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The combination of CD16A/EGFR bispecific innate cell engager AFM24 with SNK01 NK cells promotes efficacious targeting and killing of EGFR+ tumor cells

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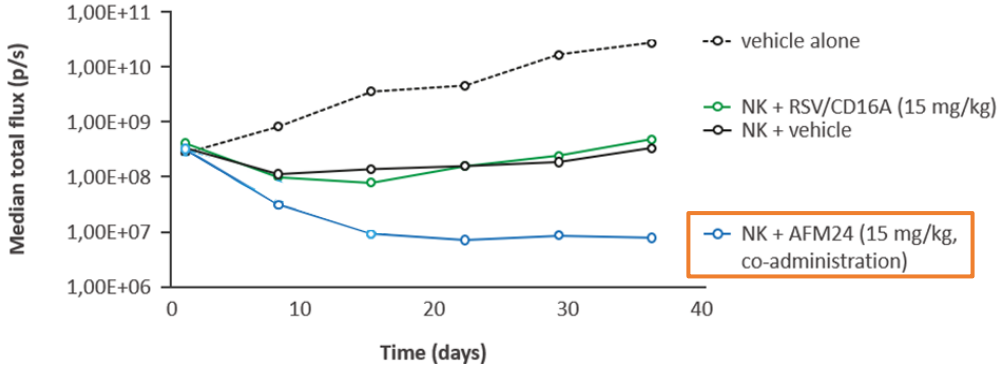
I have the following financial relationships to disclose:

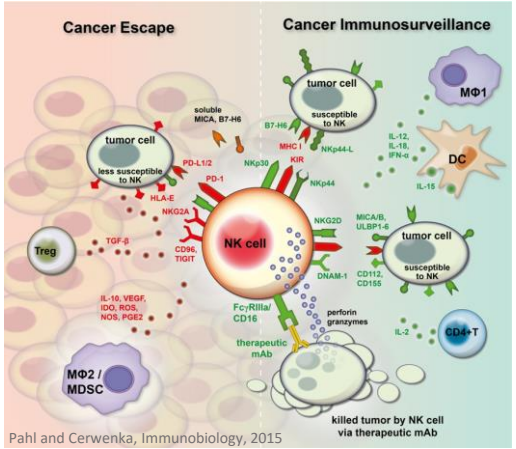
Employee of: Affimed GmbH

Background: Importance of Innate Immunity in Solid Cancers

- In solid cancers, there are lower number of NK cells and dysfunctional state compared to normal population[1]
- Patients' number of peripheral NK cells pre- and post-dose of ICE® (Innate Cell Engager) positively correlated with response to treatment.[2]
- Harnessing the power of the innate immune system to achieve an improved immune response reflects a promising approach to treat cancer patients

The combination of AFM24 with cytokine-stimulated and expanded NK cells (not SNK01) mediates tumor control in a mouse xenograft model with MDA-MB231 breast cancer cells[3]



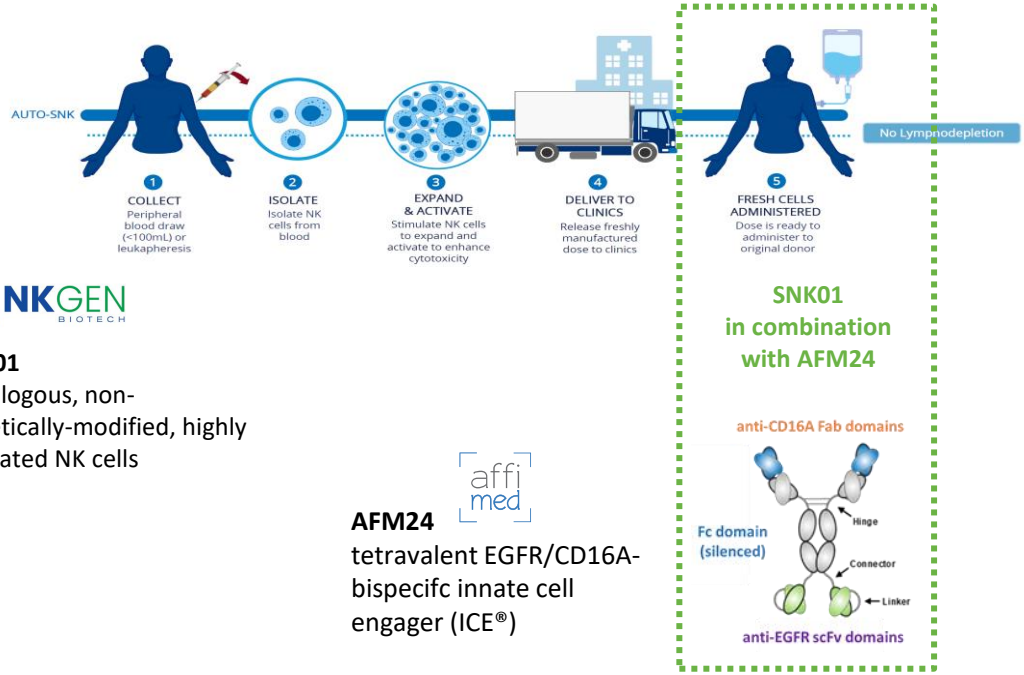


Pahl and Cerwenka, Immunobiology, 2015

[1]Pahl and Cerwenka, Immunobiology, 2015; Shin *et al.* Immune Netw., 2020; [2]Sawas et al.; 15-ICML, 2020 -AFM13; [3]Pahl *et al.* AACR2021

