Introduction

While CAR-T therapies have transformed the treatment of lymphoid malignancies, there are currently no approved adaptive cell therapies for myeloid malignancies. T cell expressing T cell Receptors (TCRs) for HLA-A*02:01 restricted minor histocompatibility antigens HA-1 and HA-2 (right panels). Cytotoxicity was measured at indicated effector to target cell ratios.

Methods and Results

To minimize potential safety risks, process variability, and costs associated with lentiviruses, our proprietary T- CR construct is based on a transposon vector. The transposon vector encodes both α and β of the TCR, under control of a strong promoter. Our transposon vector also includes a transposase gene which is used to integrate the complete TCR construct at the desired chromosomal location.

Overall trial design for TSC-100/ TSC-101 in patients undergoing HCT

Patients with AML, MDS and ALL planned for HCT with reduced intensity conditioning (RIC) from a haploidential donor (haplo) will be assigned to treatment or control arm depending on their HLA and minor antigen type. All patients with HLA-A*02:01 (~50% prevalence) will be genotyped to assign treatment arms. If they are HLA-A*02:01 positive (~100% prevalence), they will receive TSC-100. If HA-1 negative, they will receive TSC-101. Donors would need to be HLA-A2 positive and HA1-2 mismatched for either HLA or minor antigen type. Patients without HLA-A*02:01 (~60%) or without mismatched donors will be assigned to the standard-of-care arm.

References