ANV419 is a novel CD122-biased IL-2/anti-IL-2 fusion protein with potent CD8 T cell and NK cell stimulating capacity that shows additive efficacy in combination with checkpoint inhibitors and treatments acting through antibody dependent cellular cytotoxicity.

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Background

ANV419 is an IL-2/anti-IL2 antibody fusion protein for expansion of CD8 T cells and NK cells

ANV419 is an IL-2/anti-IL-2 fusion protein with natural affinity to the heterodimeric IL-2Rαβ/γ, but no affinity for IL-2RA. As a result, ANV419 induces selective proliferation of CD8 T cells and NK cells over Tregs and is currently tested in a phase 1/2 trial for the treatment of solid tumors.

Goal of the presented study was the evaluation of the activity of ANV419 on NK and CD8 T cells and its potential synergy with complementary immune-oncology mechanisms that can strengthen its NK or CD8 T cell anti-tumor response for the planned phase 2 trials.

Results

ANV419 induces Stat5 phosphorylation at comparable kinetics and magnitude as IL-2 and IL-15

Crystal structure of ANV419

IL-2 is fused to an IL-2 specific antibody that binds with high affinity to the IL-2Rα chain and are sterically blocked by the anti-IL-2 antibody.

ANV419 treatment leads to similar regulation of NK receptors compared to IL-2 and IL-15

ANV419 amplifies NK cell mediated killing independent of FcyR3a SNP F158V

Primary human NK cell killing of HER2+ HCC1954 cells in presence of 10nM ANV419 and/or 0.07 μM Herceptin was measured by live cell imaging and correlated with FcγR3A SNP F158V. Killing was normalized to Staurosporine control treated target cells.

ANV419 enhances tumor growth inhibition in combination with PD1 or CTLA4 blockade in the syngeneic H22 mouse model

Conclusions

• The data presented here support the initiation of clinical phase 2 studies assessing ANV419 treatment in indications in which NK and CD8 T cells are involved in tumor resolution as monotherapy and in combination with ADCC inducing treatments or checkpoint inhibitors

• Please visit poster 749P for more information on our phase 1 data