Rationale for AFM24 with Adoptive SNK01 NK Cells to Treat EGFR+ Solid Cancers

Abstract scope → Investigate benefit of SNK01 in combination with AFM24 towards EGFR⁺ A-431 cells *in vitro*



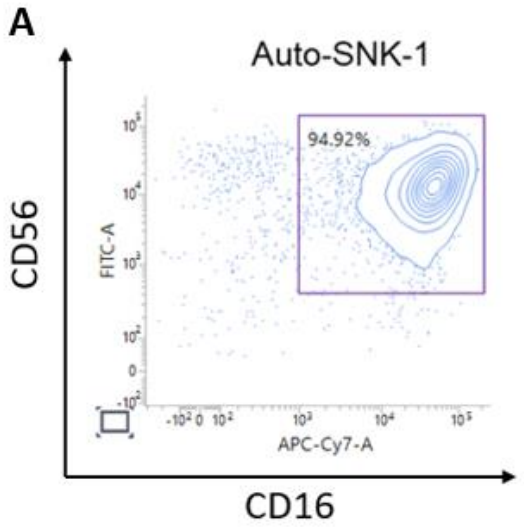
SNK01
Autologous, non-genetically-modified, highly activated NK cells

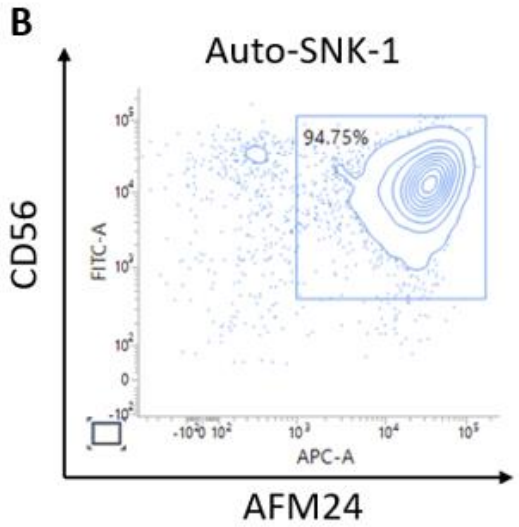
AFM24
tetravalent EGFR/CD16A-bispecifc innate cell engager (ICE®)

Summary of AFM24 + SNK01 Combination

- ✓ **SNK01: Ex-vivo activated & expanded NK Cells Potent & Cytotoxic anti-tumor activity in multiple solid tumor settings in clinical trials, regardless of patient's innate NK cell condition**
- ✓ **AFM24: Specific tumor targeting of NK cell cytotoxicity (ADCC) to EGFR⁺ tumor cells**
  - ✓ MoA (ADCC) independent of EGFR signaling cascade and its mutational status
  - ✓ MoA (ADCC) independent of CD16A allotypes, in the presence of serum IgG and at low target antigen density
- ✓ **AFM24 showed activity against numerous solid tumors and safety in preclinical studies**
- ✓ **AFM24 is currently being investigated in a Phase 1/2a monotherapy study in patients with EGFR⁺ tumors**

