Improving outcomes after CD19-targeted CAR T-cell therapy

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In this talk I will share my past and current work aimed at improving the outcomes of patients treated with T cells engineered with CD19-targeted chimeric antigen receptors (CD19 CAR T cells). I will summarize our extensive experience using defined-composition CD19 CAR T cells from approximately 200 patients with relapsed or refractory (R/R) B-cell malignancies treated on a phase I/II clinical trial at our institution. While gradually transforming the management of R/R B-cell malignancies, CD19 CAR T-cell therapy still fails to induce durable responses in most patients. In addition, a significant proportion of patients experience severe toxicities (cytokine release syndrome, neurologic toxicity), limiting access to CAR T-cell therapy to specialized centers. First, I will present our data modeling the independent impact of the CD19 CAR T-cell product type on outcomes in patients with R/R aggressive B-cell non-Hodgkin lymphoma. Next, I will discuss several strategies we investigated in clinical trials to improve outcomes after CD19 CAR T-cell therapy: i) combinatorial approaches with Bruton tyrosine kinase inhibitors and checkpoint inhibitors; ii) T cells engineered with a fully human CD19-targeted single chain variable fragment; iii) Toxicity prevention with the IL-1R antagonist anakinra.