ANKYRA

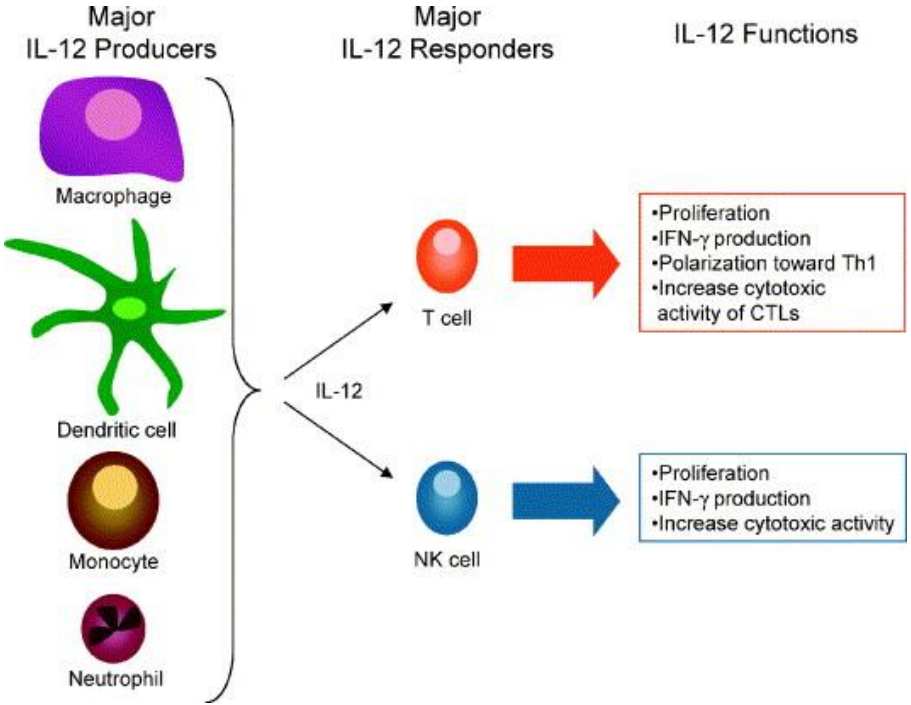
ankyratx.com

Baseline NKT cells as a potential predictive biomarker for treatment with an anchored IL-12 drug conjugate in patients with solid tumors

Lisa Sturla, PhD
Ankyra Therapeutics
Cambridge, MA

SITC Annual Meeting 2025

IL-12 is a cytokine integrating innate and adaptive immunity



- IL-12 has demonstrated potent anti-tumor activity in murine tumor models
- Systemic IL-12 has been tested in human cancer patients but was associated with significant toxicity
  - One way to mitigate poor therapeutic index is by intratumoral delivery

Watford et al. Cytokine Growth Fact Rev 2003

‘Anchored’ approach involves engineering the drugs to facilitate stable binding to aluminum hydroxide and retain them locally

