499 A FIRST-IN-HUMAN, PHASE 1/2 CLINICAL TRIAL OF TK-8001, A MAGE-A1 DIRECTED T CELL RECEPTOR IN PATIENTS WITH ADVANCED-STAGE SOLID TUMORS (THE "IMAG1NE"-TRIAL)

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Background Melanoma-associated antigen 1 (MAGE-A1) is a cancer-testis antigen with highly selective expression in testis (which is an immune privileged site) and in multiple high unmet medical need cancers. Therefore, it represents an attractive target for T cell receptor (TCR)-based therapies. TK-8001 is a MAGE-A1 directed TCR with optimized affinity and specificity, derived from the huTCR mouse platform,[1] introduced by retroviral transduction into autologous patient-derived CD8 + T cells. The anticipated mode of action of TK-8001 is to bind to MAGE-A1-epitope presenting tumor cells and eliminate them via CD8+ cytotoxic activity and interferon-γ release. Preclinical exploration of the TK-8001 TCR has demonstrated potent antitumor activity, even in low-expressing MAGE-1 positive tumor cells, and favorable benchmarking vs. existing MAGE-A1 directed TCRs derived from human donors. This abstract describes the currently launched phase 1/2 trial for TK-8001.

Methods The IMAG1NE trial (Immunotherapeutic MAGE-A1 directed Neoplasm Elimination) is a phase 1/2, first-in-human, open-label, accelerated titration, two-part clinical trial of TK-8001 (MAGE-A1-directed TCR-transduced autologous CD8+ T cells) in subjects with HLA-A*02:01 genotype and advanced-stage/metastatic, MAGE-A1+ solid tumors that either have no approved therapeutic alternative(s) or are in non-curable state and have received a minimum of two lines of systemic therapy. Major endpoints for the IMAG1NE trial will be safety, pharmacokinetics, pharmacodynamics (e.g. cytokine profiles) as well as preliminary clinical efficacy (degree of tumor mass reduction and duration of response).In Part 1 of the trial, three different doses of TK-8001 will be explored for safety and preliminary clinical efficacy in an accelerated titration design. The starting dose is set at 1x10E8 MAGE-A1 TCR transduced CD8+ T cells followed by two escalation steps. Part 2 of the trial will enroll up to 30 subjects with advanced-stage, MAGE-A1 positive cancer to confirm safety and efficacy.The study is expected to open for enrolment in Q4/2021. For further information please contact T-knife GmbH at info@t-knife.com.

REFERENCES

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