Optimization of shared neoantigen vaccine design to increase vaccine potency: *From bench to bedside and back*

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Disclosure Information

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I have the following relevant financial relationships to disclose:

Employee of: Gritstone bio, Inc.
Stockholder in: Gritstone bio, Inc.

I have no additional financial relationships to disclose.

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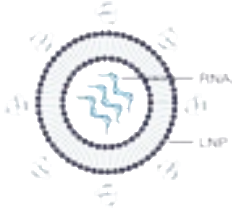
SLATE Delivers Shared Neoantigens to Selected Patients Using Gritstone's Prime/Boost Platform – Off-the-Shelf Therapy

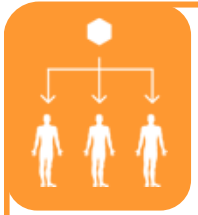
Prime

ChAd Vector

Boost



samRNA Vector



SLATE v1 Shared Neoantigen Cassette

- "Off-the-shelf" Neoantigen Immunotherapy
- 20 cancer driver mutations
- Efficient patient selection via gene panels

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SLATE Phase 1 Study Design

SLATE
off-the-shelf

High Frequency KRAS Mutation

Lung

Pancreatic

Colorectal (MSS)

Mutation Positive Tumors

PHASE 1

Objectives:
- **Safety and RP2D**
- **Immunogenicity**

Dose Level 4

Dose Level 3

Dose Level 2

Dose Level 1

ChAdV 1x10^{12} vp
Increasing doses of samRNA
Nivolumab 480 mg IV
} with 30 mg SC ipilimumab

ChAdV 1x10^{12} vp
samRNA 30 µg
Nivolumab 480 mg IV

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Safety: Immunotherapy Well-Tolerated In Patients with Previously Treated Metastatic Solid Tumors

SLATE Baseline Characteristics	n= 36
Age: mean (range)	57 (33-86)
Gender: Female/Male	22/14
Tumor Types	
Non-small cell lung cancer	17
Median number of prior therapies (range)	2 (1-4)
Prior anti-PD-(L)1 therapy	17
Microsatellite-stable (MSS) Colorectal Cancer	12
Median number of prior therapies (range)	2 (1-3)
Pancreatic ductal adenocarcinoma (PDA)	5
Median number of prior therapies (range)	1 (1-3)
Ovarian cancer	1
Number of prior therapies	4
Ampullary adenocarcinoma	1
Number of prior therapies	5

Data cut-off: 30 Nov 2021

Safety	n = 36 (all treated with concurrent nivolumab)	
	Grade 1/2	Grade 3/4
Treatment-related adverse events ≥ 5%		
Fever	13	
Fatigue	8	1
Nausea	7	
Vomiting	7	
Diarrhea	5	
Injection site reaction	5	
Arthralgia	3	
ALT increased	1	1
AST increased	1	1
Anorexia	2	
Chills	2	
Dizziness	2	
Dyspnea	2	
Generalized weakness	2	
Myalgia	2	
Pruritus	2	
Treatment-related SAEs		
Fever	2	
Hepatitis		1
Neutropenia		1
Pneumonitis		1
Rhabdomyolysis		1
Vomiting	1	

