SITC 2022

NOVEMBER 8-12 BOSTON MASSACHUSETTS

The Society for Immunotherapy of Cancer 37th Annual Meeting and Pre-Conference Programs

THE LEADING CANCER IMMUNOTHERAPY AND TUMOR IMMUNOLOGY CONFERENCE

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Society for Immunotherapy of Cancer

#SITC22

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NOVEMBER 8-12 BOSTON MASSACHUSETTS

Personalized DNA neoantigen vaccine (GNOS-PV02) in combination with plasmid IL-12 and pembrolizumab as second-line (2L) treatment for advanced hepatocellular carcinoma (HCC).

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37th Annual Meeting and Pre-Conference Programs #SITC22

DISCLOSURE

Clinical investigator on the ongoing GT-30 Phase 1b/2a clinical trial

Clinical trial sponsored by Geneos Therapeutics

INTRODUCTION

- Liver cancer is the 6th most common cancer globally and the 3rd leading cause of cancer death[1]
- HCC is the predominate subtype of liver cancer, accounting for ~80% of cases and occurring with greater frequency in Asia[2, 3]
- Atezolizumab plus bevacizumab have recently become standard of care for treatment in 1L HCC, having displaced TKIs
- 2L treatments include TKI's such as sorafenib or lenvatinib after 1L CPI combination or pembrolizumab following TKI in 1L
- Efficacy of pembrolizumab in 2L post 1L TKI is limited:
  - 13.7% - 18.3% ORR, 12.9 mo - 14.6 mo mOS[4]

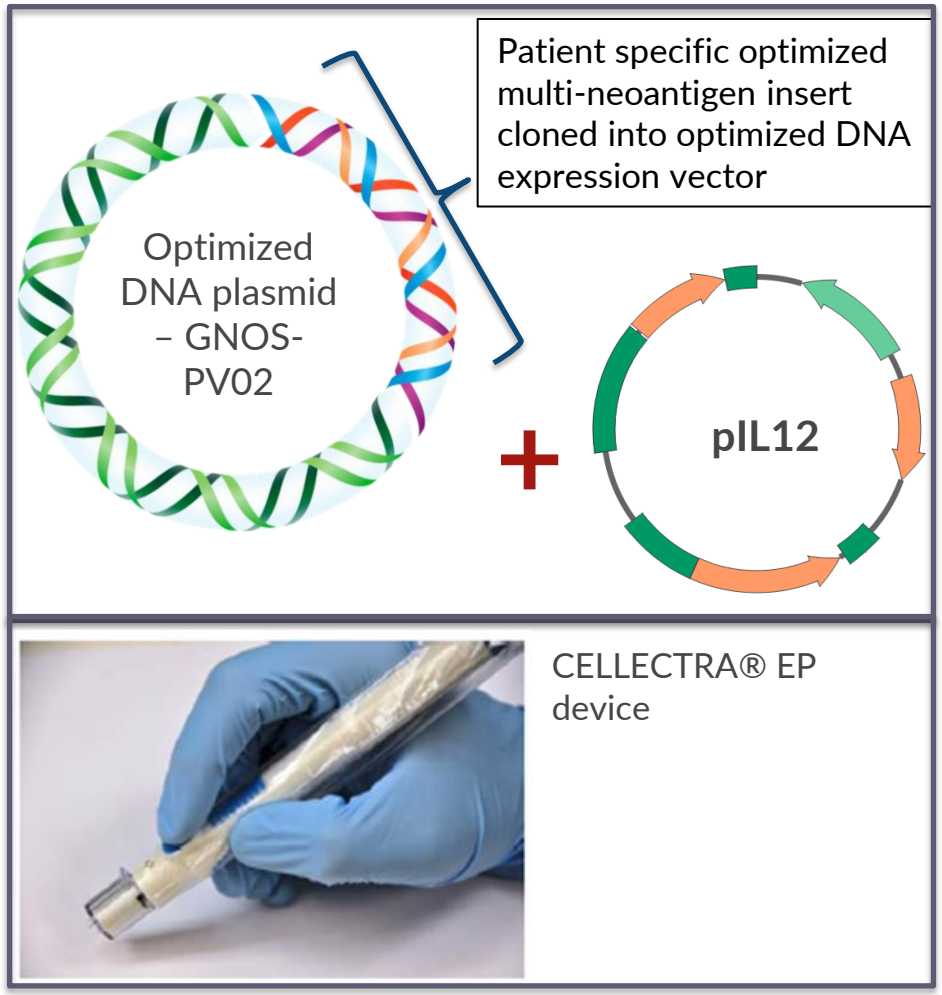
Abbreviations: HCC- hepatocellular carcinoma, TKI: Tyrosine kinase inhibitor, CPI: check point inhibitor, 1L: first line treatment, 2L: second line treatment, ORR: Overall Response Rate
[1]Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. [2] Golabi P et al. Medicine 2017, 96(9):e5904, [3] Vogel A. et al. Ann Oncol. 2021: 32(6) 801-805, [4] Keynote-394, Keynote-224, Keynote-240

