

AACR

American Association
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**ANNUAL
MEETING**
2023

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*Disease monitoring with comprehensive genomics
provides evidence of mechanism of action and
immune evasion in patients receiving an
individualized neoantigen cancer vaccine*

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Disclosure Information

Matthew J. Davis

I have the following relevant financial relationship to disclose:

- Employee of Gritstone bio, Inc
- Stockholder in Gritstone bio, Inc

- and -

I have no other financial relationships to disclose.

Safe Harbor and Forward-Looking Statements

This presentation contains forward-looking statements including, but not limited to, statements related to Gritstone bio, Inc.'s ("Gritstone", "we" or "our") proprietary drug candidates, including GRANITE, SLATE and CORAL, the timing of the start, conclusion and status of ongoing or planned clinical trials, including the timing of, and our ability to achieve, anticipated milestones, the sufficiency of our cash, cash equivalents and short-term investments, availability of funding, business strategy, the timing and outcome of regulatory decisions, future availability of pre-clinical and clinical trial data, our collaborations for our product candidates and the maintenance of those collaborations; business and results from operations; and other matters. Forward-looking statements generally contain words such as "believes," "expects," "may," "will," "should," "seeks," "approximately," "intends," "plans," "estimates," "anticipates," and other expressions that are predictions of or indicate future events and trends and that do not relate to historical matters. Because forward-looking statements are inherently subject to risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

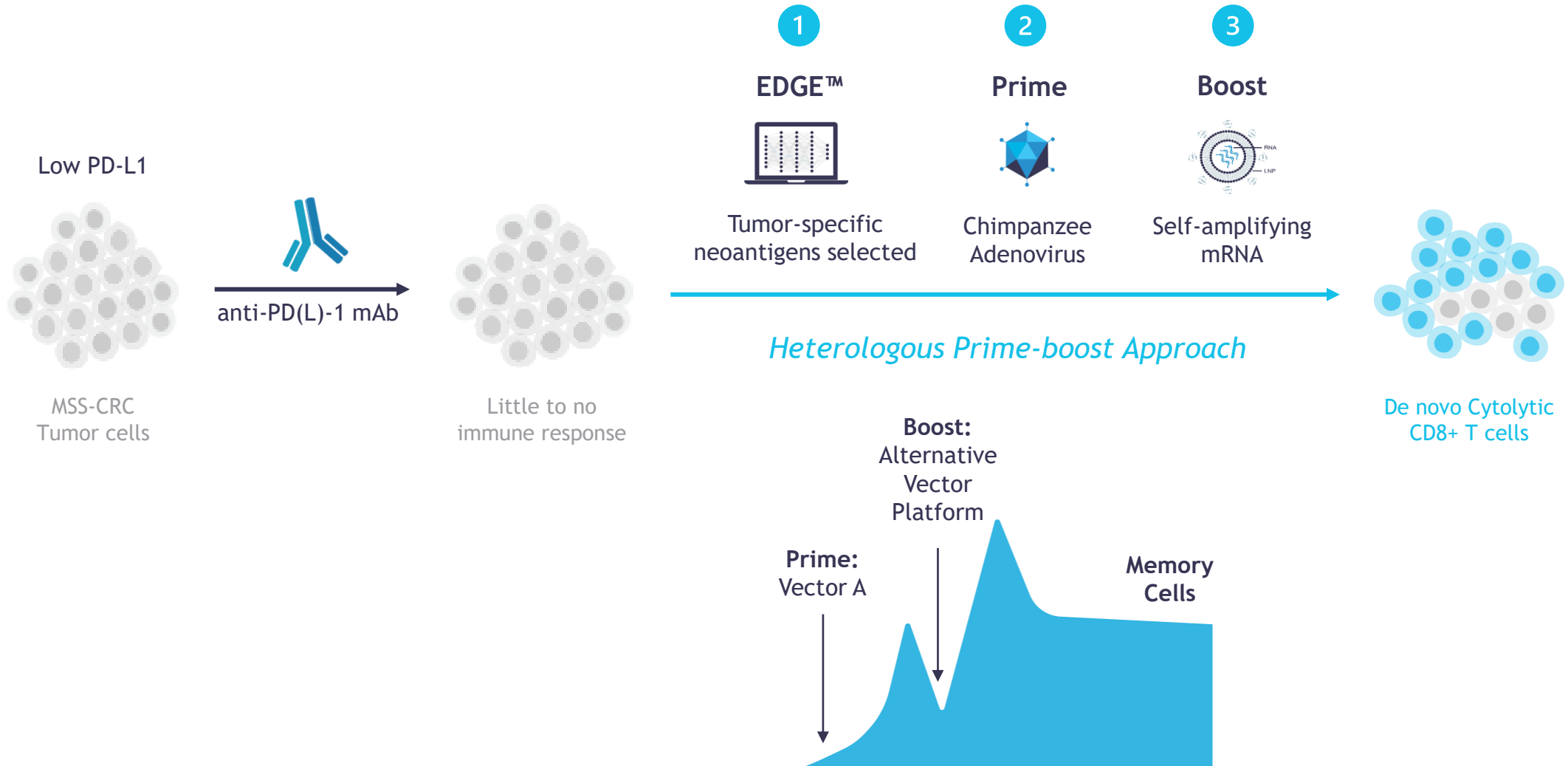
The forward-looking statements in this presentation are based on information available to Gritstone as of the date this presentation. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to our business in general, see Gritstone's most recent Annual Report on Form 10-K filed on March 9, 2023 and any current and periodic reports filed with the Securities and Exchange Commission.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