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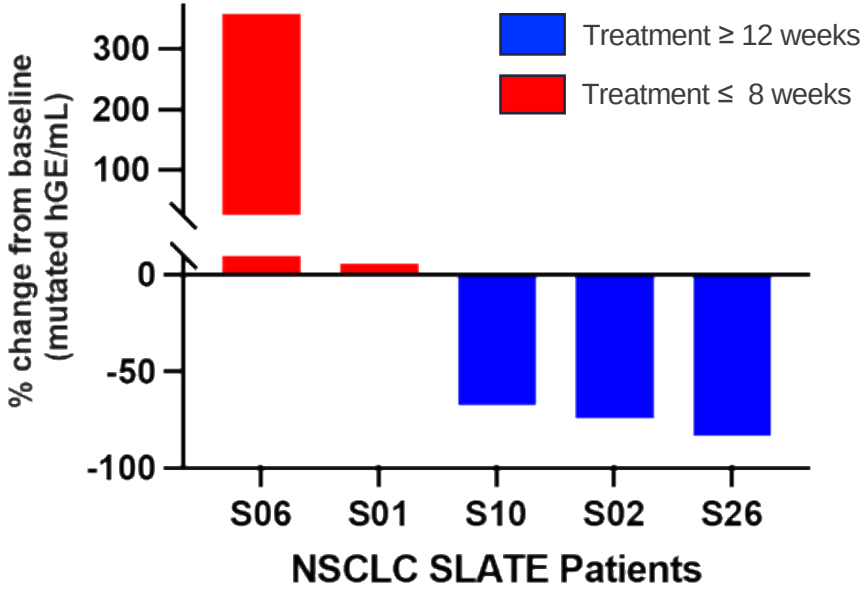
Efficacy: Several NSCLC Patients Who Progressed on Prior IO Have Experienced Decrease in ctDNA Including Patient with High Baseline Levels

Patient	Mutation	Baseline ctDNA (mutated hGE/mL)
S1	G12C	124.64
S2	G12C	26.92
S3	G12C	Not detectable
S6	G12D	21.12
S10	Q61H	77.23
S14	G12D	Not detectable
S26	G12C	3386.05



S3: Prolonged Disease Control in a Patient with NSCLC

Longer than disease control on prior anti-PD-1 mAb therapy

55-year-old male with metastatic NSCLC

KRAS G12C

→

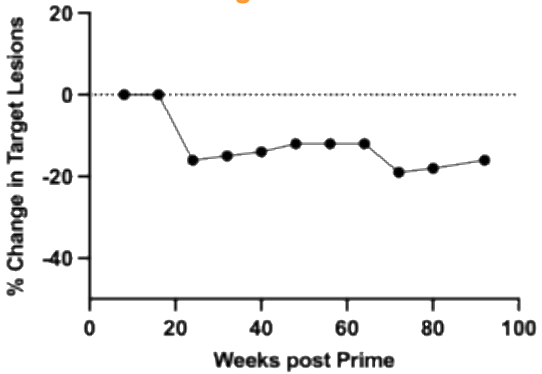
Prior Therapy

Pembrolizumab + carboplatin + pemetrexed (8 months)

PD →

Completed 2 years of study treatment (per protocol) with sustained lesion shrinkage, currently off treatment

Target Lesions



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S26: Molecular Response and Unconfirmed Partial Radiologic Response in a Patient with NSCLC

53-year-old male with metastatic NSCLC

KRAS G12C

→

Prior Therapy

Pembrolizumab + carboplatin + pemetrexed (3 months)

