AMPLIFY-7P: Phase 1 and randomized phase 2 study of amphiphile immunotherapy ELI-002 7P as adjuvant treatment for subjects with G12D, G12R, G12V, G12C, G12A, G12S and G13D Kirsten rat sarcoma (KRAS)-mutated pancreatic ductal adenocarcinoma (trial in progress)

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Background

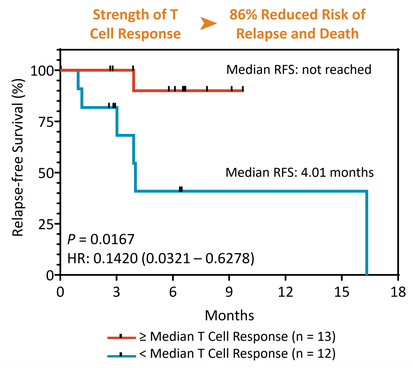
- Mutations in the RAS oncogenes KRAS, NRAS and HRAS occur in approximately 25% of all solid tumors, G12D is the most common isoform
- KRAS-specific T cells have demonstrated objective antitumor activity in several studies in pancreas cancer[1].
- Amphiphiles (Amph) are a novel cancer vaccine technology that acts by "hitchhiking" on albumin to promote delivery into lymph node-resident antigen presenting cells

AMPLIFY-201 Phase 1 Study Results

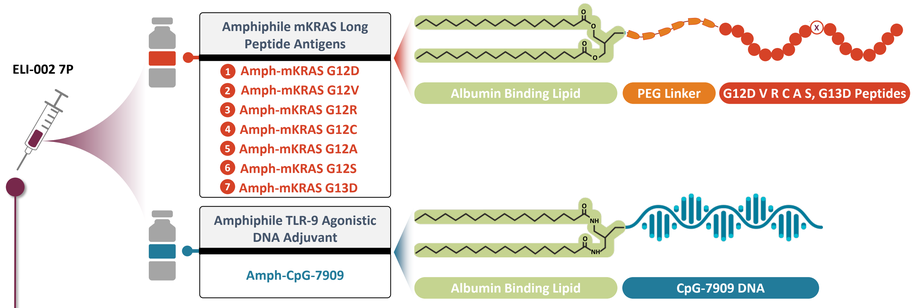
Phase 1 dose escalation of ELI-002 2P in pancreatic and colorectal cancer patients who had completed locoregional treatment but remained minimal residual disease (MRD) positive[2-4] demonstrated safety and early signals of antitumor effect including:

- Tumor biomarker reductions in 84% of patients; tumor biomarker clearance in 24% of patients
- Direct ex vivo measured T cell responses in 84% of patients; 100% of patients at the recommended phase 2 dose
- T cell responses correlated with clinical outcomes including biomarker reduction/clearance and RFS

Pant, et al. Lymph Node Targeted, mKRAS-specific Amphiphile Vaccine in Pancreatic and Colorectal Cancer: The phase 1 AMPLIFY-201 Trial. **Nature Medicine.** 2024