PERSONALIZED THERAPEUTIC VACCINATION HAS THREE COMPONENTS

- Optimized DNA plasmid encoding up to 40 neoantigens (Personalized Therapeutic Cancer Vaccine (PTCV); GNOS-PV02)
- Plasmid encoded IL-12 (pIL12) cytokine adjuvant
- CELLECTRA® in vivo electroporation device (EP) for intradermal delivery

Mechanism of Action: pIL12 and EP maximize transfection efficiency of DNA plasmids and drive induction of CD4+ & CD8+ T cells (Th1 response) faster and in a higher percent of vaccine recipients

"Needle-to-needle" in 6 - 8 weeks with path to achieve 3 – 4 weeks



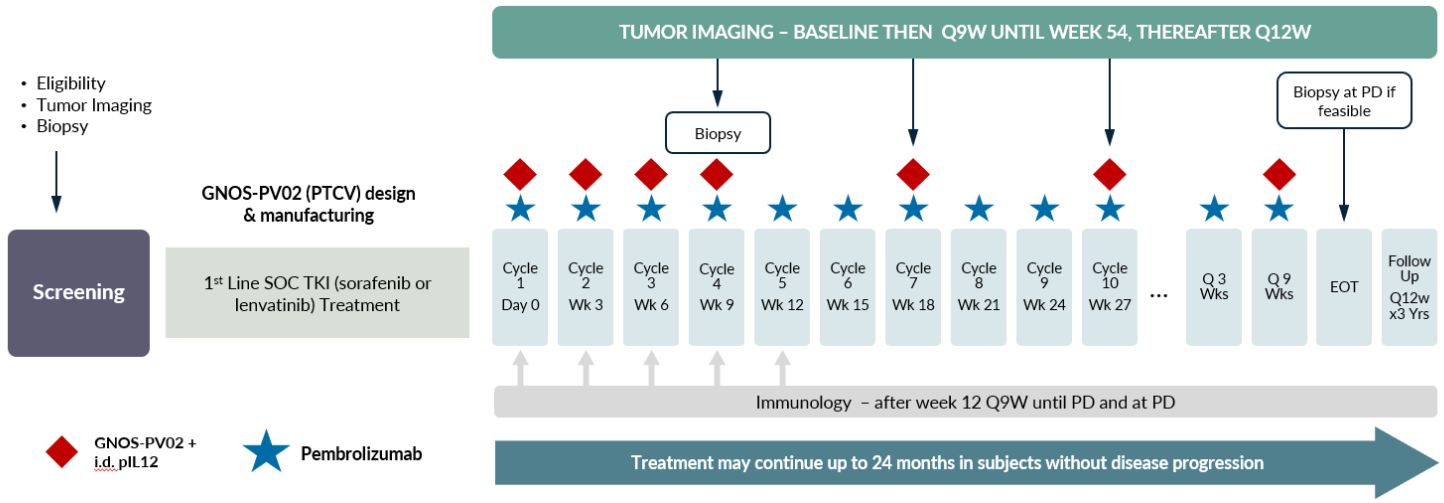
GT-30 STUDY DESIGN

24-patient, phase 1b/2a, multicenter, multiregional study in advanced HCC patients who progress during or are intolerant to 1st Line TKI treatment (sorafenib or lenvatinib)

