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Abstract 1317

AMPLIFY-7P Phase 2: T cell responses induced by lymph node-targeted amphiphile therapeutic cancer vaccine in patients with KRAS mutated pancreatic ductal adenocarcinoma

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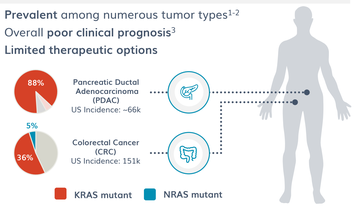
Why Target mutated KRAS with Therapeutic Immunotherapy?

1 Mutant KRAS Drives 25% of Solid Human Cancers

- **Prevalent** among numerous tumor types[1-2]
- Overall **poor clinical prognosis**[3]
- **Limited therapeutic options**



2 Mutant KRAS is a Promising Tumor Antigen

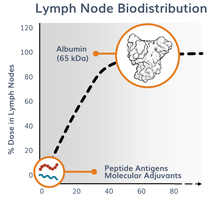
- **Truncal**: mutations occur early, expressed uniformly in all tumor cells
- **Driver**: mKRAS signaling is required for tumor growth and survival
- **Highly prevalent**: involved in ~25% of solid tumors[1-2]
- **Public neoantigen**: not centrally tolerized, cognate TCRs present in naïve repertoire[4-5]
- **Promiscuous HLA presentation**: off-the-shelf use in diverse patient population[6-8]
- **Demonstrated Clinical MOA**: 88% reduction in risk of progression or death in patients with ELI-002 2P induced mKRAS-specific T cell responses above 9.17x threshold with mOS of 28.9 months and mRFS of 16.3 months[9,13-14]
- **Multi-targeting potential**: recognition of clonal and subclonal mKRAS variants to prevent escape[10]

The AMP-Platform: Enhanced Lymph Node Delivery

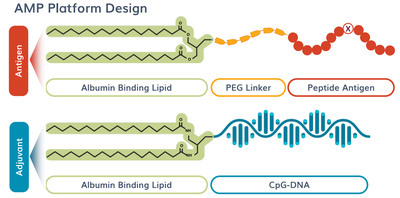
- **Smart trafficking to the lymph nodes** after subcutaneous dosing demonstrates immune responses with increased magnitude, function, and durability[11-12]
- **Designed to take advantage of potent lymph node immune mechanisms**, including activation of innate and adaptive immune cells, antigen-spreading, and improved tumor T cell trafficking / infiltration

Immunotherapy Design

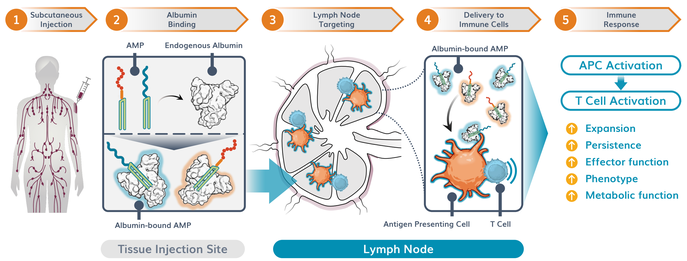
Lymph Node Biodistribution



AMP Platform Design



Mechanism of Action



Randomized, Controlled Phase 2 Study Ongoing for Adjuvant Treatment of PDAC

Randomized Phase 2

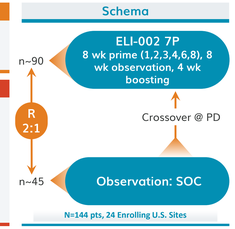
Monotherapy (no chemo, CPI combo)

- ✓ mKRAS: Expanded Antigen Coverage: G12D / V / R / C / A / S / G13D

Phase 2: Key Criteria

- ✓ Includes: mKRAS G12D / V / R / C / A / S / G13D
- ✓ Up front resectable Stage I, II or III disease (PDAC)
- ✓ Complete R0/R1 resection
- ✓ Radiographic NED status within 6 months following completion of locoregional treatment
- ✓ MRD agnostic (biomarker +/- included)

Schema



Endpoints

- Primary Endpoint: Disease-Free Survival
- Secondary: Tumor Biomarker Response (biomarker subset)
- Secondary: Overall Survival, Safety, iRECIST Overall Response Rate

