A chimeric antigen receptor-expressing T cell that targets and kills CD83 expressing cancers such as acute myeloid leukemia (AML). The CAR construct works by using a novel anti-CD83 scFv region to enable T cell targeting of CD83 expressing cancer cells and T-cell activation by incorporating co-stimulator and intracellular signaling regions. CD83 is a tumor associated antigen, and was found over-expressed on four AML cell lines. CD83 is also expressed on the surface of mature antigen presenting DCs but not on immature DCs suggesting that an anti-CD83 CAR-T cell may be an effective treatment for AML and may also help with GVHD for AML relapsed after transplant. Anti-CD83 CAR-T cell mediated killing of CD83-expressing AML cell lines was demonstrated.

COMMERCIAL OPPORTUNITY

- AML is a type of blood cancer where the bone marrow makes abnormal myeloblasts. AML accounts for nearly one-third of all new leukemia cases each year. The American Cancer Society estimates that in 2017 there will be 21,380 patients who develop AML and 10,590 AML patients will die.

- The standard of care for AML treatment has changed little over the past four decades. Intensive chemotherapy followed by hematopoietic stem cell transplantation remains the most effective treatment. However, most newly diagnosed elderly patients are ineligible for intensive chemotherapy, and there are no effective second line treatments for patients with relapse/refractory disease. As a result, the 5-year overall survival rate is 27%, and is less than 10% for patients over age 60. Around 40-60% of Hematopoietic Stem Cell transplant recipients will develop aGVHD. 30% of GVHD cases result in death.

- The marketplace is attractive for CAR-T cell development, as Novartis received approval in August 2017 for Kymriah, its anti-CD19 CAR-T therapy for pediatric B-cell ALL. The trial had an overall response rate of 82.5% (52/63). Although the list price for Kymriah is $475,000 for a one-time treatment, Novartis has said only those patients who respond by the end of the first month will need to pay. In October 2017, Gilead’s Yescarta, an anti-CD19 CAR-T, was approved for large B-cell lymphoma and is listed at $375,000. In 2017, Gilead acquired Kite Pharma for $11.7B, and in 2018, Celgene acquired Juno Therapeutics for $9B. Juno was also developing a CD-19 CAR-T therapy.

TECHNOLOGY

CD83 was found expressed on K562, Thp-1, U937 and MOLM-13 cells. Compared to mock transduced T cells, anti-CD83 CAR-T cell mediated killing of CD83-expressing cancer cells using an xCELLigence® Real-Time Cell Analysis instrument. Human CD83 CAR or mock transduced T cells were cocultured with fresh K562 or Thp-1 cells at an E/T ratio of 10:1, and a statistically significant increase in killing of AML cells was observed (P<0.0001).

PUBLICATION/PATENT

- Provisional patent application filed February 23, 2018 for Dr. Davila and Dr. Betts.

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LICENSING OPPORTUNITY