This presentation concerns drugs that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. They are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Gritstone's Approach: Induction of CD8+ T cells Against "Cold" Solid Tumors

Antigen selection + prime-boost regimen may be effective in tumors unresponsive to anti-PD(L)-1 therapy



Phase 1/2 Study Evaluating the Safety, Immunogenicity, and Clinical Activity of GRANITE in Combination with Checkpoint Blockade


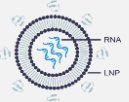
Phase 1

Dose Escalation
N=14

Phase 2

Efficacy Evaluation
N=15

Selected Endpoints

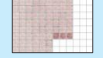
	Dose Level 1 N=3	Dose Level 2 N=3	Dose Level 3 N=2	Dose Level 4 N=6
Prime	 GRT-C901			
Boost	 GRT-R902 (dose escalation)			
Ipilimumab (SC)	-	-	30 mg	30 mg
Nivolumab (IV)	480 mg	480 mg	480 mg	480 mg

Cohort 1 <i>Microsatellite-stable Colorectal Cancer (MSS-CRC)</i>
Cohort 2 <i>Gastroesophageal adenocarcinoma (GEA)</i>
Cohort 3 <i>Non-small Cell Lung Cancer (NSCLC)</i>


Primary Endpoints
Safety and Tolerability; ORR (Phase 2); Recommended Phase 2 Dose

Secondary & Exploratory Endpoints
IMMUNE SIGNATURES


Functional assays:



ELISpot



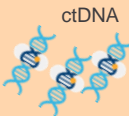
Flow




Incucyte

TUMOR SIGNATURES


Sequencing:



ctDNA



TCRs

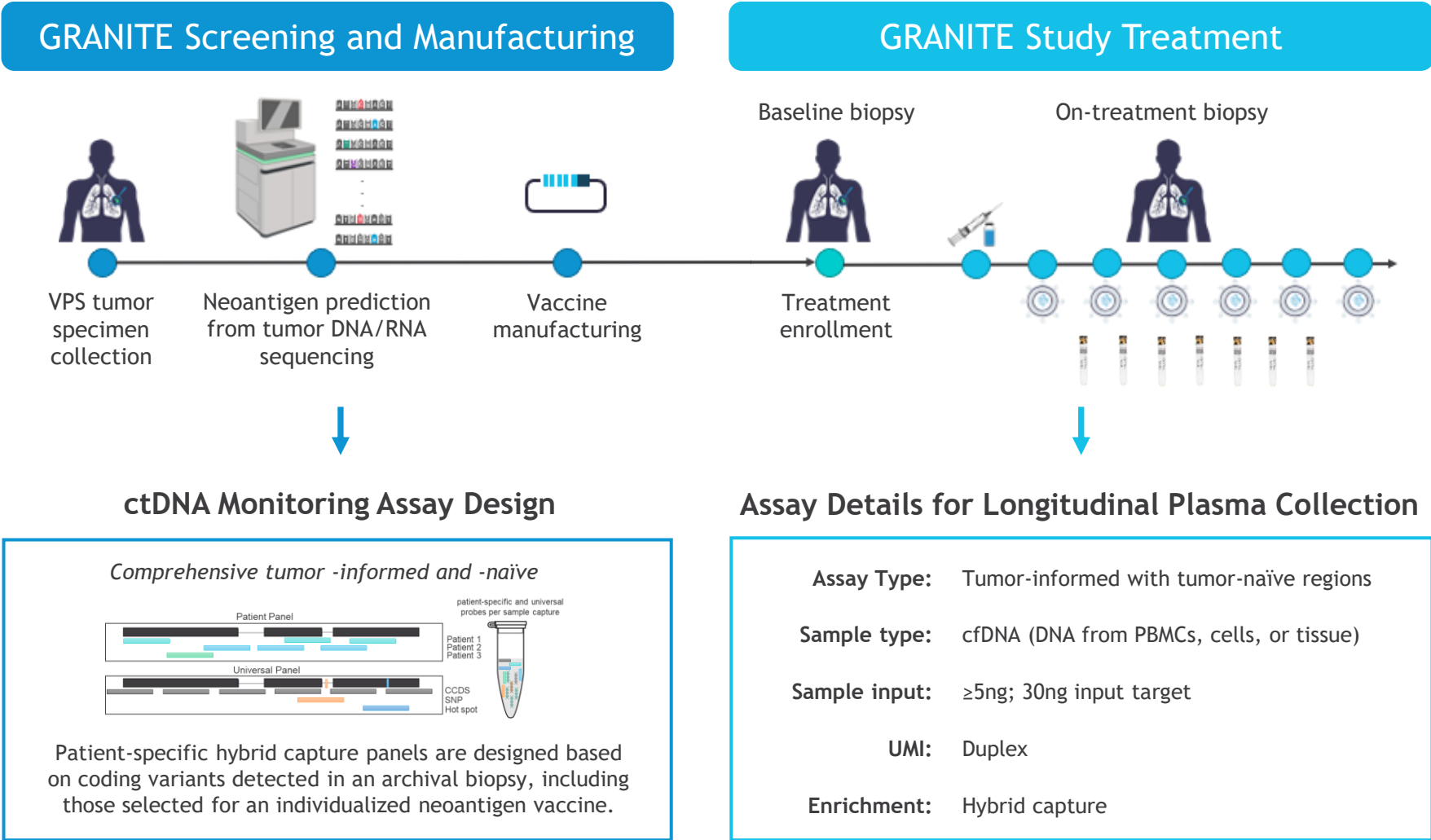


Tumor

GRT-C901 = chimpanzee adenovirus encoding 20 neoantigens
 GRT-R902 = self-amplifying mRNA in lipid nanoparticles encoding same neoantigens as GRT-C901
 NCT03639714

Liquid Biopsy: Comprehensive, Patient-specific Longitudinal Assay for an Individualized Treatment

Gritstone's approach ensures private neoantigens are monitored during treatment with long-term sample collections

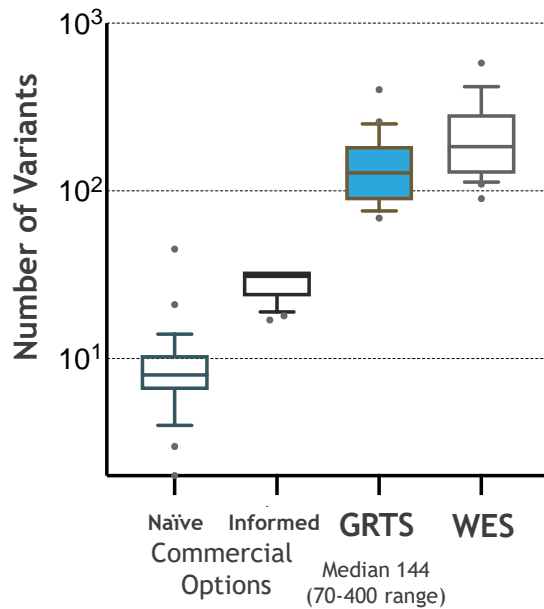


Liquid Biopsy: Gritstone's ctDNA Monitoring Assay Designed for Breadth and Depth Required for Tumor Fraction Monitoring

ctDNA monitoring assay detects >80% (median) all targeted mutations and >90% of neoantigens identified based on archival biopsy at time of study enrollment

ctDNA Assay Breadth

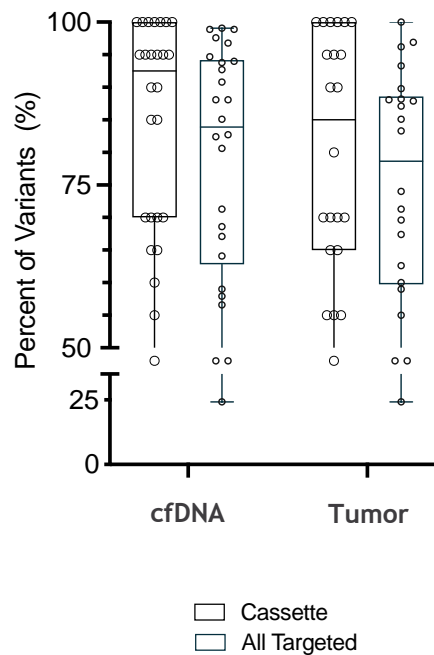
Gritstone's ctDNA assay targets a larger number of variants compared to other ctDNA assays



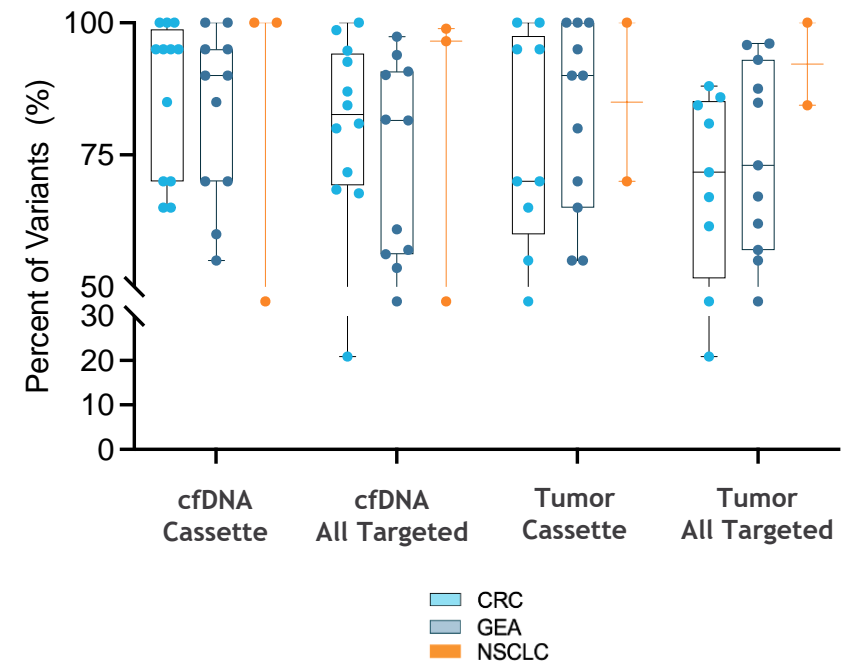
Variant Detection in cfDNA and Treatment Biopsies