Exploratory: Immunogenicity

- Direct Ex vivo T cell Analysis
- Fold change from baseline
- CD4 + CD8 T cells
- Response to mKRAS variants

Dosing

- 4.9 mg Amph-Peptides 7P + 10.0 mg Amph-CpG-7909 (6 dose priming series over an 8-week period comprised of one dose weekly for the first 4 weeks, followed by one dose every 2 weeks over the second 4 weeks, a 2 month no dose period, then a booster period with one dose weekly over 4 weeks)

Safety

- IDMC recommended that the Phase 2 trial continue to final analysis without modifications and confirmed the favorable safety profile of ELI-002 7P.

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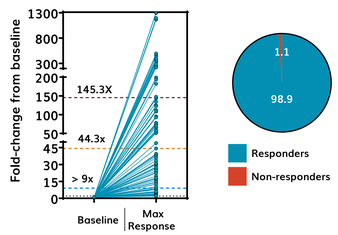
mKRAS-specific T Cell Responses in ELI-002 7P Immunized Patients

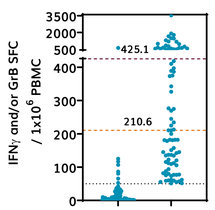
AMPLIFY-201 T Cell Fold-Changes



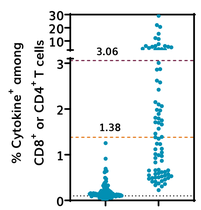
- 96 patients were randomized to ELI-002 7P and 90 patients had evaluable baseline and post-treatment PBMC timepoints
- T cells detectable by standard direct ex vivo Fluorospot and flow cytometry, with no expansion required
- **98.9% (89/90) of patients had mKRAS-specific T cell responses**
- 145.3x average fold-change in T cell numbers from baseline (median 44.3; range 2.13-1310x)
- 80% (72/90) of patients had max T cell fold-change responses above 9x over baseline, which correlated with clinical activity in two previous Phase 1 trials[9,13-14]

ELI-002 7P Generated Robust mKRAS-specific T cell Responses

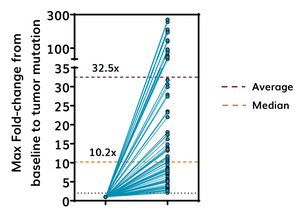
Ex Vivo Fluorospot



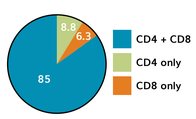
Ex Vivo ICS



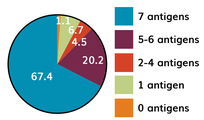
Fold-change to Tumor Mutation



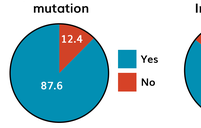
CD4 / CD8 T Cell Response



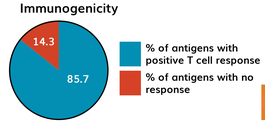
mKRAS Specificity



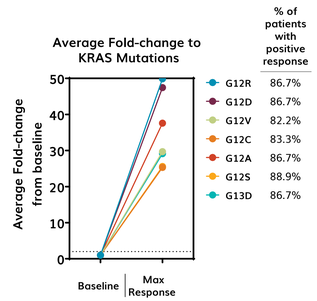
Response to Tumor mutation



Overall Immunotherapy Immunogenicity



Average Fold-change to KRAS Mutations



	% of patients with positive response
G12R	86.7%
G12D	86.7%
G12V	82.2%
G12C	83.3%
G12A	86.7%
G12S	88.9%
G13D	86.7%

- **Consistent CD4 + CD8 T cell Responses:**
  - 85% CD4 + CD8 response rate (compared to 75.0% in Phase 1)
  - Induction of combined CD4 and CD8 T cell responses correlated with clinical activity in previous Phase 1 trial
- **Consistent Responses to all included mKRAS antigens:**
  - 67.4% response rate for all 7 mKRAS antigens (compared to 50.0% in Phase 1)
  - >80% Response Rate for each individual mKRAS antigen
- **Consistent Responses to Patient-specific mKRAS Tumor antigen:**
  - 87.6% response rate to patient tumor antigen (compared to 83.3% in Phase 1)
- **Consistent Overall Immunotherapy Immunogenicity:**
  - Positive T cell responses to 85.7% (540/630) of immunotherapy antigens (compared to 66.7% in Phase 1)

AMPLIFY-7P Phase 2: Immunogenicity Methods

Immunogenicity of ELI-002 7P was assessed using longitudinally collected peripheral blood from 90 immunogenicity evaluable patients to assess specificity, polyfunctionality, and antigen breadth.