PD →

Began SLATE immunotherapy in Jan 2021

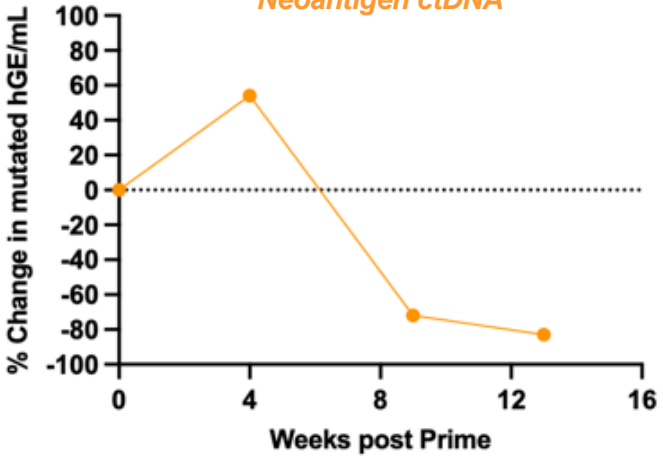
PD →

Spinal compression fracture at site of pre-existing vertebral bodies in month 5

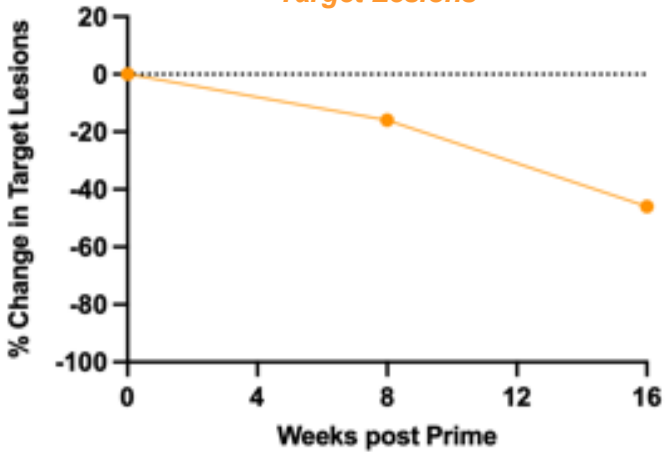
→

Tumor tissue from vertebral lesion showed increased IFNg and immune infiltrate expression signatures and increased HLA expression

Neoantigen ctDNA



Target Lesions



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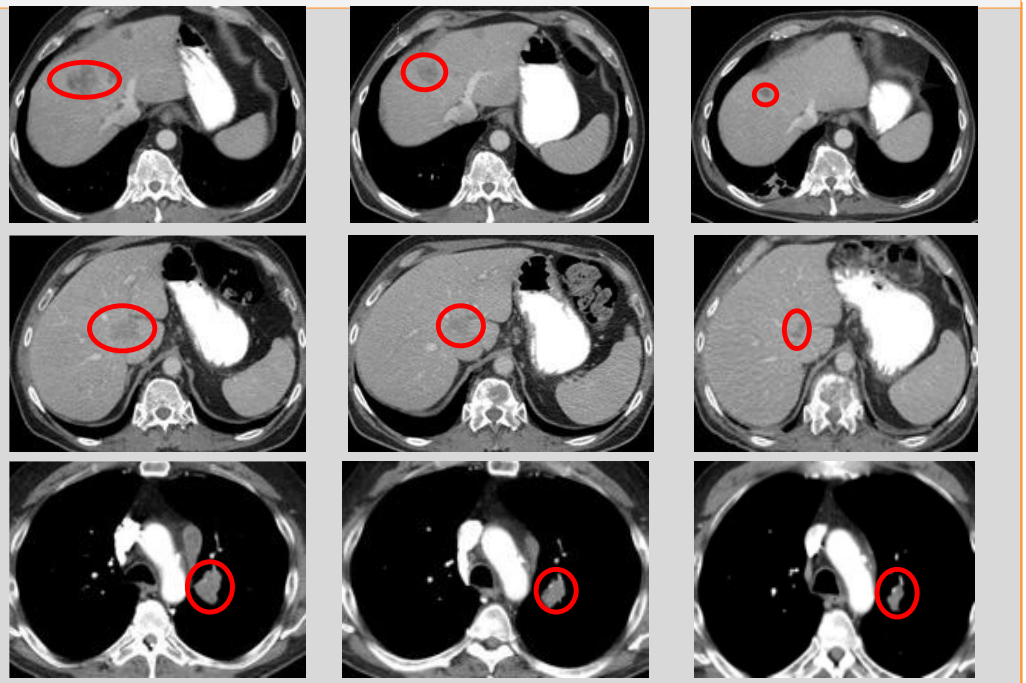
S26: Unconfirmed Partial Response with Clear Reduction in Liver and Lung Lesions

Baseline	Week 8	Week 16
113 mm*	95 mm* (-16% relative to baseline)	61 mm* (-46% relative to baseline)



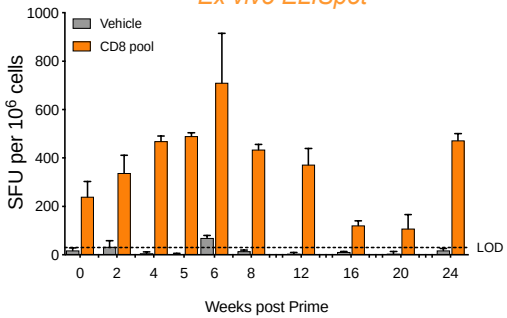
**Sum of longest diameters of two target lesions*