% of variants retained from time of neoantigen prediction using archival biopsy through study treatment – Analysis from Patients Treated on GRANITE

Variant Detection Casette vs. All Targeted



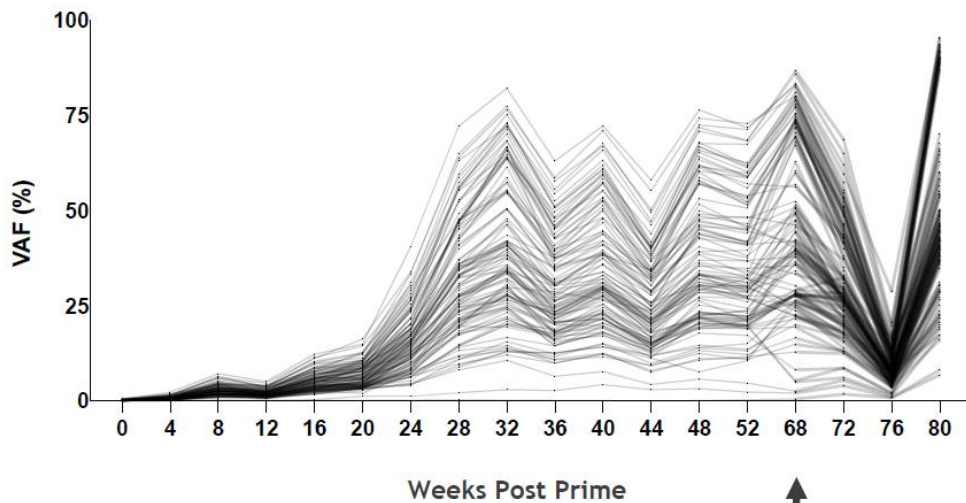
Variant Detection Across Indications Casette vs. All Targeted



Liquid Biopsy: Assay Versatility Enables Dynamic Disease Monitoring

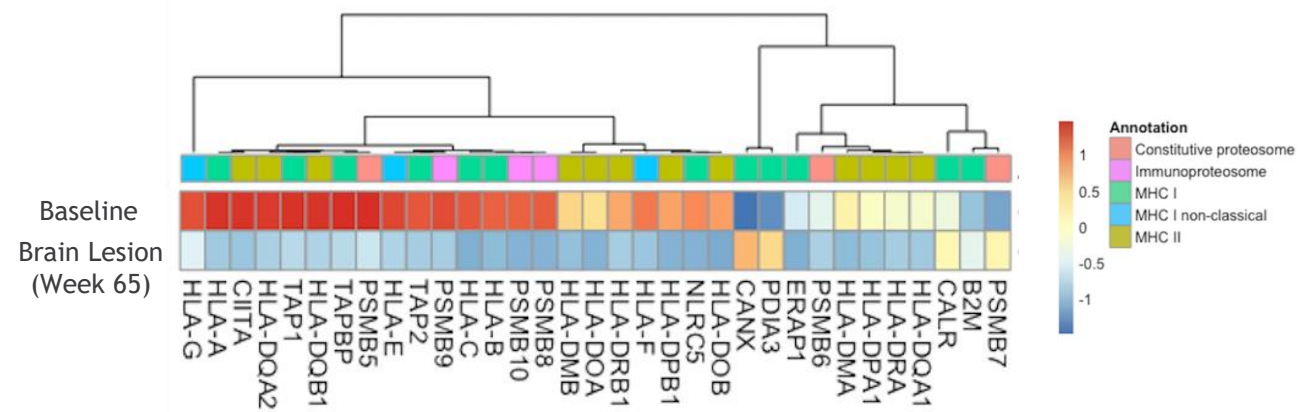
Patient with GEA who had disease stabilization followed by slow progression acquires HLA-LOH - identified in ctDNA prior to confirmation in brain lesion

Longitudinal ctDNA monitoring of > 200 tumor-informed coding somatic mutations



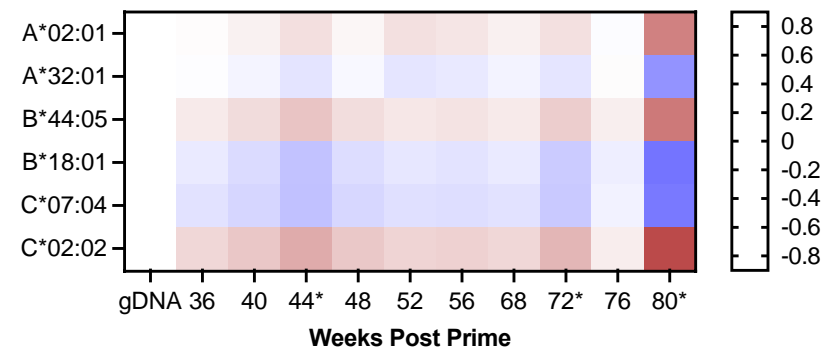
GRT-C901 Boost
Concomitant FOLFIR

Gene expression analysis from paired pre and post treatment (brain lesion) confirms loss of expression in HLA and antigen presentation pathway