PBMCs from each patient were individually stimulated with overlapping peptides for each of the seven mKRAS antigens (G12R, G12D, G12V, G12C, G12A, G12S and G13D) for evaluation of mKRAS-specific T cell responses using **direct ex vivo** assays.

T cell responses and **polyfunctionality** were determined by a direct ex vivo IFNγ/Granzyme B (GrB) Fluorospot, where a positive immune response was defined as >2-fold over baseline and at least 50 SFC per million PBMCs.

Polyfunctionality and **phenotype** of patient T cells were further characterized using an ex vivo intracellular cytokine staining (ICS) assay where responder populations were defined as >2-fold over baseline and a frequency of at least 0.1% Cytokine+. The ICS assay included markers for CD3, CD4, CD8, Memory (CCR7, CD45RA), cytokines (IFNγ, TNFα, IL2), cytolysis (GrB, Perforin), activation (CD137, CD154), and proliferation (Ki67). A positive cytolytic response (GrB and/or Perforin+) was defined as ≥ 30% increase over baseline and a frequency of at least 1.0% Cytolytic+.

Associations between HLA alleles and $\log_{10}$-transformed **maximum T cell fold change (TCFC)** were first assessed using ordinary least squares linear regression. Models included HLA allele dosage as the primary predictor. To account for the non-normal, strictly positive distribution of TCFC, parallel analyses were performed using generalized linear models (glm()) in R with a Gamma error family and log link. Regression coefficients were exponentiated to represent multiplicative changes (fold-changes) in the expected TCFC per allele copy. For each allele, nominal p-values were adjusted for multiple testing using the Benjamini–Hochberg (BH) procedure to control the false discovery rate (FDR).

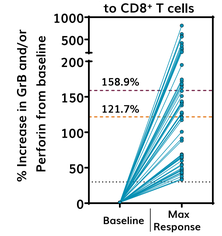
Immune Response Consistent with Observations in Phase 1 Trials of ELI-002

	ELI-002 2P (Nature Medicine) Phase 1 (n=25)	ELI-002 7P (4.9 mg) Phase 1 (n=7)	ELI-002 7P All (1.4 mg & 4.9 mg) Phase 1 (n=12)	ELI-002 7P (4.9 mg) Phase 2 (n=90)
Patients	MRD+ only	MRD+ only	MRD+ only	MRD+ & MRD-
mKRAS T Cell Response				
T cell Response Rate (%, n)	84% (21/25)	100% (7/7)	100% (12/12)	99% (89/90)
Average Fold Change[1]	58.6x	113.8x	71.1x	145.3x
Median Fold Change[1] (range)	16.4x (2.1x to 423x)	113.3x (9.5x to 351x)	18.5x (4.2x to 351x)	44.3x (2.13x to 1310x)
Threshold Above Which Clinical Activity was Correlated (% of Patients Above Threshold)	**9.17x (68% above 9.17x) 12.75x (52% above 12.75x)**	**ND**	**9.5x (75% above 9.5x)**	**TBD (80% above 9.5x)**
CD4 + CD8 T cell Response[2]	70.6%	85.7%	75.0%	85.0%
Response to 7 mKRAS Antigens[1]	57.1%	71.4%	50.0%	67.4%
Response to Patient Tumor Antigen[1]	81.0%	100%	83.3%	87.6%
Overall Antigen Response Rate (%, n)[3]	74.0% (37/50)	79.6% (39/49)	66.7% (56/84)	85.7% (540/630)