Anchor

Aluminum hydroxide (alum) locally retained for weeks

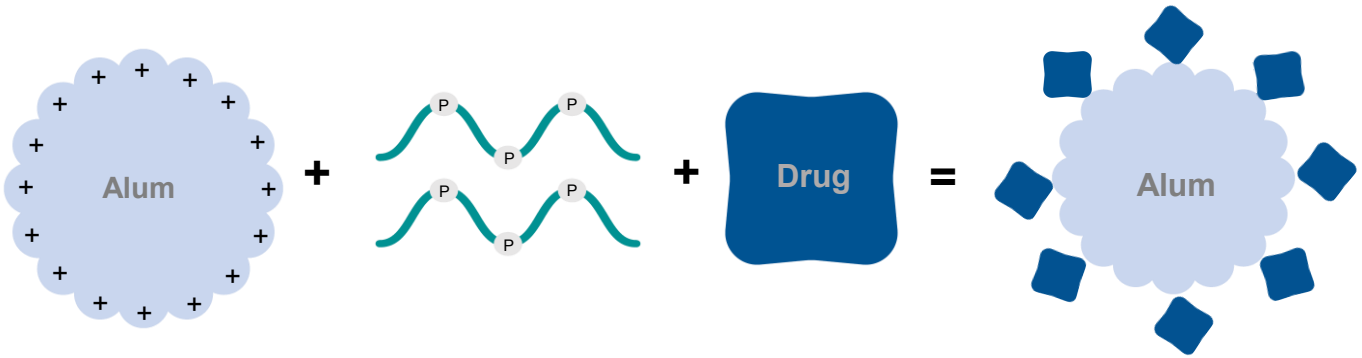
Conjugate

Alum-binding peptide (ABP) links drug to alum

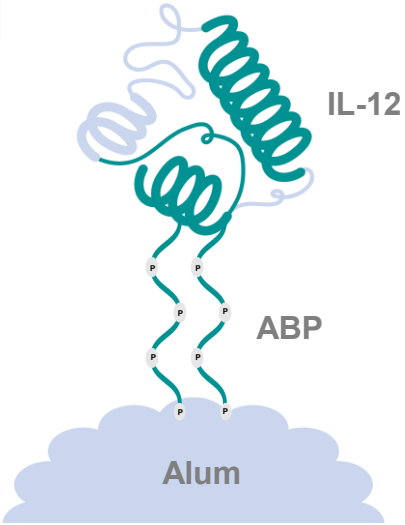
Drug

Highly potent immune modulators being delivered to tumors

Anchored Drug



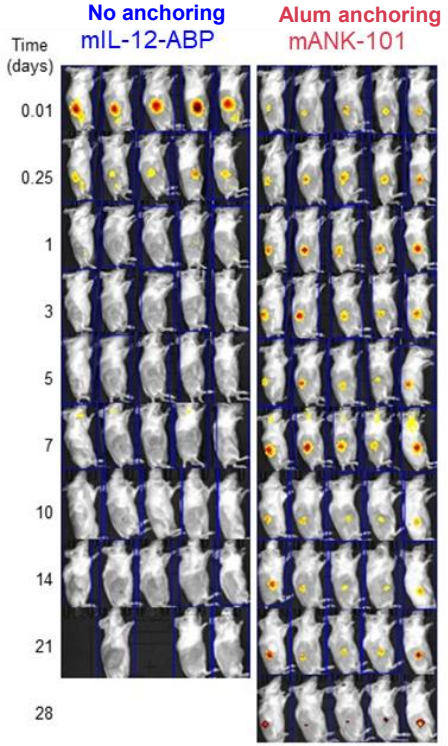
ANK-101



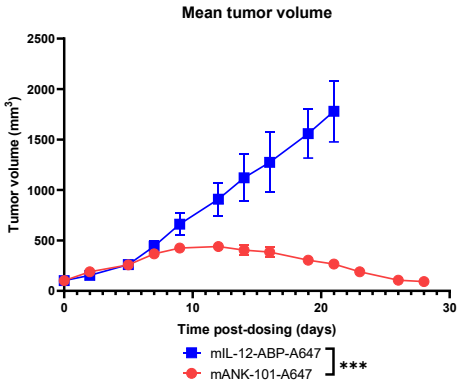
Sustained local exposure of drugs leads to:

- **Prolonged** anti-tumor immune activation
- **Minimal systemic side effects** due to less drug leakage
- Need for **fewer injections** to achieve benefit