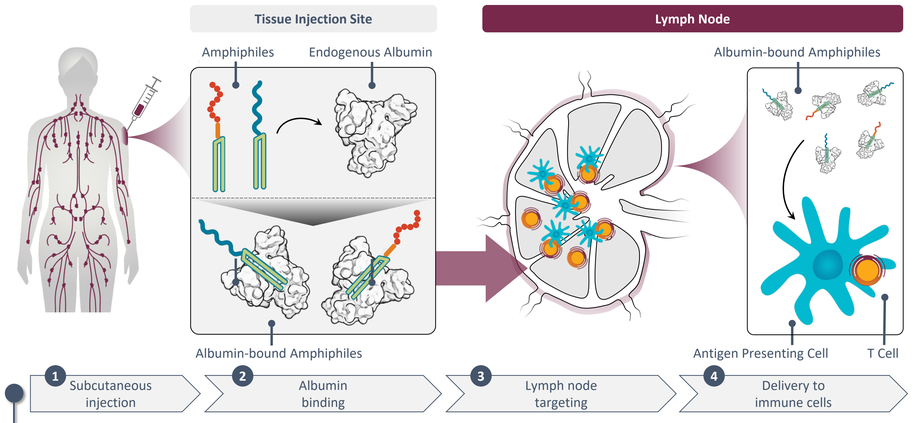


Designing a Therapeutic Vaccine Targeting mKRAS: ELI-002 7P



- Inclusion of **18-mer mKRAS peptides** allows for delivery of **diverse HLA I and II –restricted epitopes** for presentation on varied patient HLA molecules
- **Amphiphile (Amph)-modification of peptides** promotes binding to endogenous albumin at the injection site to promote collection in lymphatic vessels for **lymph node delivery**, and prevents peptide uptake into local capillaries avoiding delivery to irrelevant or tolerogenic sites
- **Amph-CpG-7909 provides** potent immune activation via TLR-9 stimulation of lymph node-resident professional antigen presenting dendritic and other key immune cells

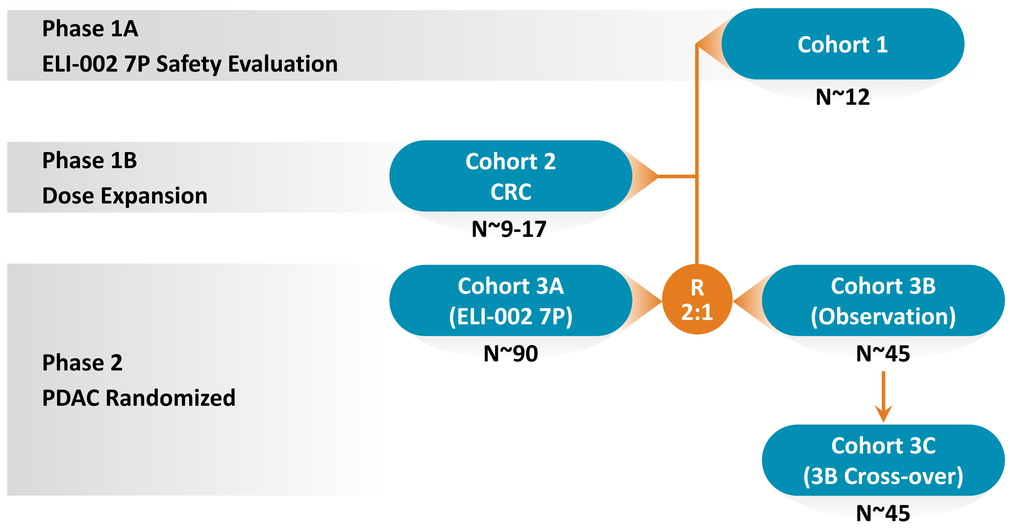
The Amphiphile Platform: Targeting the Lymph Nodes



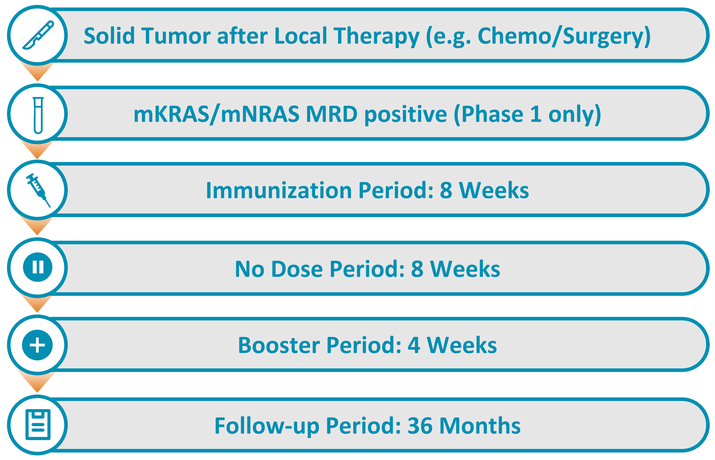
- **Conventional vaccine components** (eg. peptide antigens and molecular adjuvants) are rapidly absorbed into blood capillaries after administration leading to **poor delivery to lymph nodes where protective immune responses are orchestrated.**
- **Amph-modification promotes albumin binding to reprogram vaccines for enhanced lymph node delivery** resulting in coordinated transport of antigen and adjuvant to immune cells. Improved uptake by Antigen Presenting Cells results in enhanced **antigen-presentation and co-stimulation to cognate T cells.**
- Restricted delivery to lymph nodes **prevents systemic exposure to avoid toxic effects of potent adjuvants.**

