ABSTRACT #TPS2678

A Phase 1b, Two-Arm Study of Tolododekin Alfa (ANK-101) in Combination with an Anti-PD-1/PD-L1 Antibody in Participants with Advanced Non-Small Cell Lung Cancer (NSCLC)

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Background

- Interleukin-12 (IL-12) exerts its anti-tumor effector function through induction of IFNγ and activation of cytotoxic CD8+ T-cells and Natural Killer cells.
- Alum anchored IL-12 (ANK-101) allows prolonged retention within the tumor microenvironment with less systemic toxicity[1] (Figure 1)

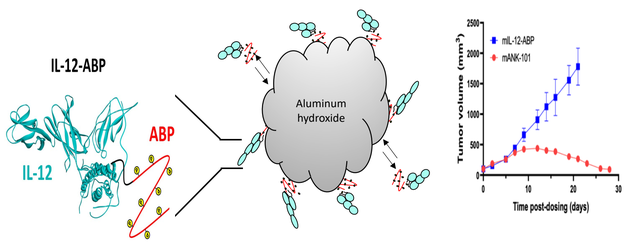


Figure 1: Ankyra anchored cancer drug therapy platform

- Native IL-12 is fused to a proprietary alum-binding peptide (ABP), phosphorylated via Fam20C co-expression, and complexed with Alhydrogel® to form ANK-101 for local retention at the injection site
- A single dose of mANK-101 (mouse surrogate) demonstrates superior efficacy versus unanchored mIL-12-ABP in the CT26 syngeneic mouse model[1]

- A significant upregulation of PD-L1 was observed with ANK-101 treatment (Figure 2A) supporting the rationale for combination with systemic anti-PD-1 antibody
- Combination of intratumoral ANK-101 and systemic PD-1 blockade demonstrated clearance of 100% of injected tumors in the MC38 (Figure 2B) and CT26 (Figure 2C and D) mouse models leading to a significant increase in overall survival[1]

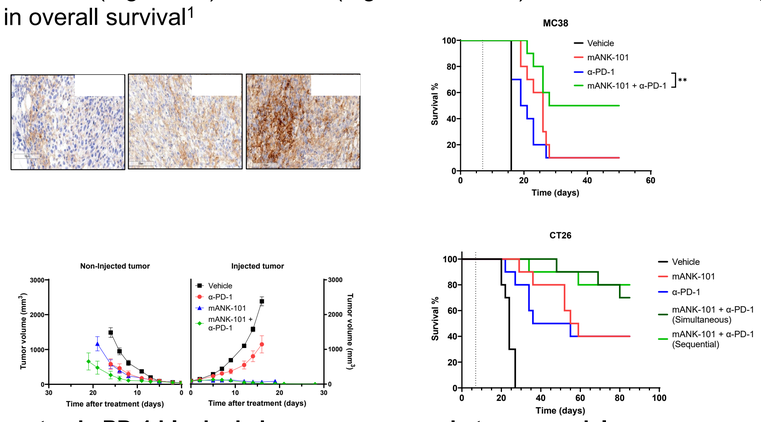


Figure 2: ANK-101 and systemic PD-1 blockade in mouse syngeneic tumor models

- ANK-101 monotherapy has been shown to be safe and well tolerated in a Phase 1 clinical trial[2]
- Combination of ANK-101 and systemic PD-1 blockade in superficial cutaneous squamous cell carcinoma (cSCC) patients is on-going
- **LANTERN trial is designed to test combination of ANK-101 and systemic PD-1 blockade in NSCLC**

Objectives

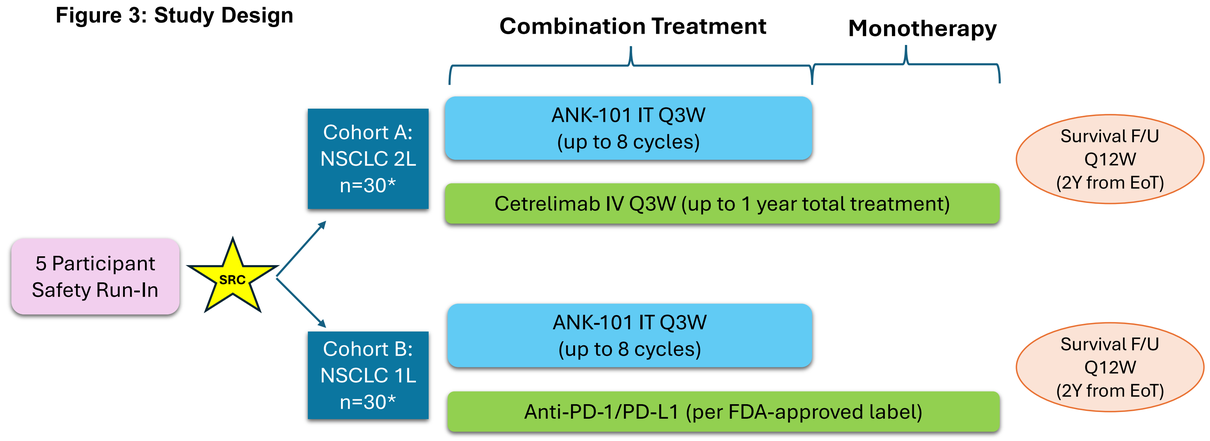
	Objectives
Primary	Determine the safety and tolerability of ANK-101 in combination with an anti-PD-1/PD-L1 antibody in participants with locally advanced or metastatic NSCLC who have progressed on prior standard of care (Cohort A) or treatment naïve with PD-L1 ≥ 50% (Cohort B)
Secondary	Evaluate the preliminary clinical activity of ANK-101 activity in combination with anti-PD-1/PD-L1 antibody in injected and non-injected lesions
	Evaluate systemic PK
	Evaluate the immunogenicity (ADA) of ANK-101 in combination with anti-PD-1/PD-L1 antibody
Exploratory	Evaluate immune responses and determine biomarker changes in participants treated with ANK-101 in combination with anti-PD-1/PD-L1 antibody