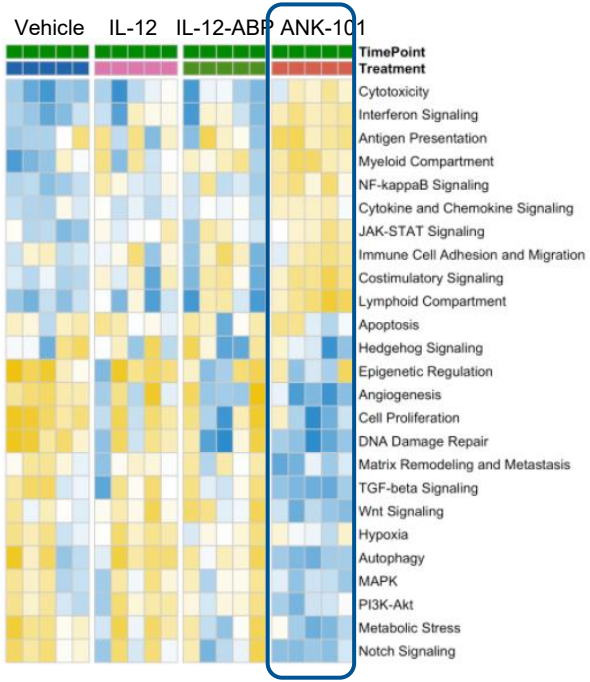
Anchored IL-12 (ANK-101) is retained in murine tumors for > 28 days and results in significant therapeutic and immune activity



Single injection

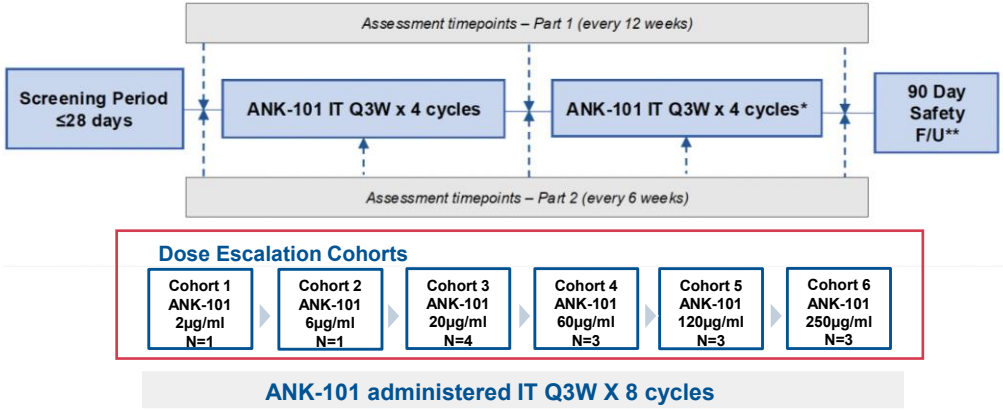


CT26 model, ***one*** 5µg dose of alexa 647 labeled IL-12-ABP+/- alum given IT and imaged by IVIS



Battula et al. JCI Insight 2023

ANK-101 FIH Phase 1 dose escalation study trial design



	Objectives	Endpoints
Primary	Determine the safety and tolerability of ANK-101	Incidence and characteristics of TEAEs according to NCI CTCAE v5.0
Secondary	Evaluate the preliminary clinical activity of ANK-101	ORR, DCR, DOR, and PFS by RECIST v1.1
	Evaluate serum PK of ANK-101	IL-12 ABP levels in serum
	Evaluate the immunogenicity (ADA) of ANK-101	ADA levels in serum
Exploratory	**Determine biomarker changes in participants treated with ANK-101**	• **Serum cytokine levels** • **Peripheral blood immune phenotyping** • **TIL analysis by IHC** • **Gene expression profiling (nanostring)**

- Part 1: Superficial tumors and Part 2: Visceral tumors
- Multiple solid tumor types
- Patients were heavily pre-treated with 73% having greater than 3 prior therapies
- 87% of patients had prior IO therapy

- ANK-101 dosed once every 21 days
- Tissue biopsies (Nanostring) and peripheral blood (Flow):
  - pre-treatment (C1D1)
  - 21 days post 1st dose (C2D1)
  - 21 days post 3rd dose (C4D1)
  - 21 days post 4th dose (C5D1)
  - End of treatment (EoT)

