AFM24 in Combination With Autologous NK Cells (SNK01) in Patients With Advanced/Metastatic Epidermal Growth Factor Receptor (EGFR) Expressing Solid Tumors: Initial Results From the Phase 1 Dose Escalation Study

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BACKGROUND

• Natural killer (NK) cells are key components of the innate immune system, responsible for eradication of transformed cells by antibody-dependent cellular cytotoxicity (ADCC).
• Autologous NK cell transfer is a promising immunotherapy that enhances the specificity and antitumor activity of anti-EGFR expanded, highly pure NK cells harvested from a patient.
• The activity of therapeutic NK cells can be enhanced in combination with innate cell engagers (ICE).

AFM24 & SNK01 COMBINATION THERAPY

• AFM24 is a tetavalent, bispecific ICE that simultaneously binds CD16A on NK cells, and EGFR frequently overexpressed on solid tumor cells, redirecting and enhancing antitumor ADCC.

• A Phase 1/2a AFM24 monotherapy study (NCT04259450) in patients with EGFR+ solid tumors revealed a well-managed safety profile and promising clinical activity at the recommended Phase 2 dose (RP2D) of 480 mg; cumulative science data revealed AFM24-mediated stimulation of the innate immune response, and indirect activation of the adaptive immune response.

• SNK01 is an autologous, NK cell-derived cellular immunity technology that can produce large scale ex vivo expanded autologous NK cells (1,000-10,000-fold expansion of NK cells with >95% purity), even in patients with low primary NK cell counts; the resulting NK cells produced are also characterized by high CD16 expression (90%+).

• SNK01 has demonstrated a tolerable toxicity profile, no risk of graft versus host disease, and promising antitumor activity as a single agent and in combination therapies in patients with rapidly progressive solid tumors.

OBJECTIVES

This study was an open-label, multicenter, proof-of-concept dose escalation (Phase 1) and dose expansion (Phase 2a) study designed to evaluate the safety, tolerability, and preliminary efficacy of AFM24 with SNK01 autologous NK cells.

STUDY DESIGN – PHASE 1: DOSE ESCALATION

Primary endpoint: To establish the maximum tolerated dose (MTD) and the RP2D of AFM24 in combination with SNK01 autologous NK cells (NCT02069949).

Secondary endpoints: To evaluate the safety, tolerability, preliminary efficacy (by assessing overall response rate (ORR) per RECIST V1.1) and pharmacokinetic (PK) of the combination.

AFM24 at 160 mg (cohort 1) or 480 mg (cohort 2) and 480 mg (cohort 3), followed by 160 mg (cohort 4) or 480 mg (cohort 5). The RP2D was determined with the combination Phase 2 dose: 60 mg AFM24 and 480 mg SNK01.

No Grade 3, 4, or 5 treatment-emergent adverse event related to study drug was observed across all dose levels.

CONCLUSIONS

• The data presented here provide proof-of-concept and support the feasibility of enhancing and redirecting the innate immune response to solid tumors by combining ICE molecules with NK cells; however, the trial will not proceed to Phase 2a.

AFM24 in combination with atezolizumab reached the planned MTD, and PK properties were similar to that of AFM24 alone.

In the AFM24-101 monotherapy study, an increase of NK cells in tumor tissue was described.

Using a population PK model, simulated AFM24 PK based on patient characteristics and PK data resulting in a median (range) of 9 (4–23) doses over a median (range) of 80 (35–209) days following the initial assessment in RECIST Status and Treatment Durations


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