Ex Vivo ICS

• 0.1 mg

× 0.5 mg

2.5 mg

5.0 mg

10.0 mg

Specificity

G12R Responses

G12D Responses

Neither

ex vivo T cell

response

(n, %)

2/3 (67%)

5/6 (83%)

4/5 (80%)

5/5 (100%)

4/4 (100%)

20/23 (87%)

ELI-002 2P vaccination generates long-lasting mKRAS-

100% (4/4) of evaluable patients maintain elevated T

cell responses above baseline post-boost immunization

An increased post-boost T cell response was observed

in 75% (3/4) of evaluable patients compared to pre-

specific T cell responses

boost T cell levels

> Tumor Biomarker Response

> 86% Reduced Risk of Relapse or Death

G12R + G12D Responses

change

113



ELI-002 Immunotherapy Induces Broad Polyfunctional T cell Responses in Subjects with High Relapse Risk KRAS Mutated Pancreatic Ductal Adenocarcinoma and Colorectal Cancer

James R. Perry¹, Lochana M. Seenappa¹, Haley VanWyk¹, Amy M. Tavares¹, Thian Kheoh¹, Esther Welkowsky¹, Christopher M. Haqq¹, Peter C. DeMuth¹, and Lisa K. McNeil¹

¹ Elicio Therapeutics, Inc. 451 D St., Ste 501, Boston, MA 02210

Why Target mutated KRAS with Therapeutic Vaccination? KRAS mutant **Mutant KRAS Drives 25% of Solid Human Cancers** NRAS mutant **Prevalent** among numerous tumor types¹⁻² Overall **poor clinical prognosis**³ Limited therapeutic options **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 tumors¹⁻² Public neoantigen: not centrally tolerized, cognate TCRs present in naïve repertoire⁴⁻⁵ **Promiscuous HLA presentation**: potential off-the-shelf use in diverse patient population⁶⁻⁸ Proven Clinical MOA: mKRAS-specific T cells known to mediate antitumor efficacy⁴⁻⁵ **Colorectal Cancer (CRC) Pancreatic Ductal** Multi-targeting potential: recognition of clonal and subclonal mKRAS US Incidence: 151k Adenocarcinoma variants to prevent escape⁹ US Incidence: ~56k **ELI-002 2P: Advancing Innovation for mKRAS Cancer Vaccines** 1 Technological Innovation: Amphiphile Lymph Node Targeting Platform¹⁰⁻¹¹ 2 Clinical Innovation: Treatment in High Relapse-Risk Adjuvant Setting Targeting surgically debulked tumors enables T cells to address minimal residual **Smart trafficking to the lymph nodes** after subcutaneous dosing generates disease to potentially eliminate remaining tumor cells and protect against immune responses with increased magnitude, function, and durability. Takes advantage of potent lymph node immune mechanisms, including activation Activating the immune system **before loss of HLA expression** in the tumor of innate and adaptive cells, antigen-spreading, and improved tumor T cell trafficking / infiltration. microenvironment in a chemotherapy-free window of opportunity. Mutant KRAS peptides provide a validated antigen for application of the Other oncology vaccines have typically been used in later lines of therapy for advanced disease, after onset of tumor immune resistance. Amphiphile platform. In the adjuvant setting, tumor biomarkers (ctDNA, serum tumor antigen) are Lymph node delivery of potent adjuvants minimizes systemic exposure to early predictors of disease control or recurrence. **Amphiphile mKRAS Long** ^^^^ **Peptide Antigens** ~~~~ 1 Amph-mKRAS G12D 2 Amph-mKRAS G12R G12D or G12R Peptide **Amphiphile TLR-9 Agonistic DNA Adiuvant** ^^^^ Amph-CpG-7909 **CpG-7909 DNA**

Inclusion of 18-mer G12D and G12R mKRAS peptides allows for delivery of diverse HLA I and II – restricted epitopes for presentation on varied patient HLA

node delivery, and prevents peptide uptake into local capillaries avoiding delivery to irrelevant or tolerogenic sites.

Tissue Injection Site

Albumin-bound Amphiphiles

poor delivery to lymph nodes where protective immune responses are orchestrated.

Screening Period

G12R+ or G12D+

NED

Imaging Negative

ctDNA+ or

serum biomarker+

Surgery

Neoadjuvant

Adjuvant

Chemotherapy

Patients

Safety

binding

Restricted delivery to lymph nodes minimizes systemic exposure to avoid toxic effects of potent adjuvants.