Longitudinal ctDNA monitoring with tumor-naive panel identifies HLA-LOH in ctDNA at week 44, 72 and 80

G01 Change in HLA Allele Fraction

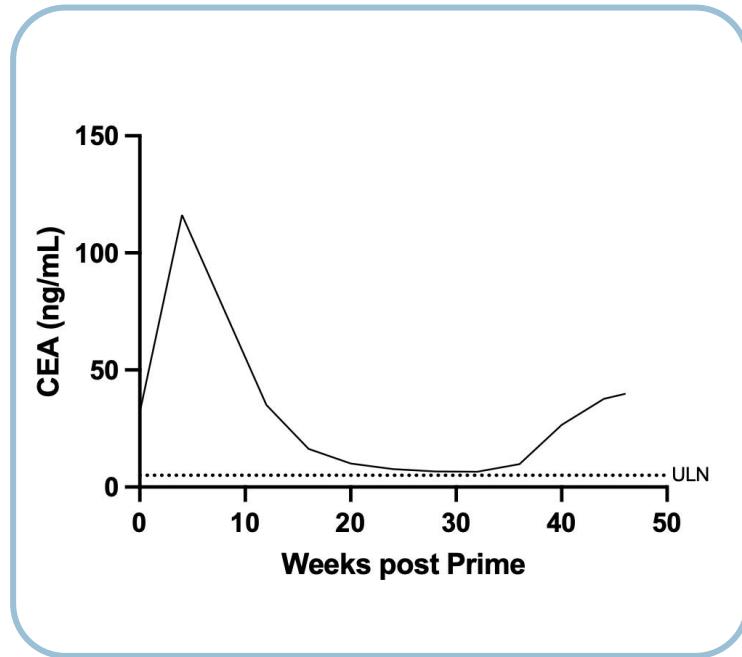


HLA-LOH
HLA-A (32:01),
HLA-B (18:01)
HLA-C (07:04)

Liquid Biopsy: Assay Versatility Enables Dynamic Disease Monitoring

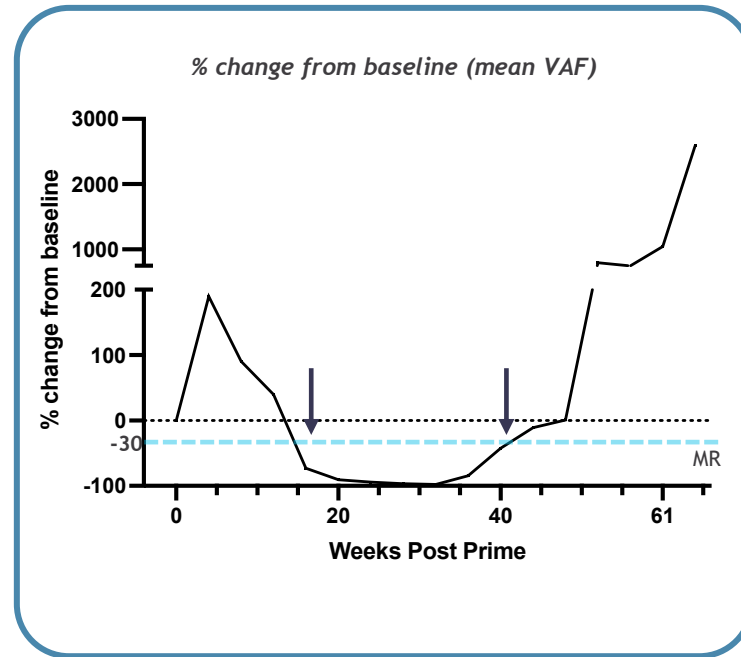
Patient with MSS-CRC who had stable disease per RECIST had prolonged molecular response followed by acquired immune evasion detected after 12 months of treatment