The goal is to demonstrate safety, immune responses, and enhanced efficacy compared to single agent anti-PD1 therapy

Key Eligibility Criteria:

- Histologically confirmed HCC
- BCLC Stage C or B disease not amenable to or progressed after loco-regional therapy
- Child-Pugh class A
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1



Primary endpoints: Determine safety and efficacy of PTCV and evaluate preliminary immune response
Secondary endpoints: Evaluate the anti-tumor activity

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PATIENT BASELINE CHARACTERISTICS

Demographic Information (n=24)		Number (%)
Median age, years (range)		66.5 (40-78)
Gender	Female	6 (25%)
	Male	18 (75%)
Race	White	14 (58%)
	Asian	7 (30%)
	Other (Black or Pacific Islander)	3 (12%)
ECOG PS	0	17 (71%)
	1	7 (29%)
BCLC Stage	B	10 (42%)
	C	14 (58%)
Etiology	HBV	5 (21%)
	HCV	8 (33%)
	HBV+HCV	1 (4%)
	Non-Viral	10 (42%)
PVI		5 (21%)
Baseline AFP, ng/mL	≥400	4 (17%)
	<400	20 (83%)

Abbreviations:
AFP: alpha-fetoprotein
BCLC: Barcelona Clinic Liver Cancer
ECOG PS: Eastern Cooperative Oncology Group Performance Status
HBV: hepatitis B virus
HCV: hepatitis C Virus
PVI: Portal vein invasion

SAFETY SUMMARY

Serious Adverse Events (SAE)

- 7/24 patients experienced an SAE
- No SAEs attributed to PTCV, pIL12 or electroporation
- One SAE (immune nephritis) related to pembrolizumab; led to discontinuation of treatment

Adverse Events

- 19 patients experienced an AE; most common were injection site reactions
- All AEs mild and self-resolved
- *Treatment-related AEs attributed specifically to PTCV, pIL12 or EP were all Grade 1 or 2*

Treatment-Related Adverse Events (n=19)	Grade 1-2
Injection Site Reaction (discomfort, erythema, pain, pruritis, swelling)	9 (47%)
Fatigue	6 (34%)
Pain (abdominal, feet, knee, muscle)	4 (21%)
Rash	3 (16%)
Itching	3 (16%)
Hypothyroidism	2 (11%)
Fever	2 (11%)
Gastroesophageal reflux	1 (5%)
Joint Aches	1 (5%)
Stiffness (hands, fingers)	1 (5%)
Hypophosphatemia	1 (5%)
Diarrhea	1 (5%)
Anemia	1 (5%)
Dry skin	1 (5%)
Immune nephritis	1 (5%)
Loss of appetite	1 (5%)
Exacerbation of skin tags	1 (5%)

