MUC16 CAR-T therapy to treat ovarian cancer

Ovarian cancer is the leading cause of death from gynaecological malignancies in the Western world. CAR-T cell therapy has been tested against various targets in ovarian cancer and one of the candidates is the MUC16 ectodomain. This ectodomain remains on the cell surface after cleavage of cancer-antigen 125 (CA125). CA125 is the domain distal from the membrane, which is currently used as a serum biomarker for ovarian cancer. Scientists at Oslo University hospital have demonstrated the suitability of the CA125 as a target for CAR-T cell therapy.

Business Opportunity

In vitro and in vivo results, including PDX studies, demonstrate that the CA125 domain of MUC16 represents an excellent target for treating MUC16-positive malignancies. Inven2 seeks collaboration with industrial partners and licensors who can support the clinical development of K101 CAR T cell therapy in patients with ovarian cancer.

Technology Description

A series of antibodies raised against the CA125 extracellular repeat domain of MUC16 were tested and adapted to CAR format. Comparisons between these candidates, and against an existing CAR targeting the MUC16 ectodomain, identified K101 as having high potency and specificity. A high efficacy of K101CAR T cells was observed against cell lines and patient-derived tumours, in vitro and in vivo. It was also demonstrated that K101CAR functionality was not impaired by the soluble antigen. In direct comparisons, K101CAR, which targets the extracellular repeat domains, was shown to have comparable efficacy to the previously validated 4H11CAR, which targets the MUC16 ectodomain.

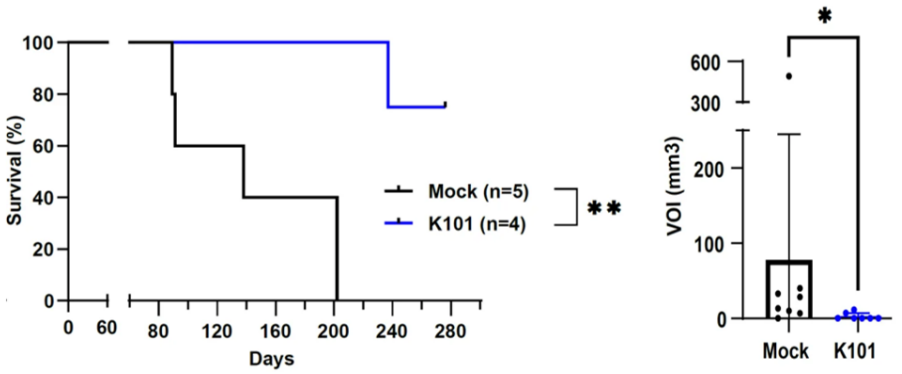

Fig. 1: K101CAR T cells control an orthotopic PDX model. PDX26 cells (1x10^5) were engrafted orthotopically in the bursa of the ovary in immunodeficient mice. These were allowed to engraft for 22 days, prior to two injections (d22 and d24) of T cells (Mock or K101CAR). Left: Kaplan-Meyer curve of Mock- and K101CAR-T cell treated mice (GvHD events excluded). n=4-5, Log-rank test *p<0.05, **p<0.01. Right: Spherical volume of interest (VOI) analysis of Mock- and

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K101CAR-T cell treated PDX mice at day 86. Columns are presented as Mean ± S.D., n=7-8, Mann-Whitney test, *p<0.05

Intellectual Property

A patent application was filed in 2024

References

1. Casey NP, Kleinmanns K, Forcados C, et al(April 11, 2024) , https://jitc.bmj.com/content/12/4/e008179, https://jitc.bmj.com/, 12, e008179