CEA Dynamics



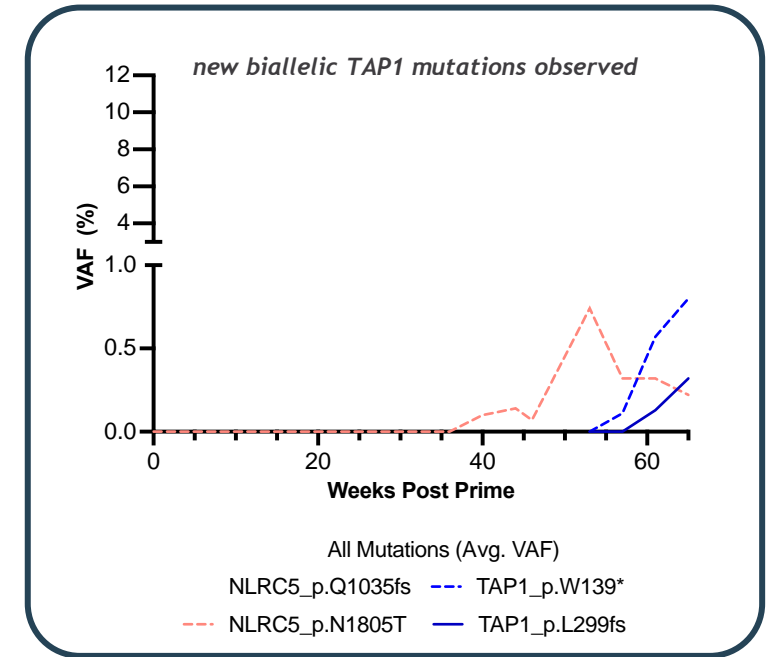
ULN= upper limit of normal

Molecular Response



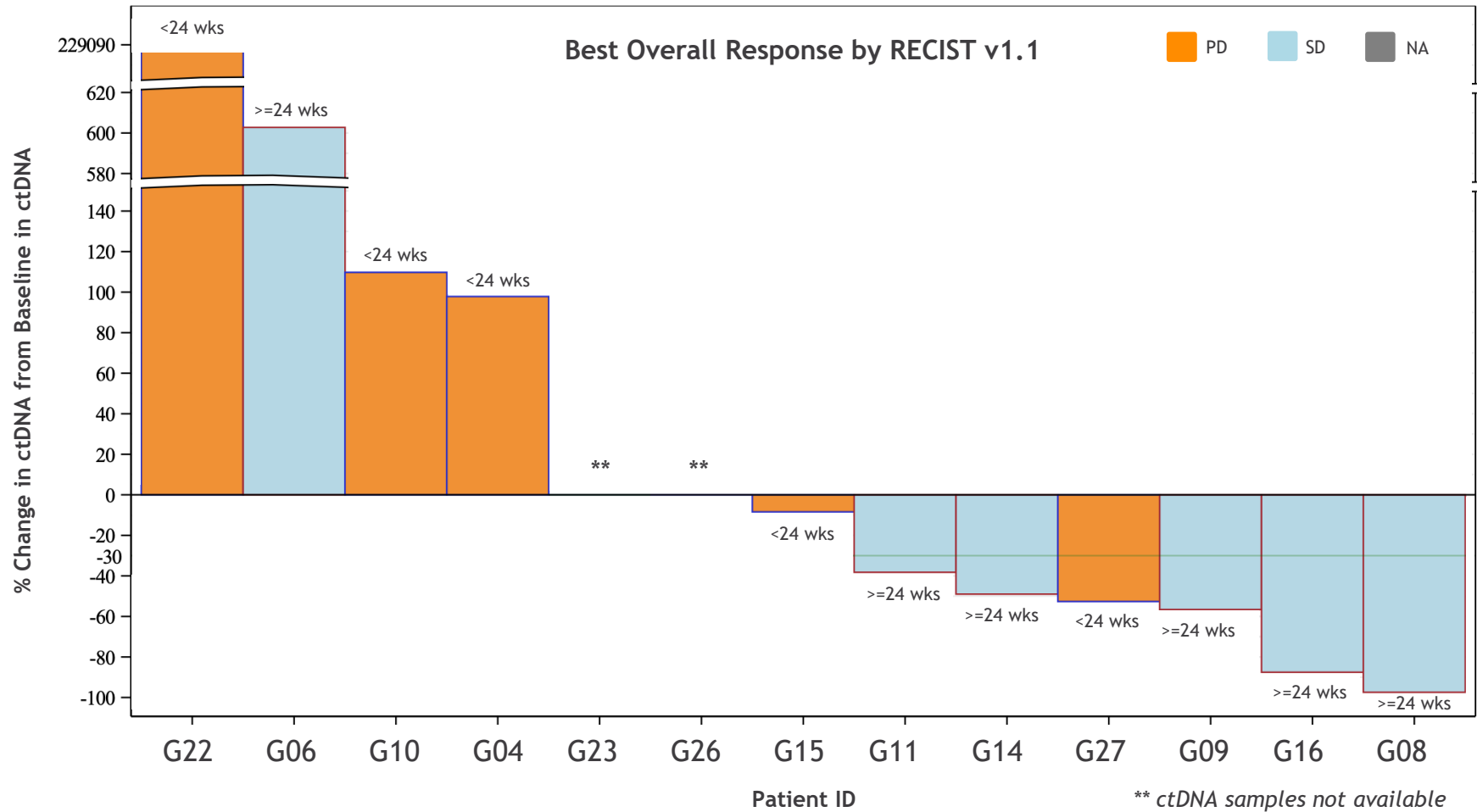
MR = Molecular Response

ctDNA recurrence around 12 months



Molecular Response: Multiple Patients with MSS-CRC Have a Molecular Response with Associated Clinical Benefit