SLATE V1: CD8+ T Cells Consistently Induced Against Multiple KRAS Driver Mutations but *ex vivo* ELISpot Positive in Subset of Patients Only

SLATE drives detectable CD8+ T cell responses against single neoantigens

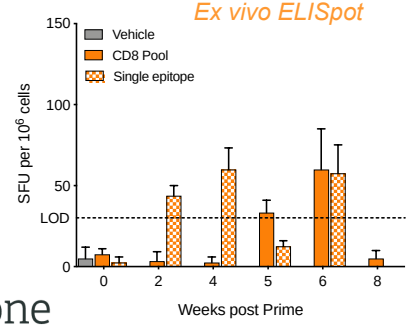
S2 *KRAS G12C*

Ex vivo ELISpot

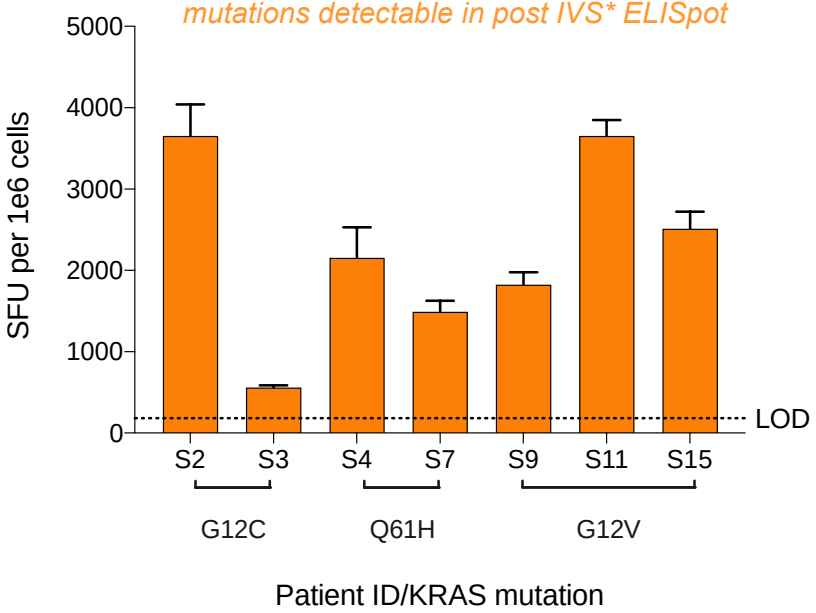


S4 *KRAS Q61H*

Ex vivo ELISpot



CD8+ T cell responses against single neoantigens from multiple KRAS driver mutations detectable in post IVS ELISpot*



**IVS – In vitro stimulation*

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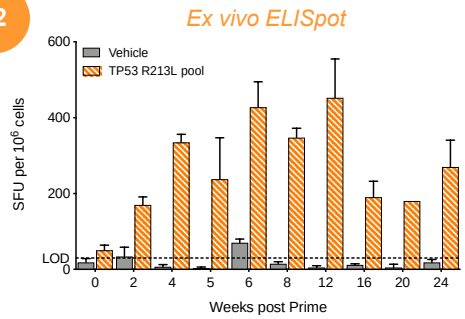
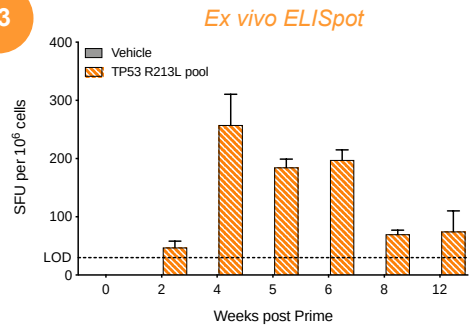
SLATE V1: TP53^{mut} Neoantigens Seem Immunodominant – Although Rarer than KRAS^{mut} Neoantigens, they Drive Strong CD8^{+} T Cell Responses

Responses to 3/3 TP53 mutations tested to date; mutations presented by 3 different Class I HLA alleles