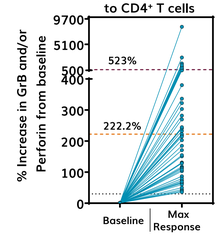
[1] Responses shown are best overall responses vs baseline for assessable patients at any timepoint during the assessment period, measured among T cell Responders; ND = Not Determined; TBD = To be Determined; MRD = Minimal Residual Disease
[2] Measured among evaluable patients with samples assessable by Ex Vivo ICS assay; [3] Overall Antigen Response Rate calculated as the percentage of positive mKRAS-specific T cell responses among all evaluated patients against all immunotherapy antigens
The Company remains blinded to the trial efficacy outcomes and the correlation of T cell responses to antitumor response; ELI-002 2P: Data cutoff 24-Sept-24; ELI-002 7P Phase 1: Data cutoff 24-Sept-24; ELI-002 7P Phase 2: 22-Aug-25

ELI-002 7P Treatment Amplifies mKRAS-specific Cytotoxic CD4+ and CD8+ T cells

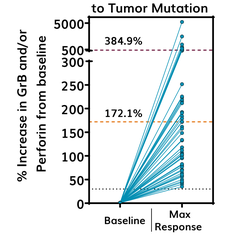
Cytotoxic response to CD8+ T cells



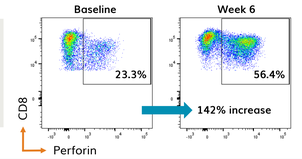
Cytotoxic response to CD4+ T cells



Cytotoxic response to Tumor Mutation



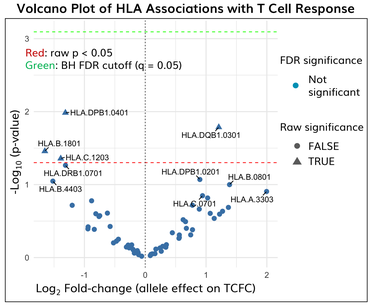
CD8+ mKRAS-specific cytotoxic T cells



- PBMCs were stimulated with individual mKRAS antigens in a direct ex vivo ICS assay to assess the cytotoxic markers, Granzyme B (GrB) and Perforin
- 86.8% (66/76) of patients induced cytotoxic mKRAS-specific T cell responses; 75% (57/76) induced CD8+ cytotoxic T cells, 75% (57/76) induced CD4+ cytotoxic T cells and 63.2% (48/76) induced both CD4+ and CD8+ cytotoxic T cells
- 78.9% (60/75) of patients induced cytotoxic T cells to their specific KRAS tumor mutation

No Association Between HLA Type and ELI-002 7P Induced T cell Response

Volcano Plot of HLA Associations with T Cell Response



- Blood was collected from each patient at baseline for high resolution HLA typing by NGS (n = 89 ELI-002 7P immunized patients).
- A two-variable analysis of maximum T cell fold-change (TCFC) versus the presence of various HLA alleles was performed, highlighting alleles with FDR < 0.05. Analyses were restricted to alleles with a carrier frequency ≥5% (≥5 patients) to reduce instability from sparse data.
- No associations were seen between HLA allele and T cell fold-change (either increased or decreased T cell response), indicating that patient HLA background was not associated with mKRAS-specific T cell response induced by ELI-002 7P.
- The 89 ELI-002 7P treated patients had very diverse HLA Class I and Class II backgrounds, with 1132 unique HLA alleles out of 1398 total HLA alleles in assessed patients.

TAKE HOME MESSAGES

Lymph node-targeted mKRAS specific cancer immunotherapy ELI-002 7P generated robust T cell responses in ongoing randomized Phase 2 AMPLIFY-7P trial:

- ➢ Robust expansion of mKRAS-specific T cells
- ➢ Consistent CD4 + CD8 T cell responses
- ➢ Consistent responses to all included mKRAS antigens
- ➢ Consistent responses to patient-specific mKRAS tumor antigen
- ➢ Consistent overall immunotherapy immunogenicity
- ➢ Increased CD4+ and CD8+ mKRAS-specific cytotoxic T cells after immunization with ELI-002 7P
- ➢ No associations between HLA allele and mKRAS-specific T cell fold-change
- ➢ Disease-free survival final analysis expected in Q4 2025; correlation of DFS/OS to T cell responses will be assessed

✓ Phase 3 will be a randomized, blinded trial; primary endpoint will be investigator assessed DFS using modified RECIST (new lesions confirmed by biopsy/imaging)