The Combination of CD16A/EGFR Innate Cell Engager, AFM24, with SNK01 Autologous Natural Killer Cells in Patients with Advanced Solid Tumors

Anthony El-Khoueiry¹, Paul Y. Song², Jennifer Rubel³, Dorna Pourang⁴, Christa Raab⁵, Gabriele Hintzen⁶, Michael Emig⁷, Pilar Nava-Parada⁸

BACKGROUND
- Epidermal growth factor receptor (EGFR) is frequently overexpressed on the cell surface in solid tumors making it an ideal therapeutic target¹
- Overexpression is typically a strong prognostic indicator, but not all patients respond to EGFR inhibitors², and in patients who are responsive, acquired resistance invariably occurs³; therefore, novel therapies acting independently of EGFR signaling are required
- Natural killer (NK) cells are a critical component of the innate immune system involved in the eradication of transformed cells via antibody-dependent cellular cytotoxicity (ADCC)
- Autologous NK cell transfer is a treatment that provides immune enhancement using highly pure NK cells harvested from a patient and represents a promising treatment strategy, with ex vivo expansion and activation enhancing the specificity and anti-tumor activity of NK cells⁴

AFM2 & SNK01 THERAPY
- AFM24 is a tetravalent bispecific innate cell engager (ICE)® derived from the redirected optimized cell killing (ROCK®) antibody platform
- AFM24 engages CD16A on NK cells and macrophages, with a higher affinity than monoclonal antibodies, and triggers ADCC and antibody-dependent cellular phagocytosis, respectively, directed at EGFR-expressing cancer cells⁵
- Preclinical data have shown that, independent of EGFR mutational status, AFM24 can induce NK cell-mediated killing of EGFR-expressing (EGFR⁺) solid tumor cell lines⁶
- An ongoing phase 1/2a study (NCT04259450) is seeking to establish the safety and efficacy of AFM24 monotherapy in EGFR⁺ solid tumors; this study has shown that patients had a well-managed safety profile with AFM24, and the recommended Phase 2 dose was established as 480 mg⁷
- SuperNK cell therapy (SNK01) is an ex vivo expanded autologous NK cell-derived adoptive cellular immunotherapy; the expansion process yields >5,500 of highly activated cytotoxic NK cell immunotherapeutic agent with >95% cell purity⁸
- SNK01 is characterized by increased CD16 expression (~90%); and, has demonstrated a tolerable toxicity profile with no risk of graft vs. host disease in patients with rapidly progressive solid tumors⁹
- Clinical data has shown anti-tumor activity in solid tumors as a single agent and in combination therapy with ex vivo expansion and activation further enhancing the specificity and anti-tumor activity of NK cells⁹

OBJECTIVE
To investigate AFM24 in combination with SNK01 autologous NK cells in patients with advanced or metastatic EGFR⁺ solid tumors

METHODS
- An ongoing Phase 1/2a open-label, non-randomized, multicenter, dose escalation (Phase 1) and dose expansion (Phase 2a) study was initiated in November 2021 (NCT05099549) to evaluate the safety, tolerability and efficacy of AFM24 in combination with SNK01 autologous NK cells in EGFR⁺ solid tumors
- AFM24 will be administered at an escalating dose as weekly intravenous (IV) infusions; the starting dose (160 mg) and dose escalations for each cohort are based on results from the ongoing AFM24 monotherapy trial and in agreement with the Safety Review Committee (SRC). SNK01 NK cells will be given at a fixed dose (4.0 x10⁹ cells) as a weekly IV infusion followed by AFM24
- Subjects will receive combination therapy until disease progression, intolerable toxicity, subject withdrawal or termination at the Investigator’s discretion

STUDY PARAMETERS
Key inclusion criteria:
- Eligible subjects at least 18 years of age must have advanced or metastatic disease with EGFR-positive immunohistochemical staining (defined as >1% of tumor cells) and be refractory to standard-of-care treatment
- One or more measurable tumor lesions by RECIST v1.1
- Eastern Cooperative Oncology Group performance status of 0 or 1
- Adequate bone marrow, hepatic and renal function

Key exclusion criteria:
- Untreated or symptomatic central nervous system metastases
- No resolution of specific toxicities related to any prior anti-cancer therapy to Grade ≤ 1 according to the NCI-CTCAE v5.0
- Treatment with systemic anticancer therapy or an investigational device within 4 weeks, or within 5 half-lives of the prior to the first dose of study treatment
- Clinically significant cardiovascular disease
- Autoimmune disease requiring therapy; immunodeficiency, or any disease process requiring systemic immunosuppressive therapy

STUDY ENDPOINTS
Primary endpoints:
Phase 1
- To determine the maximum tolerated dose and/or recommended Phase 2 dose
- To establish the overall response rate (as per RECIST v1.1) in EGFR⁺ disease specific cohorts

Secondary endpoints:
Phase 1
- Safety and tolerability of AFM24 in combination with SNK01 cells
- Preliminary efficacy; assessed by evaluating progression-free survival (PFS) and overall survival (OS) (as per RECIST v1.1)

Phase 2a
- Safety and tolerability of AFM24 in combination with SNK01 cells
- PFS, OS, duration of response clinical benefit rate

Secondary endpoints for both phases include treatment-emergent adverse events, serious adverse events, pharmacokinetics (maximum observed plasma concentration, time to maximum concentration, area under plasma concentration-time curve) and immunogenicity and anti-drug antibodies assessed up to 24 months. Pharmacodynamic and biomarker analyses will also be explored.

REFERENCES