Clinical Sites



Study Design

Figure 3: Study Design



- Multicenter, Phase 1b, two-part, open-label study of intratumoral (IT) injection of ANK-101 administered in combination with an anti-programmed cell death protein 1 (PD-1)/programmed cell death ligand 1 (PD-L1) antibody in participants with locally advanced or metastatic non-small cell lung cancer (NSCLC)
- Participants with epidermal growth factor receptor (EGFR)- or anaplastic lymphoma kinase (ALK)-mutated NSCLC will be excluded from both Cohorts A and B
- Initial sample size will be 30 participants in each cohort (total 60)
- The first 5 participants enrolled in the study (regardless of cohort) will be included in a safety run-in
- Participants will receive ANK-101 administered on Day 1 of each 21-day cycle (once every 3 weeks [Q3W]) by IT injection in combination with an anti-PD-1/PD-L1 antibody. Cetrelimab is an investigational, humanized anti-PD-1 antibody used in this study
- Imaging will be conducted at baseline and every 6 weeks
- Blood and tumor biopsies will be collected for PK and immune analyses

Study Eligibility

Key Inclusion Criteria	Key Exclusion Criteria
≥ 18 years of age	**Cohort A only:** Participants with Grade 3 or higher toxic effects or treated with anti-tumor necrosis factor (TNF) or anti-interleukin-6 (IL-6) agents to manage AEs from previous treatment with immunotherapy are excluded from receiving cetrelimab. **Cohort B only:** Prior therapy with an immune checkpoint inhibitor. **Note:** Adjuvant therapy, prior to the development of metastatic disease, is allowed ≥ 6 months prior to C1D1 or neoadjuvant therapy ≥ 3 months prior to C1D1, provided participants have recovered from any prior AEs to Grade 1 or lower.
Have histologically or cytologically confirmed locally advanced or metastatic NSCLC (per the 8th American Joint Committee on Cancer [AJCC]). **Cohort A only:** Have documented disease progression or be refractory to an anti-PD-1/PD-L1 antibody and a platinum-based chemotherapy regimen approved for NSCLC, either in combination or sequentially. **Cohort B only:** Have not received prior systemic treatment for locally advanced or metastatic NSCLC and have PD-L1 ≥ 50% by local testing using an FDA-approved assay or in a Clinical Laboratory Improvement Amendments (CLIA)-approved laboratory.	Have known EGFR or ALK mutations by local testing. Prior treatment with recombinant interleukin-12 (IL-12). Have primary or acquired immunodeficient states (e.g., leukemia, lymphoma). Have active autoimmune disease or medical conditions requiring chronic steroid (i.e., ≥ 10 mg/day prednisone or equivalent) or other immunosuppressive therapy within 28 days prior to the start of C1D1; participants.
Have measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1	Have known active uncontrolled hepatitis B virus, or hepatitis C virus.
Cohort A only: Last dose of previous anticancer therapy (including investigational agents) ≥ 28 days, radiotherapy ≥ 14 days (targeted palliative radiotherapy is allowed for lesions not planned for injections), or surgical intervention ≥ 21 days prior to C1D1. **Cohort A only:** Thyroid-stimulating hormone (TSH) within normal limits. If TSH is not within normal limits at baseline, total T3 or free T3 and free T4 must be within normal limits.	Have uncontrolled bleeding disorders within 28 days prior to C1D1 or known bleeding diathesis.
Have adequate bone marrow, hepatic function and renal function defined as creatinine clearance ≥ 50 mL/min as determined by the Cockcroft-Gault equation.	Have a history of allogeneic tissue/solid organ transplant.

Study Status

For additional information clinicaltrials.gov identifier NCT # NCT07027514

References

[1]Battula S. et al 2023: Intratumoral aluminum hydroxide-anchored IL-12 drives potent antitumor activity by remodeling the tumor microenvironment: JCI insight 8(23): 1-19.
[2]Park et al 2025: Interleukin-12 anchored drug conjugate (tolododekin alfa) in patients with advanced solid tumors: first in human Phase 1 trial: Nature Communications 16: 8567.

Acknowledgments

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