ABSTRACT # 677

A Phase 1, Open-Label, Dose Escalation Study of the Safety and Tolerability of ANK-101 in Advanced Solid Tumors*

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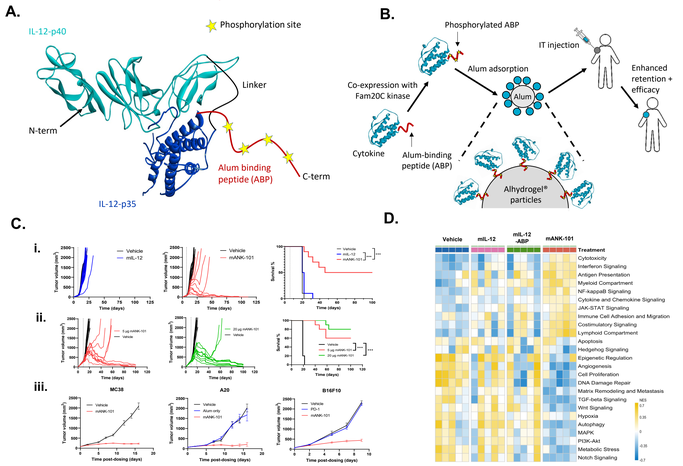
Background

- Cytokines have demonstrated anti-tumor activity in patients with cancer but usually require high doses resulting in significant systemic toxicity
- Human interleukin-12 (IL-12) is composed of a p35 and p40 subunit (Fig. 1A) and exerts its effector function through activation of T and NK cells and induction of interferon-gamma
- Systemic IL-12 promotes potent anti-tumor effects but was associated with serious systemic toxicity in clinical trials
- ANK-101 is a novel anchored IL-12 drug composed of IL-12 linked to aluminum hydroxide (Alhydrogel®) via an alum-binding peptide (ABP) (Fig. 1B)1
- ANK-101 allows prolonged retention of IL-12 within the tumor microenvironment without systemic toxicity [2-3]

Figure 1: Schematic of ANK-101 complex



***A**. Single-chain human IL-12 with wild-type p40 and p35 sequences was genetically fused at its C-terminus to an alum-binding peptide (ABP) to form IL-12-ABP, and complexed with a 10X mass excess of Alhydrogel© to form ANK-101.*
***B**. Cytokines and other potent immune agonists are genetically fused to a proprietary ABP and co-expressed with Fam20C kinase to phosphorylate the peptide at multiple serine residues. The phosphorylated fusion proteins are mixed with the Alhydrogel® (aluminum hydroxide) to form a spontaneous complex. Cytokine/Alhydrogel© complexes are administered IT where they are locally retained due to their size and charge, leading to a cytokine depot that promotes potent and long-lasting local immune activation.*
***C**. (i) Tumor volume (TV) and survival for BALB/c mice (10/group) bearing ~80 mm^3 CT26 tumors that were administered a single IT injection of vehicle, 5 µg mIL-12, or 5 µg mANK-101. (ii) Tumor growth curves and survival of BALB/c mice bearing ~300 mm^3 CT26 tumors administered two IT doses of vehicle, 5 µg or 20 µg mANK-101 ten days apart. (iii) 5 µg mANK-101 was tested for anti-tumor response in various syngeneic tumor models.*
***D.** C57Bl/6 mice bearing MC38 tumors were administered a single IT injection of vehicle or 5 µg of mANK-101. Tumors were harvested 7 days post-treatment and transcriptional analysis was performed by Nanostring (PanCancer IO 360 panel).*

Objectives

Primary Objectives:

- The safety and tolerability of escalating doses of ANK-101
- To determine the RDE of ANK-101

Secondary Objectives:

- To evaluate the PK of ANK-101
- To evaluate the immunogenicity (ADA) of ANK-101
- To evaluate the preliminary clinical activity of ANK-101

Exploratory Objectives:

- To determine immune responses and biomarker changes in participants treated with ANK-101
- To assess the QOL while on ANK-101 treatment

Study Design

- The study is comprised of 2 parts: Part 1, superficial tumors, and Part 2, visceral tumors. Both parts have dose-escalation and dose-expansion cohorts (Fig. 2)
- Part 1 will be restricted to superficial lesions and Part 2 will enroll subjects with visceral disease; Part 2 cohorts may begin following the DLT period of cohort 1 in Part 1 dosing cohort
- Dose-escalation cohorts in Part 1 and Part 2, the accelerated dose-escalation method with a single subject for the first 3 dose levels (DL) will be used followed by the standard 3+3 design for the next 3 DLs
- There will be a 21-day DLT period after the first dose at each cohort
- Subjects will receive four doses every 3 weeks and may repeat an additional four doses in the absence of disease progression or significant toxicity (Fig. 3)
- Response assessment will be conducted at baseline and every 12 weeks for Part 1 and every 6 weeks for Part 2
- Blood and tumor biopsies will be collected for PK and immune analyses

