Dr. Budde:

CD 19 CAR-T therapy, approved in 2017 for Kymriah and Yescarta, is the next “game changer” for cancer therapy since immunotherapy, such as Ibrutinib, was approved in 2014, and Rituxan, in 1997. CAR-T combines cellular, genetic manipulation, and immunotherapy. There are currently 265 CART T trials in the US, 206 in China, and 101 in Europe. Of the 3 locations mentioned China has the least regulation around research, raising for Dr. Budde concern about risk and safety.

Dr. Jacobson:

The 3 best known US trials are in DLBCL are Kite’s ZUMA-1, Novartis’ JULIET, and Juno’s TRANSCEND. See [https://www.cancer.gov/about-cancer/treatment/research/car-t-cells](https://www.cancer.gov/about-cancer/treatment/research/car-t-cells) for a description of how the treatment works. T-cells are removed from the body and then genetically modified (called a CAR) to make them seek the B-cell lymphoma cells. The CAR-T cells are then given back to the patient. Each trial has a slightly different design for the genetic manipulation, and each group hopes that their trial will be the most successful in reducing adverse effects present in the earlier CAR-T designs.

Several types of CAR-T toxicities were described, and suggestion made that doing CAR-T earlier in a patient’s treatment would lower the risks of adverse effects. Dr. Jacobson suggested that a person’s 6 month response post CAR-T predicts their 12 month response.

Research challenges include finding the right tumor protein target within the cell, getting the CAR-T cells to the reach the tumor environment, and finding a way to affect the tumor environment to promote, not suppress, the activity of the CAR T cells that successfully reach the tumor.

Approaches to CAR T cell therapy include finding a more potent gene editing combination, a more regulated “conditional switch”, and shorter delivery and production time, including “custom” vs “off the shelf/universal” CAR’s using donor Lymphocytes.

Next steps on CAR-T: Combining CAR-T therapy with immune checkpoint blockade of other Immunotherapy agents, 3rd generation CARs, CAR-T cells that recognize more than one tumor protein, armored CAR’s, engineered to secrete proteins that improve CAR-T cell activity, safer and more finely regulated CAR’s that require a more complex and specific set of interactions with the tumor cell for activity, and expanding indications for additional NHL’s including MCL.