Exploratory biomarker data presentation for Part 1 superficial tumors only n=15

Park et al. Nature Comm 2025

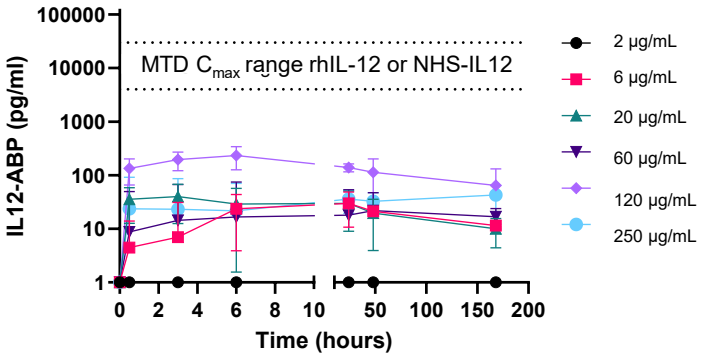
ANK-101 is well-tolerated without dose limiting toxicity (DLT)

Treatment Related Adverse Events

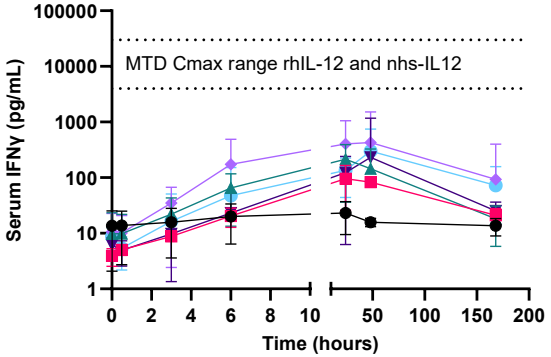
	Part 1 N=25
Any TRAE [n (%)]	14 (56)
Grade ≥ 3, [n (%)]	1 (4)
Most common any TRAE events [n (%)]	
Fatigue	5 (20)
Chills	5 (20)
Myalgia	4 (16)
Pyrexia	4 (16)
Malaise	3 (12)

Date updated: 14AUG2025

Serum IL-12-ABP



Serum IFNγ

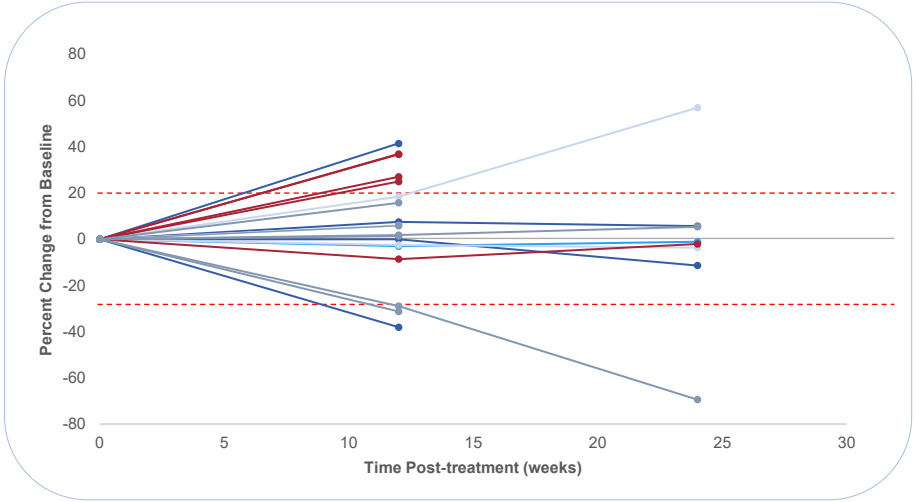


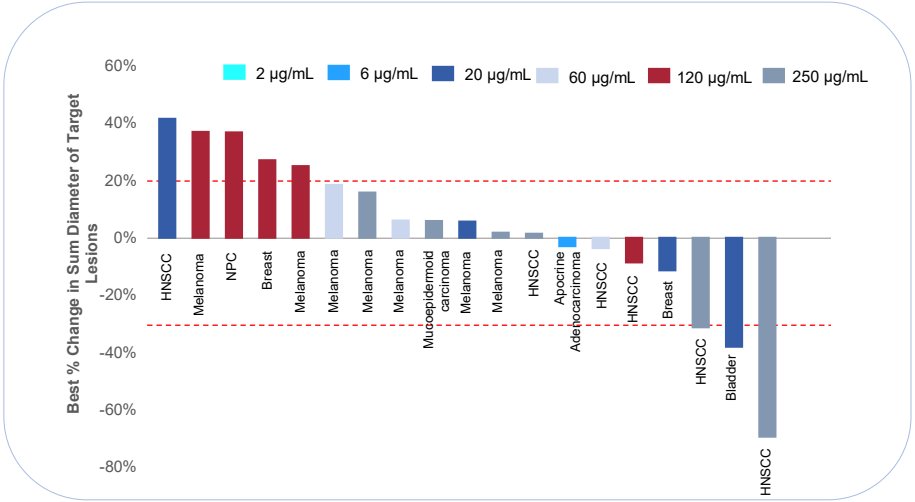
- **No DLTs observed**
- Most TRAE's were mild Grade 1-2
- ADA's detected in 5 out of 25 patients (patient response not affected)