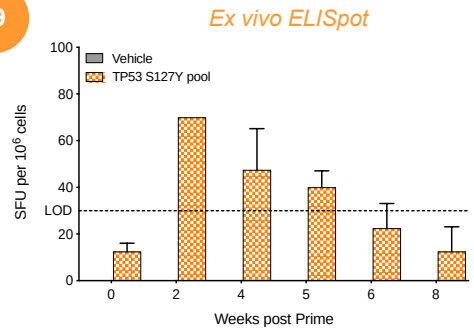
S2



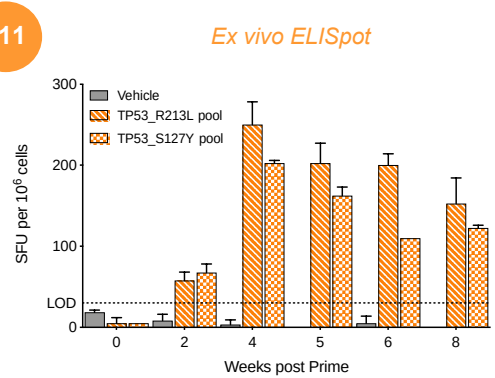
S3



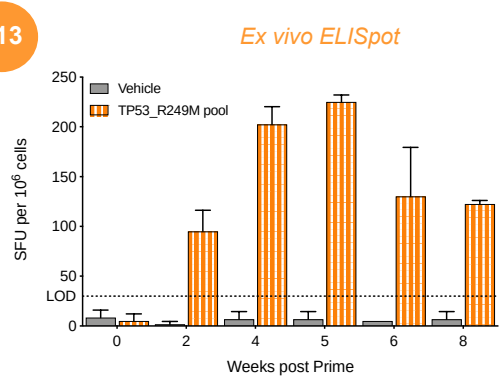
S9



S11



S13



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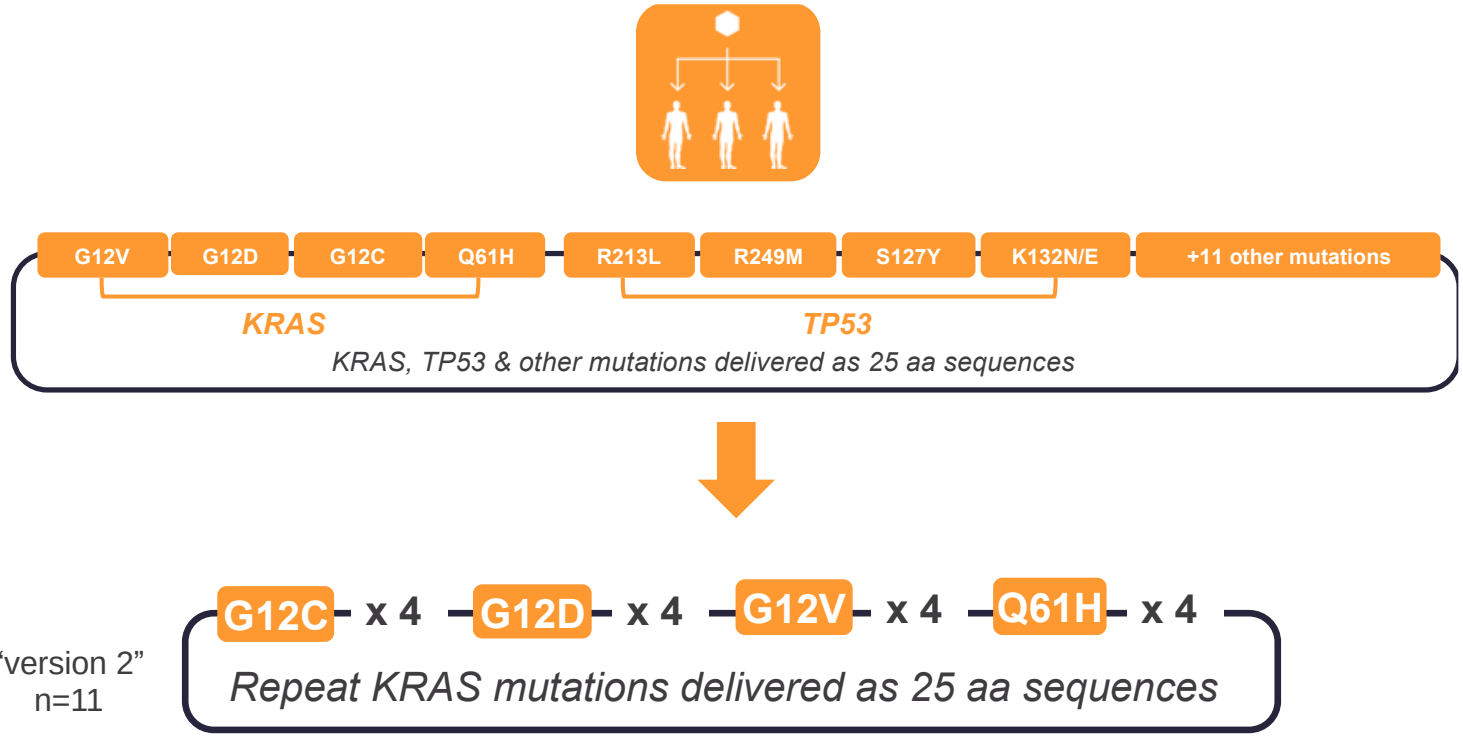
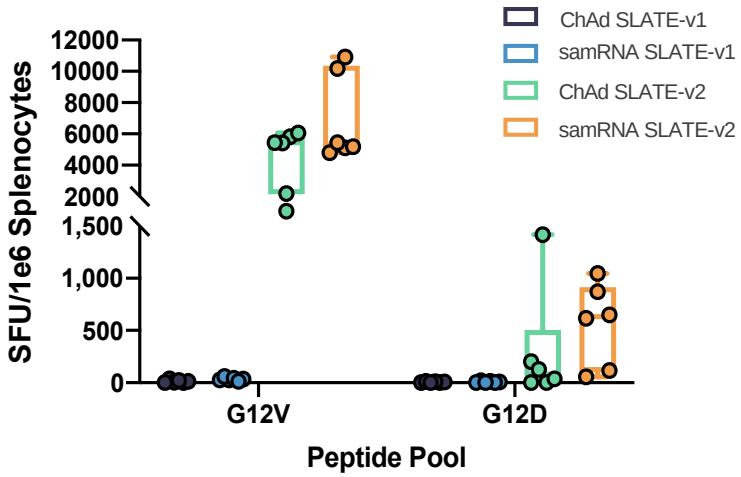
Optimizing Cassette to Mitigate TP53 Immunodominance and Enhance KRAS Immunogenicity