Figure 2: Phase 1 dose-escalation and dose-expansion schema

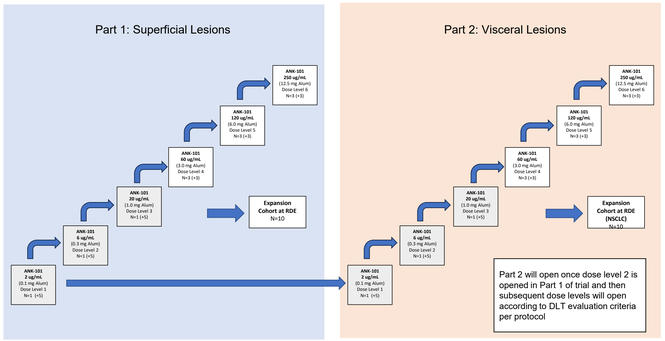
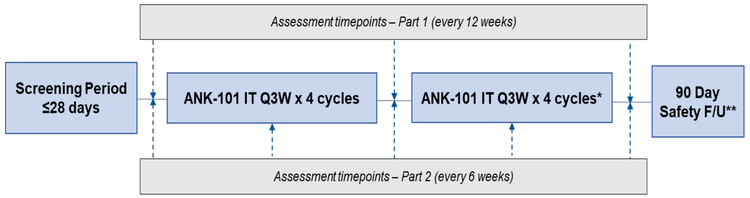


Figure 3: Treatment plan



*if there is no significant clinical deterioration as determined by the Investigator, or unacceptable toxicity at Week 12, participants may receive four more cycles provided they continue to meet eligibility criteria
**The 90-day Safety Follow Up/EOS visit is to occur either by phone or in clinic 90 days from the last dose of ANK-101. If the visit occurs in-clinic, then all assessments should be performed. If this visit is by phone, then only AEs and concomitant medications will be collected.

Study Status

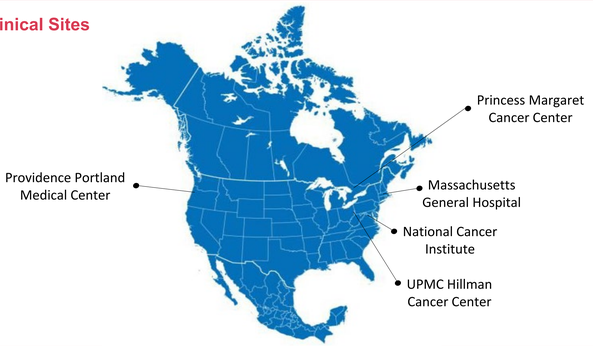
As of October 15th, 2024, a total of 15 participants have been enrolled in the study. 12 participants in Part 1 and 3 participants in Part 2. For additional information clinicaltrials.gov identifier NCT # 06171750

Study Eligibility

Key Inclusion Criteria	Key Exclusion Criteria
≥ 18 years of age	Injectable tumors impinging upon major airways or blood vessels
Have histologically or cytologically confirmed advanced solid tumor malignancy. Participants with metastatic disease will be eligible. **Part 1 only:** Tumor(s) must be cutaneous, subcutaneous, soft tissue, or nodal in locations that are visible, palpable, or detectable by ultrasound. **Part 2 only:** Participants must have at least one tumor located in deep viscera able to be accessed by interventional radiologic or endoscopic procedures for injection (e.g., ultrasound or computed tomography [CT] guided). **Part 2 Dose Expansion Cohort only:** Histologically confirmed Stage III or Stage IV NSCLC.	Prior treatment with recombinant interleukin-12 (IL-12). Have received live vaccines within 28 days prior to the start of ANK-101 treatment (C1D1). **Note:** Administration of attenuated vaccines is allowed. Have primary or acquired immunodeficient states (e.g., leukemia, lymphoma). Have had prior organ or hematopoietic stem cell transplantation. Have known active central nervous system (CNS) metastases
Have measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1	Have known history of hepatitis B virus, known active hepatitis C virus.
Have documented disease progression, be refractory to, or intolerant of existing standard of care (SOC) therapy(ies) known to provide clinical benefit for their condition (including surgical cure) or not be eligible for SOC therapy(ies).	HIV-infected participants with a history of Kaposi sarcoma and/or Multicentric Castleman Disease.
Have adequate renal, hepatic, and bone marrow function.	Have active autoimmune disease or medical conditions requiring chronic steroid treatment (i.e., ≥ 20 mg/day prednisone or equivalent).

Clinical sites

Figure: 4 Clinical Sites



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