- Serum IL-12-ABP levels **<1% of administered dose;** highest level detected was **1ng/mL**
- **Significantly lower IFNγ levels** compared with other systemic IL-12 delivery approaches

Strauss et al 2019: Clin Cancer Res. 25 (1): 99-109
Atkins et al 1997: Clin Cancer Res. 3(3): 409-17

ANK-101 demonstrates clinical activity in phase 1





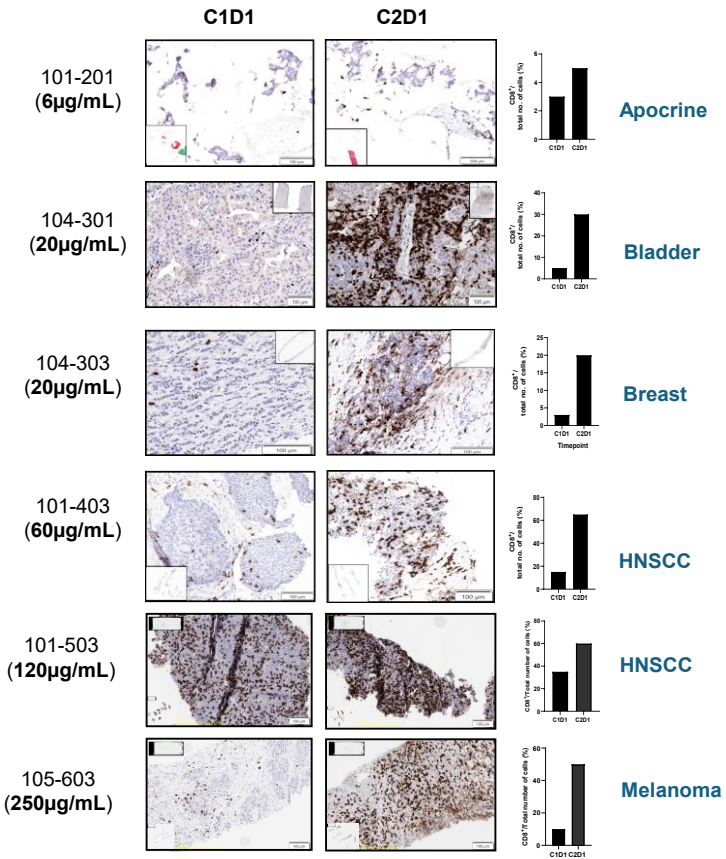
NPC: Nasopharyngeal carcinoma
HNSCC: Head and Neck Squamous Cell Carcinoma

- Disease control rate of 60-70% with objective responses observed at 250 µg/mL dose
- On-going response assessment in progress

