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A Phase I Clinical Trial Combining Chimeric Antigen Receptor T-cell Therapy with Autologous Hematopoietic Stem Cells in Patients with Relapsed or Refractory Hematologic Malignancies

Chimeric Antigen Receptor (CAR) T-Cell therapy is a novel immunotherapy using genetically modified autologous T-cells to treat relapsed or refractory hematological malignancies. Currently, CAR T is indicated as a second line therapy for non-Hodgkin Lymphoma, third-line therapy for Acute Lymphoblastic Leukemia, and fifth-line therapy for Multiple Myeloma. While response rates look promising, CAR T is associated with unique toxicities such as cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, macrophage activation syndrome as well as post-infusion cytopenias and increased infection risk. Moreover, eligible patients receive several rounds of genotoxic chemotherapy prior to T cell collection since CAR T is currently indicated as a therapy for relapsed disease. This increases the risk of pre-lymphodepletion cytopenias which are associated with reduced CAR T-cell efficacy, increased treatment related toxicity, and post-infusion cytopenias.

To address these treatment related risks and in efforts to improve CAR T-cell efficacy, we designed a phase I, single arm clinical trial combining autologous hematopoietic stem cells and any FDA approved CAR T-cell product at Cedars Sinai Medical Center in Los Angeles, California. Patients with relapsed or refractory non-Hodgkin B-Cell lymphoma, B-Cell precursor acute lymphoblastic leukemia, and multiple myeloma are eligible to enroll in this trial and, based on their disease, will receive one of the following FDA approved CAR T-cell products: axicabtagene ciloleucel, tisagenlecleucel, brexucabtagene autoleucel, Idecabtagene vicleucel, ciltacabtagene autoleucel or lisocabtagene maraleucel. The co-primary endpoints of this trial are to determine the feasibility of collecting the target cell dose (2×10^6 to 5×10^6) of autologous hematopoietic stem cells in at least 50% of the patients and the safety of adding autologous hematopoietic stem cells to the planned CAR T treatment within the first 60 days following CAR T dosing.

In this trial, enrolled patients will undergo a mobilized blood stem cell collection after T cell collection and prior to CAR T infusion. Patients will be risk stratified according to their baseline inflammation and hematopoietic reserve. They will receive an autologous hematopoietic stem cell boost 14 days after CAR T-cell infusion should they meet one or more of the following criteria: high CAR HEMATOTOX score (≥ 2), any platelet counts < 75×10^9/L on one day post CAR T infusion (Day 0 – 14), absolute neutrophil count < 1000/mm^3 on any day post CAR T infusion (Day 0 – 14), ≥ grade 2 cytokine release syndrome, ≥ grade 2 immune cell activation neurotoxicity syndrome. If a patient has baseline platelet counts < 150×10^9/L or absolute neutrophil counts < 1500/mm^3, they will receive the CD34+ stem cell infusion regardless of the other criteria.

With this trial, we hope to improve the therapeutic efficacy of CAR T and minimize its treatment related risks.