Amphiphile (Amph)-modification of peptides promotes binding to endogenous albumin at the injection site to promote collection in lymphatic vessels for lymph

♦ Amph-CpG-7909 provides potent immune activation via TLR-9 stimulation of lymph node-resident professional antigen presenting dendritic and other key immune

Conventional vaccine components (e.g. peptide antigens and molecular adjuvants) are rapidly absorbed into blood capillaries after administration leading to

Amph-modification promotes albumin binding to reprogram vaccines for enhanced lymph node delivery resulting in coordinated transport of antigen and

AMPLIFY 201: Trial Design¹²

adjuvant to immune cells. Improved uptake by Antigen Presenting Cells results in enhanced antigen-presentation and co-stimulation to cognate T cells.

Lymph node

targeting

Lymph Node

Amph-Peptides 2P 1.4 mg + 0.1, 0.5, 2.5, 5 or 10 mg Amph-CpG-7909

Albumin-bound Amphiphiles

Antigen Presenting Cell

Delivery to

immune cells

References

2457-2467

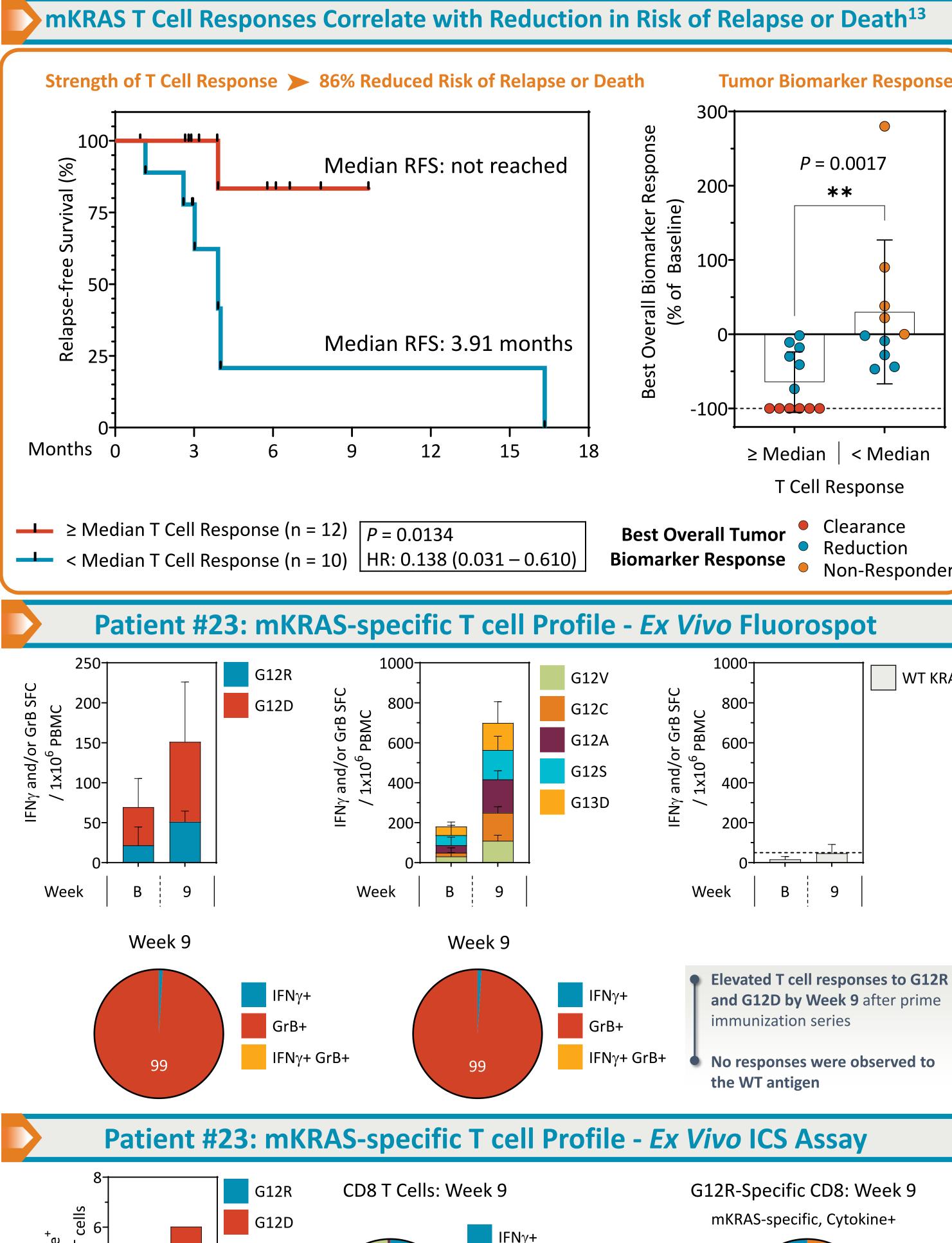
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Increased mKRAS-specific Memory T cells Assessed by IVS **IVS Fluorospot** IVS ICS • 0.1 mg 100-× 0.5 mg 2.5 mg 5.0 mg **1**0.0 mg • 100% of patients induce mKRAS-specific memory T cell responses after in vitro stimulation Increased Polyfunctionality of mKRAS-specific T cells after ELI-002 2P Immunization Proliferation: Week 9 T Cell Activation: Week 9 Cytolysis: Week 9 Patient #23 **Polyfunctional T cell Profile:** Increased activation. cytolysis, and 7.81 0.71 proliferation after vaccination **ELI-002 2P Immunization Elicits Durable mKRAS-specific Immune Responses**

