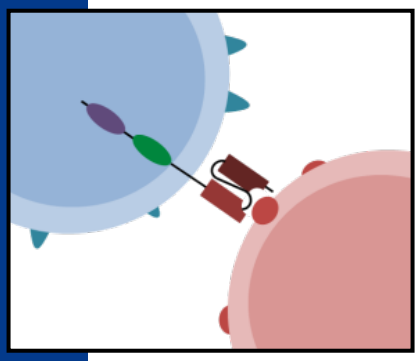
CAR-T cells to Kill Neuroendocrine Tumors Expressing Somatostatin Receptor 2 (SSTR2)



A CAR construct was made to target the Somatostatin Receptor 2 that is highly expressed on neuroendocrine tumors (NETs). Instead of an scFv, the CAR construct has a dual octreotide molecule, an octapeptide that mimics natural somatostatin pharmacologically but is a more potent inhibitor of growth hormone, glucagon and insulin, and is used for the treatment of growth hormone producing tumors. Dual Octreotide anti-SSTR2 CAR-T cells demonstrated 60% better killing efficacy in-vitro as compared to control, and in-vivo resulted in a 65% reduction in tumor growth. Moreover, the CAR-T cells also induced necrosis in NET xenograft models in the absence of pathological alterations of SSTR-expression tissues.

COMMERCIAL OPPORTUNITY

- According to ASCO, it is estimated that more than 12,000 people in the United States are diagnosed with a NET each year, and a study from Spain suggested that about 43% of patients have metastases. NETs are typically incurable in the metastatic setting. Most NETs overexpress receptors for somatostatin. Somatostatin inhibits the release of many hormones and other secretory proteins, and the somatostatin receptor is a G protein-coupled receptor.
- Current management strategies for NETs include surgery, radiological intervention, cytotoxic chemotherapies, somatostatin analogs and biological agents such as sunitinib and everolimus. Standard immunotherapy treatments have not yet demonstrated significant activity in well-differentiated neuroendocrine tumors.
- The marketplace is attractive for autologous CAR-T cell therapies, as Novartis received approval in August 2017 for Kymriah, its anti-CD19 CAR-T therapy for pediatric B-cell ALL with an ORR of 82.5%. 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 March 2021, Bluebird and BMS' Abecma, an anti-BCMA CAR-T, was approved for multiple myeloma. In 2017, Gilead acquired Kite Pharma for $11.7B, and in 2018, Celgene acquired Juno Therapeutics for $9B. Juno's anti-CD19 CAR-T Breyanzi was approved in February 2021. In 2020, Kymriah had annualized sales of $422M, and Yescarta had annualized sales of $592M. Also, CMS in 2018 set Medicare Part B reimbursements for CAR T-cell therapies at $500,000 for Kymriah and $400,000 for Yescarta in the outpatient setting.

TECHNOLOGY

Anti-SSTR2 CAR-T cells and un-transduced (UT) T cells were incubated for up to 72 hours with NET cell lines at an effector: target (E:T) ratio of 1:1. By in vitro bioluminescence imaging assay, anti-SSTR2 CAR-T cells induced cell death in up to 60% of Luc+ NET cell lines as compared with UT T cells. Immunodeficient, four-to-six-week-old, NSG female mice (n=66) were subcutaneously injected with either Luc+ BON1 or CM NET cell lines. When the mean tumor volume reached 1 mm^3, mice were randomized to receive PBS (n=11), UT T cells (n=11) or anti-SSTR2 CAR-T cells (n=11) by tail vein injection. Treatment with anti-SSTR2 CAR-T cells significantly reduced the growth of both BON1 and CM xenografts by about 65% by day 28

PUBLICATION/PATENT

- PCT application was filed in June 2021 for Drs. Abate-Daga, Strosberg and Cives.

CONTACT

The Innovation Office
813.745.6828
InnovationMarketing@Moffitt.org

LICENSING OPPORTUNITY

MOFFITT CANCER CENTER