The AMPLIFY 7P trial: Lymph node targeted vaccine ELI-002 7P in patients with RAS mutated pancreatic and colorectal tumors after locoregional treatment

ELI-002-201 Cohort Schematic



ELI-002-201 Study Design



Key Inclusion / Exclusion Criteria

1 Inclusion Criteria

- KRAS mutation G12D, G12V, G12R, G12C, G12A, G12S or G13D
- Phase 1 only: MRD positive (ctDNA, CA19-9, CEA)
- PDAC: Up front resectable stage I, II, or III pancreatic adenocarcinoma within 6 months following completion of locoregional treatment with or without radiation, R0/R1 surgery, radiographic NED
- CRC: stage II (T4NO), III, or oligometastatic stage IV following completion of locoregional treatment, R0/R1 surgery, radiographic NED
- Absolute Lymphocyte Count ≥1.0 x 10^9/L (or pre-chemo baseline)
- ECOG 0 or 1

2 Exclusion Criteria

- Previous ELI-002 or cancer vaccine
- Use of immunosuppressive drugs

Hypotheses

- Immunotherapy is anticipated to succeed in the adjuvant setting since the trafficking of T cells into tumor and the ratio of effector T cells to target tumor cells may be enhanced prior to visible disease
- Phase 1: ELI-002 7P is safe and leads to tumor biomarker reduction in ≥30% of patients
- Phase 2: ELI-002 7P prolongs Disease Free Survival vs Standard of Care (Observation)

Study Design

- Phase 1 patients received fixed 10.0 mg doses of AMP-CpG adjuvant at one of two AMP-Peptides 7P dose levels (1.4 mg or 4.9 mg)
- Phase 2 patients are randomized 2:1 to receive the RP2D (10.0 mg AMP-CpG with 4.9 mg AMP-peptides 7P) or to observation
- Phase 2 crossover at confirmed radiographic disease progression (iRECIST)

1 Primary and Secondary Endpoints

- Primary: Disease free survival per investigator (iRECIST)
- Secondary: Evaluate biomarker reduction and clearance compared to baseline
  - Median overall survival (OS)
  - Assess safety
  - ORR (objective response rate) per iRECIST (in cross-over cohort)
- Exploratory: Immunogenicity of ELI-002 7P compared to baseline

2 Treatment

- Immunization Period: 6 ELI-002 7P doses
- Booster Period (2 months after Immunization Period): 4 additional ELI-002 7P doses
- Follow up continues x 36 months

3 Statistics

- Phase 2 interim analysis using group sequential design for control of overall alpha 0.10

4 Biomarker Evaluations

- ctDNA and serum tumor biomarker
- Apheresis for T cells - mechanism of action biomarkers
- High Resolution HLA typing

STUDY INFORMATION

- **Status: Phase 2 Recruiting**
- **Phase 1A has been completed with no dose-limiting toxicities**
- **An IDMC reviewed Phase 1A and opened Phase 2 (PDAC) to enrollment**
- **Phase 1B (Colorectal) is planned (currently not active)**
- **ClinicalTrials.gov: NCT05726864**

References

1. Tran, et al., **NEJM.** 2016
2. O'Reilly et al., **ASCO 2023 Annual Meeting.** 2023: Abstract 2528
3. Wainberg et al., **AACR Special Conference on Pancreatic Cancer.** 2023: Abstract C092
4. Pant et al. **Nature Medicine.** 2024

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