing effects of the T cell lymphocyte to fight the disease for months or years. The whole process, called “vein-to-vein” time, is about 22 days, though advances are also being made in production time as well. While the cells are being developed, a patient will typically receive chemotherapy to prepare their immune system to support the CAR-T cells once they are given back. This is done in a hospital, where the patient can be monitored closely.

Patients receiving CAR-T cell therapy typically develop temporary low blood cell counts from the treatment, with fatigue, increased risk of infection, and need for transfusion support. There are also potentially serious side effects that can occur after CAR-T cell therapy. One is cytokine release syndrome (CRS). CRS occurs in about 85% of patients receiving CAR-T cell therapy. The onset of symptoms can occur within minutes or hours, but can also develop days or sometimes weeks later. Effects are usually reversible and resolve in a matter of days. Symptoms are mild and manageable and include fever, low blood pressure, or difficulty breathing. Rarely, the adverse effects are long-term and can include cardiac dysfunction, bleeding, and kidney and/or liver failure. These more severe reactions are usually treated with tocilizumab, or Actemra, an inflammation-reducing treatment that was successful in managing CRS during clinical trials of CAR-T cell therapy. Another potential side effect of CAR-T cell therapy is a mass
die off of B cells, known as B-cell Aplasia. The healthy B cells are killed by the infused CAR-T cells. To compensate, patients must receive immunoglobulin therapy, which provides them with the necessary antibodies to fight off infections. The most serious and potentially life threatening side effect is cerebral edema.

To help ensure the safety of CAR-T cell therapy, Novartis is limiting availability to around 30 to 35 medical centers where personnel have had extensive training with the treatment. They also plan to post Novartis employees at hospitals using the therapy and to follow patients for up to 15 years.

Typically, cancer patients take one or several drugs until they stop working, then switch to other drugs. This type of treatment and any associated side effects can go on for years. CAR-T cell therapy however, is given as an infusion only once. As of September 2017, the AWP listed on Red Book for the single infusion of Kymriah is $570,000. This price does not include the cost of any pre-infusion treatment, administration of the therapy, hospitalizations that may occur due to adverse effects, or any associated follow-up care. When the cost of Kymriah is added to potential associated costs, a year of treatment is estimated to be $640,000. This is based on experience from clinical trials.