631 PHASE I DOSE ESCALATION STUDY IN PATIENTS WITH ADVANCED SOLID TUMORS WITH ANV419, A NOVEL FUSION PROTEIN SELECTIVE FOR IL-2Rβ/γ

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Background ANV419 is a fusion protein of an anti-IL-2 antibody and human-IL-2 with selective signaling through IL-2Rβ/γ thus limiting the side effects of activating the IL-2Rα/β/γ ANV419 is investigated in a phase I dose finding study in patients with advanced solid tumors (ANV419-001).

Methods The primary objective of ANV419-001 is safety and tolerability of ANV419. Secondary objectives include response rate (RECISTv1.1), pharmacokinetic and pharmacodynamic evaluation. ANV419 is administered as a 15 minutes intravenous infusion Q2W. As of 29th June 2022, 26 patients with Eastern Cooperative Oncology Group (ECOG) Performance Status 0 or 1 and a range of primary tumor types with multiple previous lines of therapy have been enrolled and dosed in 9 cohorts up to 243µg/kg.

Results ANV419 was generally well tolerated across multiple cycles, with no dose-limiting toxicities (DLTs) up to and including 243µg/kg. The most frequent ANV419 related adverse events (AEs), reported in at least 10% of patients, were chills, fever, fatigue, nausea, vomiting, cytokine release syndrome (CRS) and increased liver function tests, mainly Grade 1 and Grade 2. All drug related events were responsive to supportive care therapy and reversible.

A dose proportional increase in ANV419 plasma concentration results in an increased estimated half-life up to 28 hours at higher doses.

In this study, IL-6, IL-8, TNF-α, and IFN-γ levels (10-Plex Panel) were transiently increased at high doses (108 and 243µg/kg), 4 hours after infusion.

Pharmacodynamic evaluation of ANV419 on day 4 post-dosing (cycle 1 and 2) showed a selective and dose dependent proliferation of $CD8^+$ T and NK cells, with a lower increase of proliferating Tregs. As typical for IL-2 related lymphocyte sequestration, a transient dose dependent lymphopenia was observed in all patients lasting up to at least 72 hours after ANV419 infusion, followed by a dose dependent increasing lymphocyte counts up to 5.4-fold of baseline. Lymphocyte numbers keep increasing over multiple cycles up to 3.8-fold after 2 cycles (243µg/kg). In 21 patients with at least one post-baseline tumor response assessment, 52% of patients (n=11) achieved a response of SD or PR, with 10 SD, 1 PR and 10 PD.

Conclusions ANV419 maintains a favorable safety profile, while inducing a systemic inflammatory response in cancer patients with preferential proliferation of effector cells compared to high dose of IL-2. Dose escalation is ongoing. The preliminary efficacy data shows a potential for ANV419 as therapeutic option for patients with progressing/relapsing cancer. Updated data will be shared at the meeting.

Trial Registration NCT04855929

Ethics Approval The study ANV419-001 has been approved by the following Ethics committee:

- HM Hospitals Drug Research Ethics Committee (CEIm) (ID: 20.12.1736-GHM)
- EKNZ – Ethikkommission Nordwest und Zentralschweiz (ID 2021-00911)
- London – Surrey Borders Research Ethics Committee (ID: 21/LO/0213)

Written consent was obtained from all patients prior taking part into this study.

Consent Written informed consent was obtained from the patient for publication of this abstract.

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