Patient 16

Patient 18

Patient 20

Patient 11

Expansion of mKRAS-specific T cells by ELI-002 2P Immunization

Specificity

7 antigens

5-6 antigens

2-4 antigens

Amph-

CpG Dose

Level

0.1 mg

0.5 mg

2.5 mg

5.0 mg

10.0 mg

Total

1 antigen

Ex Vivo Fluorospot

CD4 / CD8 Response

CD4 + CD8 T cells

G12R

G12D

G12V

G12C

G12A

G12S

G13D

No Response

CD8 T cells

CD4 T cells

Fold-change

Responders

Non-responders

Responders

Weeks post-vaccination T Cell Response **MOA Correlated to:**

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Lymph node-targeted Therapeutic mKRAS-specific Cancer Vaccine ELI-002 2P:

Direct ex vivo mKRAS-specific T cell responses observed in 87% of patients and IVS responses were observed in 100% of patients

50% of patients generated both CD4 and CD8 T cell responses

- T cells exhibited robust functional quality: activation, cytokine production, cytolytic capacity, proliferation, memory phenotype
- 100% (4/4) of patients evaluable for durability maintained elevated T cell responses above baseline

✓ Phase 1, randomized Phase 2 Study of ELI-002 7P (NCT05726864) in PDAC patients: targeting G12D, R, V, C, A, S, G13D

AMPLIFY 201: Immunogenicity Methods

Immunogenicity of ELI-002 2P was assessed using longitudinally collected peripheral blood from 23 evaluable patients to assess specificity, polyfunctionality, antigen breadth, and phenotype of mKRAS-specific T cells.

44% had Grade 1-2 TEAEs: e.g. injection site reaction, fatigue, headache, nausea12

Baseline Characteristics: 20 Pancreatic (PDAC), 5 Colorectal (CRC) were evaluated for safety as of data cutoff: April 25, 2023

Safety: No TEAEs ≥ Grade 3, no Dose Limiting Toxicities, no Cytokine Release Syndrome observed across all dose levels;

- 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) and the WT antigen, for evaluation of mKRAS-specific T cell responses using both direct ex vivo and in vitro stimulated assays
- T cell responses and polyfunctionality were determined by a direct ex vivo IFNγ/Granzyme B (GrB) Fluorospot and a 10-day in vitro stimulated (IVS) IFNy/TNF α Fluorospot assay, 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 and IVS 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, CD45RO), cytokines (IFNγ, TNFα, IL2), cytolysis (GrB, Perforin, CD107a), activation markers (CD69, CD137, CD154), and proliferation

● 87% of Patients generated direct ex vivo detectable mKRAS-specific T cell responses following ELI-002 2P Immunization, with 100% Responders at the highest dose levels (5.0 and 10.0 mg) Ex Vivo Responders ≥ Median | < Median T Cell Response Reduction Non-Responder Patient #23: mKRAS-specific T cell Profile - Ex Vivo Fluorospot WT KRAS - -<u>-</u> - - - - - - -| - - - -Cohort 11222223333444445555123 CD4 and CD8 T cell responses were observed, with 50% generating mixed CD4 + CD8 responses Elevated T cell responses to G12R \bullet mKRAS-specific **T cells were polyfunctional** (IFN γ , TNF α , IL-2), specific to both immunizing and non-immunizing mKRAS antigens and G12D by Week 9 after prime immunization series No responses were observed to Patient #23: mKRAS-specific T cell Profile - Ex Vivo ICS Assay G12R-Specific CD8: Week 9 mKRAS-specific, Cytokine+ IFNγ+ IL2+ TNFα+ Effector Memory Naïve Central Memory TEMRA CD4 T Cells: Week 9 G12R-Specific CD4: Week 9 mKRAS-specific, Cytokine+ TNFα+ Week Patient #23 mKRAS-specific Memory T cell Profile - IVS % Cytokine Secretion in G12R WT KRAS <u>의 1000 J</u> Fluorospot: Week 9 ∑ 8 1500-600 IFNγ+ 7 × 1000 G12R G12D After IVS stimulation, greatly increased T cell responses to G12R and G12D at Week 9 post prime immunization series No responses were detected for the WT antigen

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