SLATE: Version 2 of the *KRAS^{mut}* Antigenic Cassette Induces Stronger T-Cell Responses to Multiple KRAS Neoantigens in Both Mice and Patients

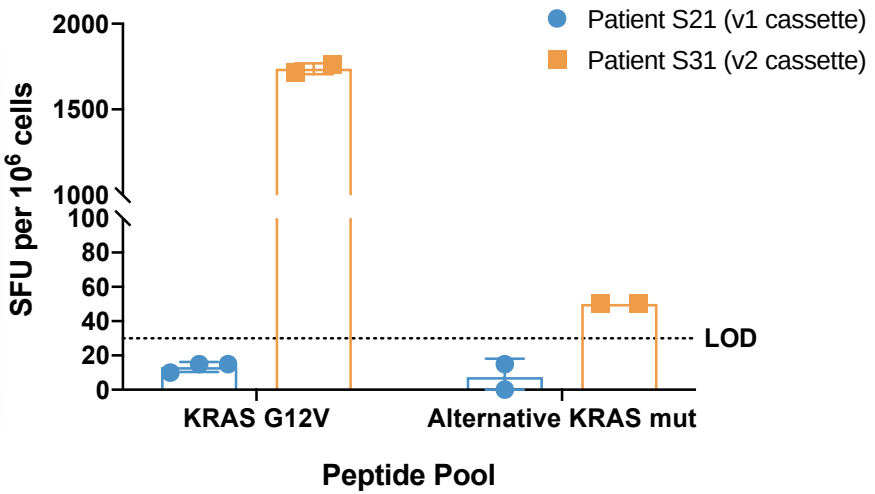
No ex vivo T-cell responses observed in transgenic mice or representative patient with SLATE v1 cassette

HLA Class I Transgenic mice



Overnight stimulation with peptide pool containing 38 minimal epitopes. Background subtracted.