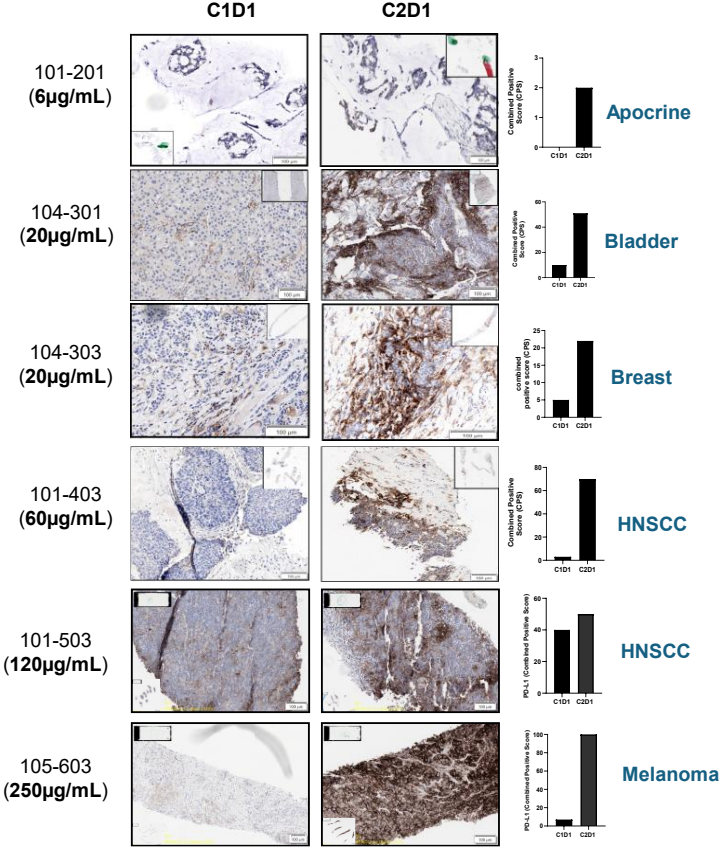
Date updated: 14AUG2025

ANK-101 induces local immune cell activation across tumor types

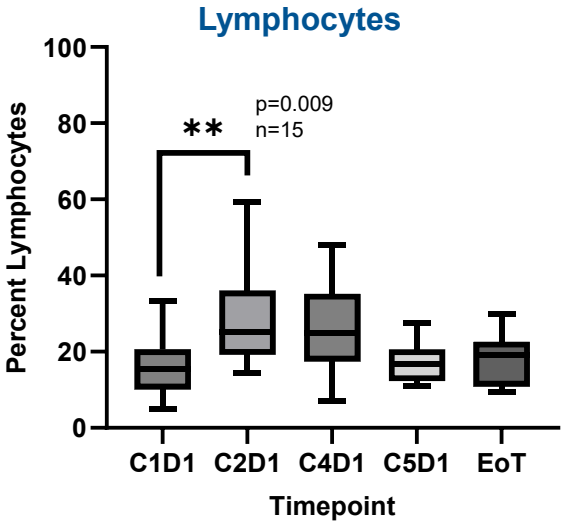
CD8⁺ T cell Infiltration

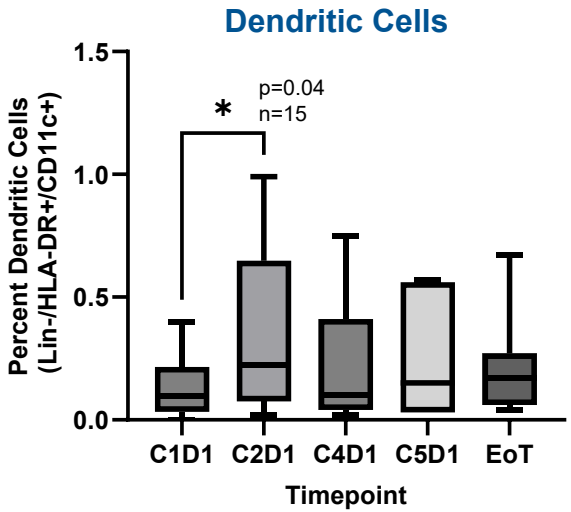


PD-L1 Expression



Peripheral lymphocytes and dendritic cells were increased in whole blood following ANK-101





Treatment Timepoint ID	Description
C1D1	Pretreatment
C2D1	21 days post 1st dose
C4D1	21 days post 3rd dose
C5D1	21 days post 4th dose
EoT	End of treatment

Following the first dose of ANK-101 the following was observed in 15 patients across 6 dosing cohorts:

