Celyad Oncology

CAR T cell therapy vs. CAR NK cell therapy

Recently researchers have tried to modify natural killer (NK) cells with chimeric antigen receptors (CAR) to increase potential to bind and destroy cancer cells, known as NK cell therapy. Here we describe the differences between CAR T cell therapies and CAR NK cell therapies to consider when developing cancer treatments for patients.

CAR T cell therapy		CAR NK cell therapy
T cells are part of the adaptive immune system and are intended to generate a long-lasting protective immune response. By engineering T cells with the Natural Killer Group 2D (NKG2D) receptor, they become NKG2D CAR T cell therapies.	Base cell type	NK cells are a part of the innate immune system and are the first line of defense against foreign infections and cancer cells. Their primary role is surveillance, early detection of foreign cells and initial immune system activity. By engineering NK cells with a CAR receptor, they become CAR NK cell therapies.
1-12 months (memory T cells).	Half life	7 days for mature NK cells. Some early evidence suggests this could be several months for certain 'memory' NK cells.
Non-modified T cells infiltrate solid tumors at higher but variable frequency as compared to NK cells. T cell infiltration seems associated with prognosis.	Tumor Infiltration	NK cells appear to have restricted capacity to infiltrate into solid tumors. If found, high levels of NK cells are associated with improved prognosis.
No HLA matching or mismatching required for Celyad allogeneic CAR T cells. HLA matching is used for others allogeneic CAR Ts. Knockdown or knockout of the T cell receptor. Graft-versus-Host (GvH) activity of allogeneic T cells requires persistence.	Allo-reactivity	KIR mismatched (e.g. haploidentical donors) to avoid inhibitory receptor activity. Will the expression of a CAR overcome the effects of inhibitory receptors? No TCR to drive Graft-versus-Host-disease (GvHD). Short-term persistence likely ensures no GvH activity in the KIR mismatched situation.
Cytokine reactive syndrome (CRS), neurological symptoms likely target and disease specific. Only mild and reversible occurrences of GvHD reported to date in the allogeneic setting but limited numbers of patients.	Adverse events	No evidence of GvHD in the allogeneic setting to date though limited numbers of patients treated. Most studies have focused on haploidentical donors to avoid KIR activity. Short persistence likely to avoid long term deleterious effects.
Four licensed products: three CD19 and one BCMA CAR T. Major activity in the CAR T space exploring more targets Initial activity in solid tumors non-oncology applications.	Clinical activity	Primary NK cells have been used in the transplant setting. No clinical activity in one study using NK cells in melanoma (NCI) Much work in the NK space has focused on the use of an irradiated cell line NK-92. Engineered cord blood-derived CAR NK cells showed initial promise in hematological malignancy (11 pts).