KRAS G12V enrolled patients



Overnight stimulation with peptide pool containing 38 minimal epitopes.
Timepoint collected post-second SAM administration.

S31: Partial Response at First Scan at 8 Weeks with Shrinkage in Both Target Lesions

Durable tumor shrinkage with decrease of 28% on confirmatory scan at 18 weeks (scan delayed due to COVID infection)

41-year-old male with metastatic NSCLC

KRAS G12V

→

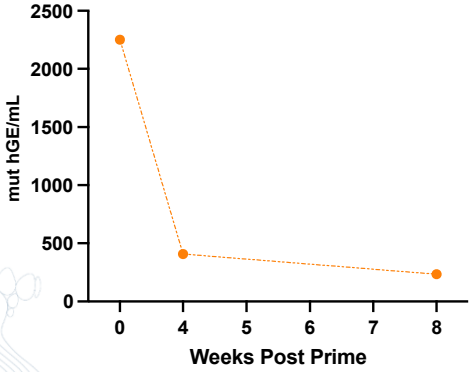
Prior Therapy

Pembrolizumab/ carboplatin/ pemetrexed (16 months)

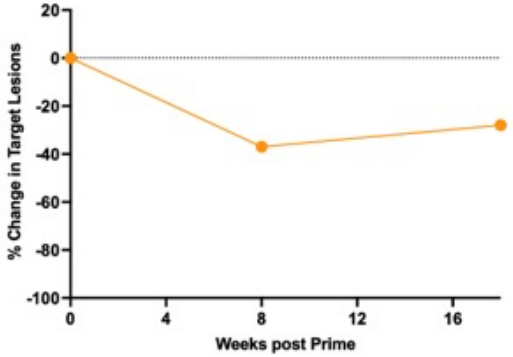
PD →

Began SLATE immunotherapy in Oct 2021

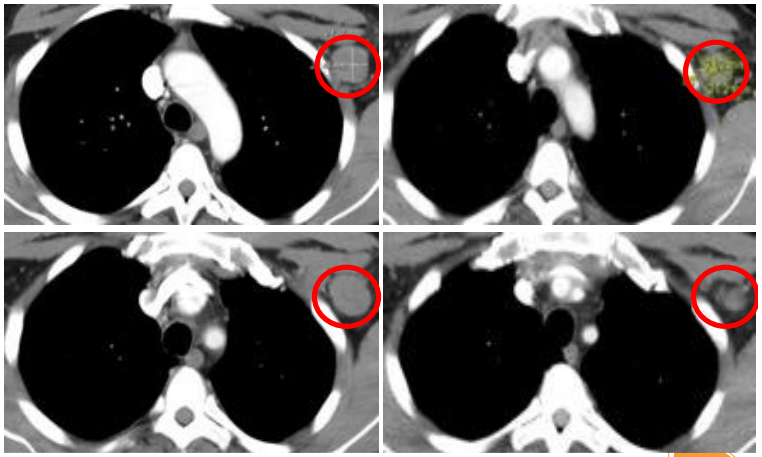
Neoantigen ctDNA



Target Lesions



Baseline	8 weeks (-37%)



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SLATE Highlights

Safety & Tolerability

- Neoantigen immunotherapy appears to have a favorable safety and tolerability profile

Efficacy

- Even in advanced NSCLC patients who have progressed on prior chemo-immunotherapy we observe molecular responses and tumor shrinkage in patients with durable clinical benefit
- One patient completed two years on study treatment and now off all treatment

Translational approach

- An emerging hierarchy of neoantigen immunodominance is emerging that may be related to peptide-HLA complex density on tumor cell surface

Clinical Development Strategy

- We aim to move into earlier disease settings to amplify efficacy signals and drive the survival curve plateau higher

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Thank you!