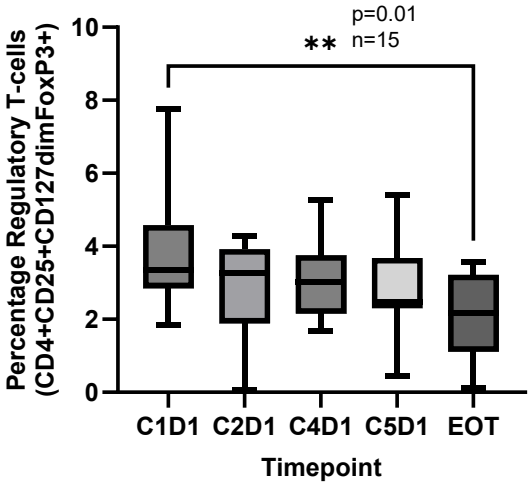
- Significant increases in **Lymphocytes** and **Dendritic Cells**
- Trend towards a decrease in **Granulocytes (data not shown)**
- No significant change in **B cells and NK cells (data not shown)**

Immune cell type quantification expressed as percentage of total immune cells

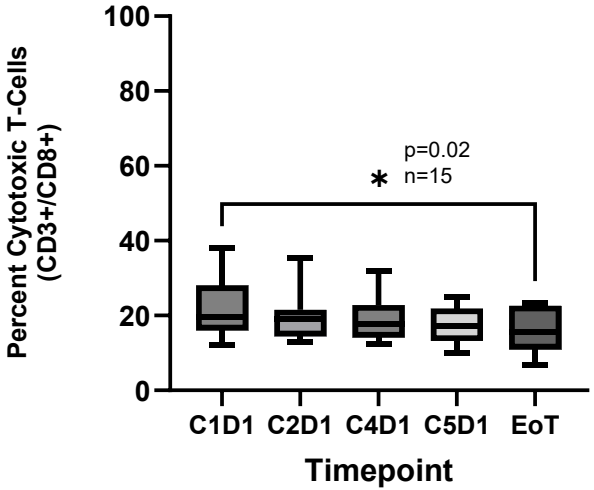
ANK-101 induced changes in peripheral T-cell populations

Peripheral regulatory T-cells (Treg) and cytotoxic CD8⁺ T cells decrease while intratumoral cytotoxic CD8⁺ T cells significantly increase in patients with disease control