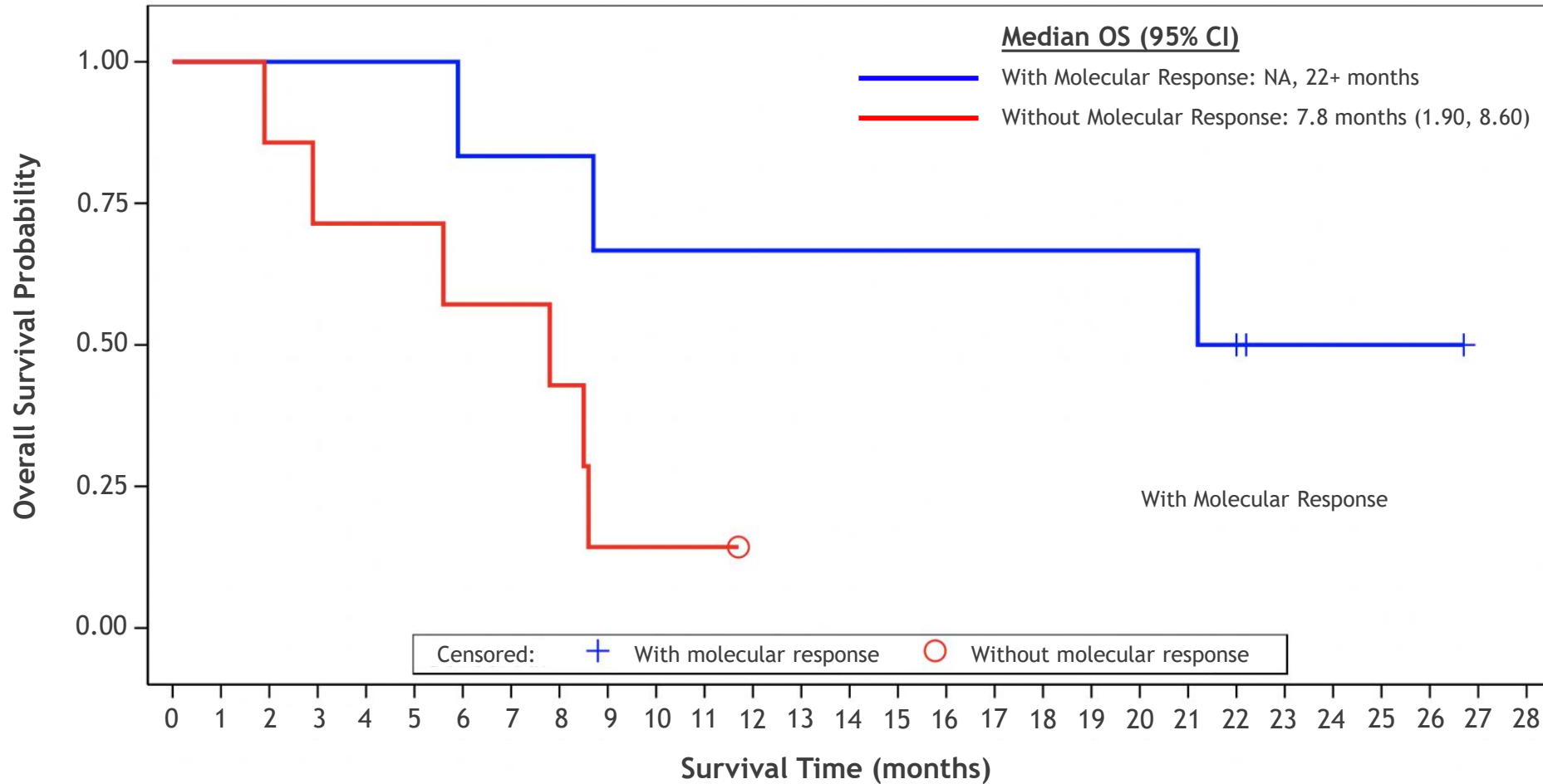
Data cut-off 31 Aug 2022



Molecular response defined as a reduction of at least 30% in mean variant allele frequency (VAF) relative to baseline at any time following initiation of study treatment. Duration of treatment annotated as < or >= 24 weeks per patient.

Molecular Response: Patients with Molecular Response Have Prolonged Overall Survival Compared to Those without Molecular Response

Median overall survival not reached, extending beyond 22 months in molecular responders Data cut-off 31 Aug 2022

