**BACKGROUND**

**Rucaparib**
- Rucaparib is a small molecule poly(ADP-ribose) polymerase (PARP) inhibitor that has demonstrated activity in BRCA-mutant tumors through synthetic lethality.
- Rucaparib has also been shown to synergize with checkpoint inhibitors by increasing DNA damage, intratumoral CD8+ T cell infiltration and activating the immune system.

**NKTR-214**
- NKTR-214 is a biased agonist that targets the IL-2 pathway, providing sustained signaling through the heterodimeric IL-2 receptor pathway (CD2+ and natural killer (NK) cells) compared to IL-2 alone.
- NKTR-214 has demonstrated a 44% response rate in metastatic castration-resistant prostate cancer and is currently being tested for efficacy in multiple clinical trials.

**NKTR-214 Experiments**

**Rucaparib and NKTR-214 Combination Therapy Provides Survival Benefit in Genetically Relevant Orthotopic Brca1-/- Ovarian Cancer Model**

- Kaplan-Meier Survival
- Combination therapy significantly increased survival compared to the vehicle control. Further improvement was observed with the combination.

**CONCLUSIONS**

- The combination of rucaparib and NKTR-214 resulted in enhanced survival in Brca1-/- and Brca2-/- mutant ovarian mouse models.
- The combination also increased intratumoral immune cell infiltration and enhanced the expression of genes involved in multiple immune signaling pathways.

**METHODS**

- **TCR CDR3 Sequencing**
  - Nanoliter gene expression profiling and T cell receptor (TCR) sequencing were performed on individual BRCA1-/-AKT tumors and Brca1-/- tumors treated with the combination of rucaparib and NKTR-214.
  - The soft tissue score measures relative abundance of the T cell population based on the expression levels of marker genes.
  - The diversity score measures the frequency and total number of each TCR clone. Tumors treated with the combination of rucaparib and NKTR-214 contained more T cells with increased CD3 diversity. Clonality of the TCR CDR3 repertoire in individual tumors from each cohort was presented in a Tree of the T cell repertoire.

**REFERENCES**