Binding of AFM24 to SNK01 Up To Saturation Level

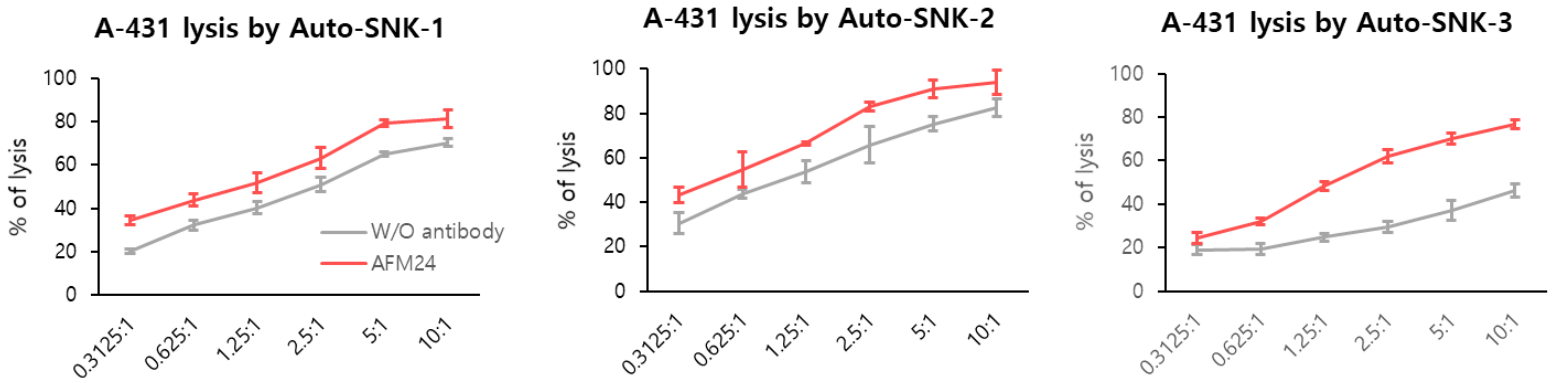




>80% SNK01 cells homogenously express high levels of CD16A as detected by flow cytometry

AFM24 binding levels match CD16A expression levels, indicating saturation of CD16 on SNK01 by AFM24

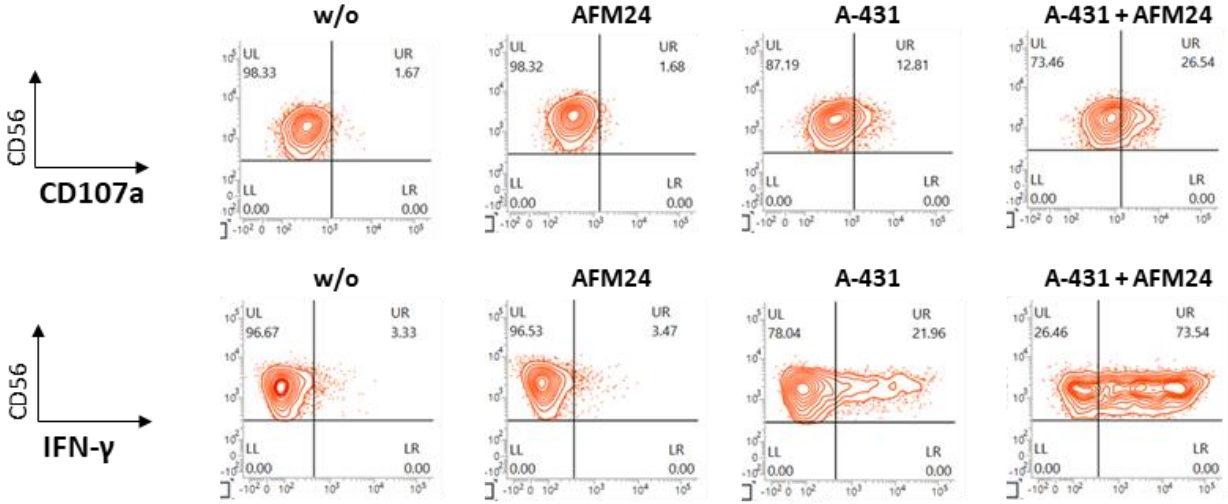
AFM24 Enhances the Killing of EGFR+ Tumor Cells by SNK01 NK Cells



Auto-SNK-1, Auto-SNK-2, Auto-SNK-3 representing NK cell products prepared from 3 different donors

AFM24 + SNK01 show favorable cytotoxic activity

AFM24 + SNK01 Enhanced Degranulation & IFN-γ towards EGFR+ Tumor Cells



AFM24 + SNK01 substantially increases degranulation (CD107a up-regulation) and intracellular IFN-γ in response to A-431 target cells

Note that in the absence of target cells, AFM24 + SNK01 does not show enhanced degranulation or IFN-γ

Conclusions

The combination of AFM24 with SNK01 NK cells is intended to:

- Introduce highly cytotoxic CD16+ SNK01 in EGFR+ tumor with an autologous platform
- Enhance the targeting ability of SNK01 + AFM24 in EGFR+ tumors
- Stimulate SNK01 cell cytotoxicity (ADCC) towards EGFR+ cell lines regardless of the mutational status of the EGFR signalling pathway and CD16A allotypes

Clinical development path of combining AFM24 + SNK01:

- Phase 1/2a Study: Collaboration between NKGen Biotech & Affimed
- Open-label, non-randomized, multi-center, US only, dose escalation and expansion trial in adult patients with EGFR+ tumors
- Phase 1: Establish safety and maximum tolerated dose or recommended phase 2 dose of AFM24+SNK01, PK, PD
- Potential Phase 2a: Evaluate the preliminary efficacy of AFM24 in combination with SNK01
- First-patient-in anticipated in H2/2021

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Thank you for your interest

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