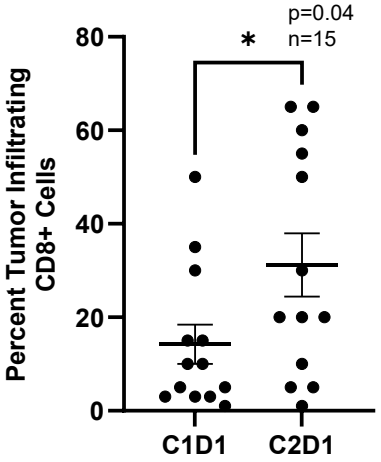
Peripheral regulatory T-cells



Peripheral CD8⁺ T-cells



Tumor infiltrating CD8⁺ T-cells

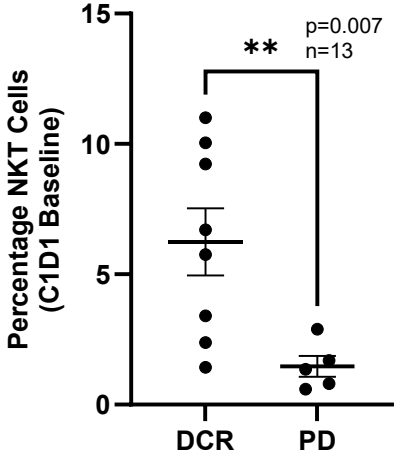


Flow cytometry

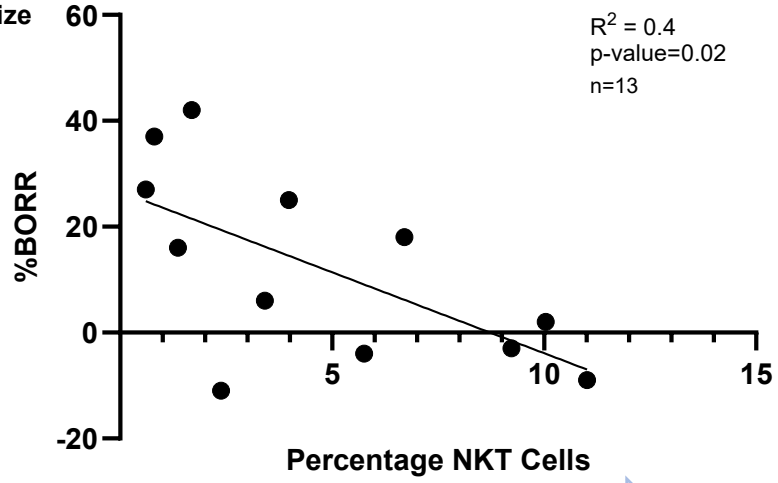
Immunohistochemistry

Immune cell type quantification expressed as percentage of total immune cells

Pre-treatment levels of circulating NKT cells are associated with disease control following ANK-101 treatment



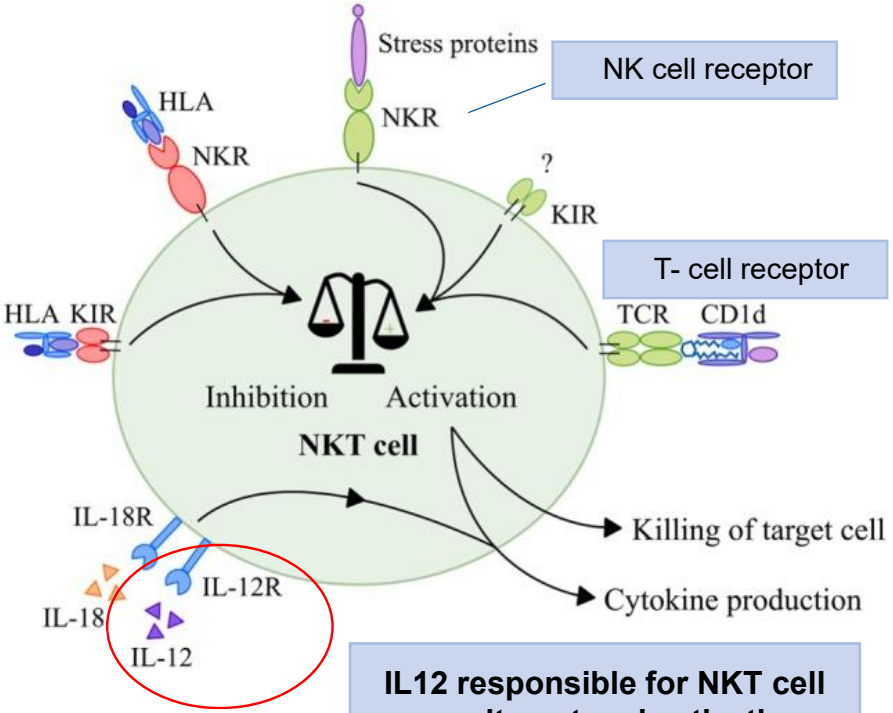
Lesion Size



DCR: Disease control (stable disease/objective response)
PD: Progressive disease

Peripheral NKT cell numbers are significantly higher at baseline in patients with disease control during ANK-101 treatment

Baseline NKT cells may be a predictive biomarker of response to IL-12 treatment



- Natural Killer T (NKT) cells constitute 2-4% of lymphocytes sharing markers like CD1d, NK1.1, CD161, and IL2R with T cells and NK cells
- NKT cells possess a constitutive "effector-memory" phenotype
- Involved in immune surveillance and show potential for immunotherapy
- Patients with elevated baseline NKT cells appeared to be more likely to achieve disease control with anchored IL-12 treatment

Further studies are warranted to better define the role of NKT cells as a predictive biomarker of response to IL-12 immunotherapy

Krijgsman et al 2018: Frontiers in Immunology 9 (367)