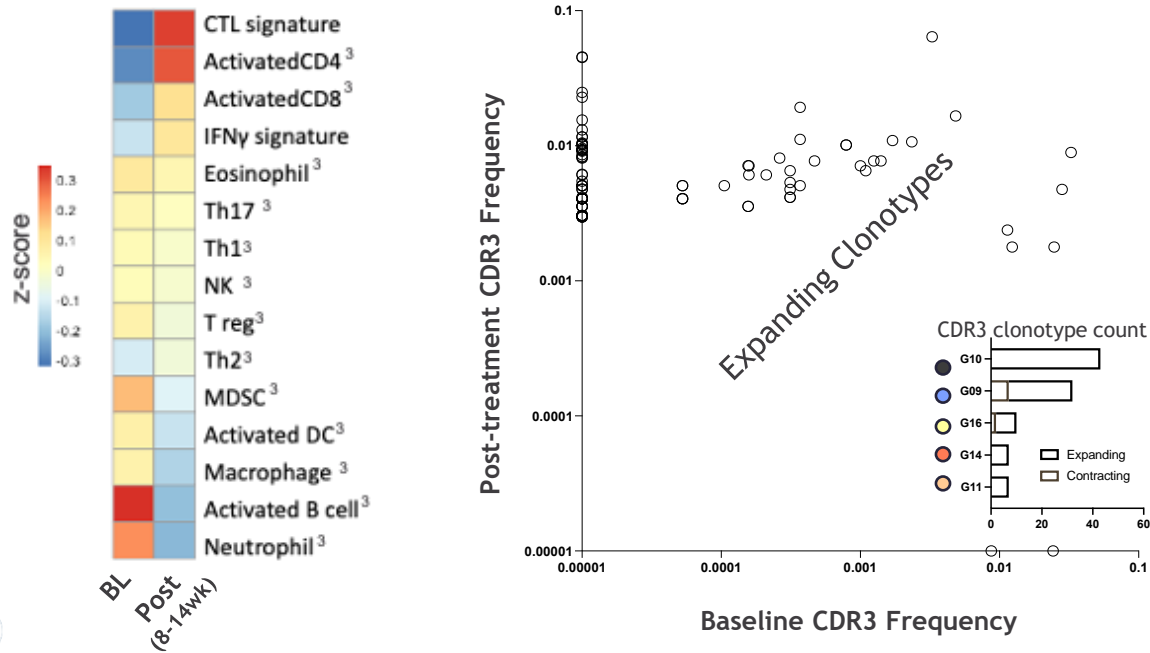


	Number at Risk				
	0	2	4	6	8
With Molecular Response	6	5	4	4	1
Without Molecular Response	7	4	0	0	0

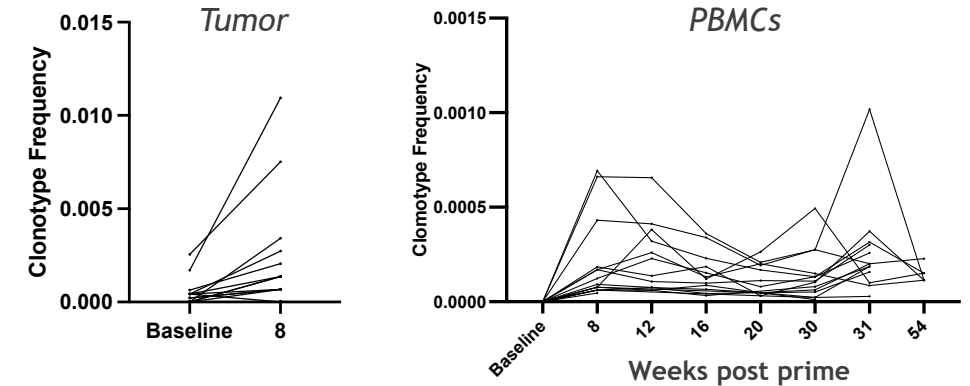
Biomarkers: Association of Joint Tumor and Peripheral TCR Expansion with Increased CD8 Effector T Cell Infiltration Gene Expression Post Treatment

Paired pre and post treatment tumor RNAseq and TCRseq with accompanying longitudinal clonotype tracking from 5 patients with MSS-CRC

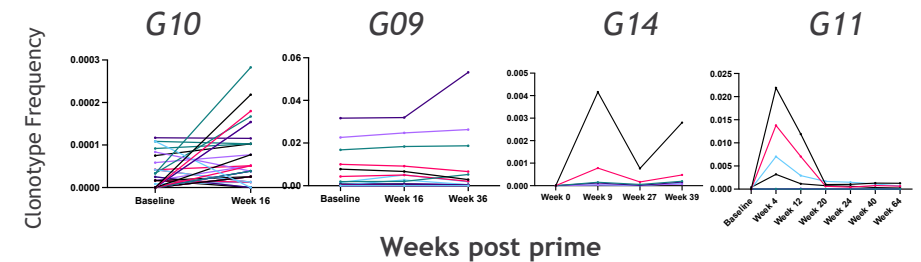
MSS-CRC Paired pre and post biopsy immune infiltration associated gene expression signatures (left) and TCRseq CDR3 clonotype differential abundance (right)



Peripheral TCR clonotype kinetics identified in paired pre- and post- tumor tissue Patient Example: G16 TCR clonotype kinetics in tumor (left) and PBMCs (right)



Significantly expanded or contracted tumor TCR clonotypes identified in PBMCs



³Immune subtype signatures (PMID: 29628290)

Significant tumor TCR CDR3 expansion determined via a binomial test with Benjamini-Hochberg correction and P value <0.01, analyzing TCRs with two cells or more in either timepoint
CDR3 = complementary determining region

Conclusions



Highly Sensitive Assay for ctDNA Detection

- ctDNA monitoring assay designed to capture all coding mutations detected in neoantigen prediction biopsy
- >90% of predicted neoantigens detected in ctDNA (>80% of all coding mutations) - detection is more accurate than in tumor tissue
- Tumor informed and naïve approach allows versatile disease monitoring including capturing evidence of vaccine-induced immune evasion



Clinical Efficacy

- Molecular response (reduction in ctDNA) observed in 55% (6 out of 11 evaluable) of patients with CRC
- Molecular response associates with improved overall survival in patients with CRC



MOA

- Evidence of vaccine-induced immune evasion through acquired biallelic loss of function TAP1 mutations and HLA-LOH
- T cell expansion is associated with increased Immune infiltration (based on gene expression signatures) in paired pre- and post- treatment tumor specimens
- Differentially expanding T cell clones are found both in the periphery and in the tumor



Future Directions

- These data lead to a randomized Phase 2/3 study in patients with CRC which is currently enrolling and treating patients (NCT05141721)



Thank You

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