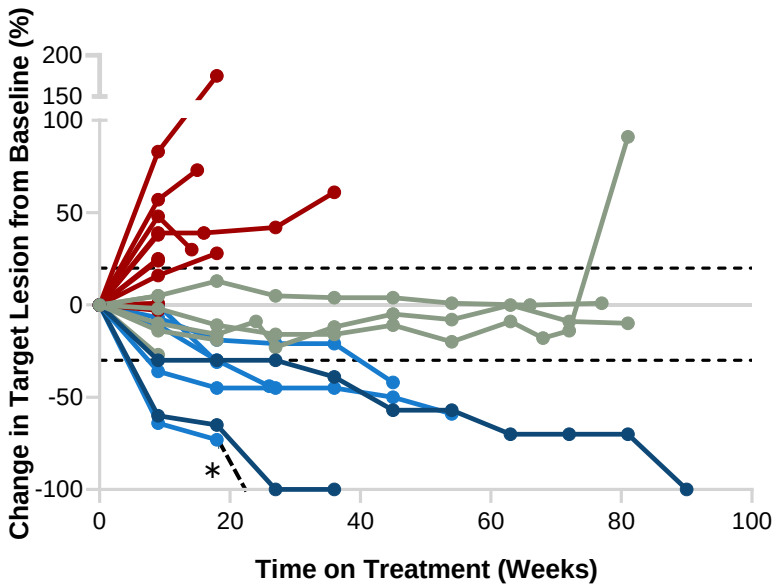
Treatment Related AEs are determined by the investigator for those adverse events deemed as possibly, probably, or definitely-related to PTCV, IL-12, EP and/or CPI

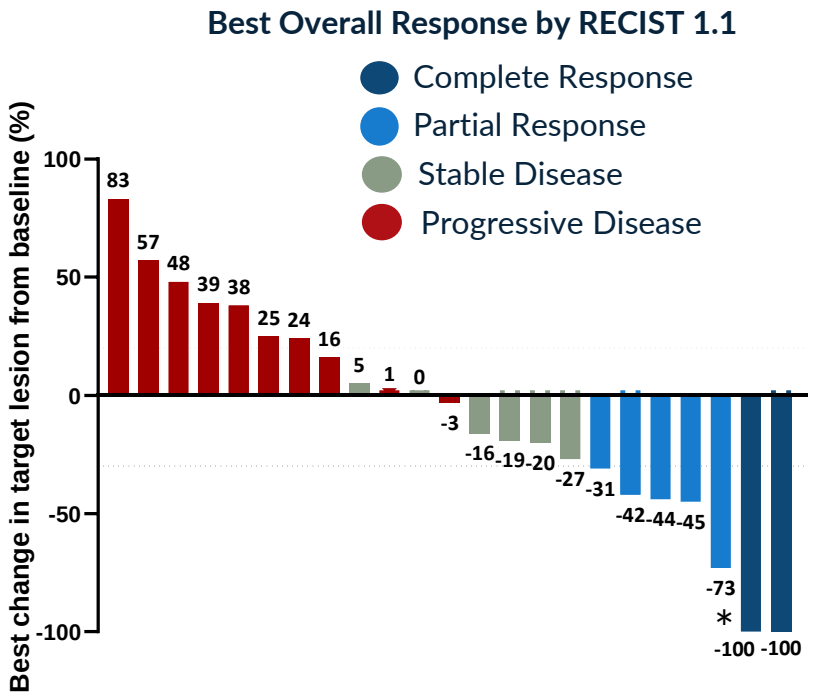
EFFICACY SUMMARY: 29.2% ORR (n = 24 PATIENTS; 2 CR, 5 PR)

% Change from Baseline over Time# & Best Overall Response#

Data from First 24 Patients

(as of June 30, 2022)





To date: 2 CR, 5 PR, 6 SD, 10 PD

- A third subject (*) with liver primary and two lung mets, PR by RECIST1.1, achieved secondary resectability due to tumor shrinkage; now has no remaining evidence of cancer
- ITT: ORR 29.2%, DCR 54.2% by RECIST 1.1
- One patient elected early termination after 1st dose due to unrelated SAE; is non-evaluable
- By evaluable patients, ORR 30.4%, DCR 56.5%

#One patient was not evaluable

Abbreviations: CR: Complete response, PR: Partial response, SD: Stable disease, PD: Progressive disease, ITT: intent to treat, ORR: Overall response rate, DCR: Disease control rate, RECIST: Response evaluation criteria in solid tumors

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GT-30-Pt#17: COMPLETE RESPONSE

73 yo white male, Hep C Cirrhosis

HCC (Aug2019)

Microwave ablation (Aug2019)

TACE (Dec2020 and Jan2021)

Lenvatinib (Jun2021; BOR SD)

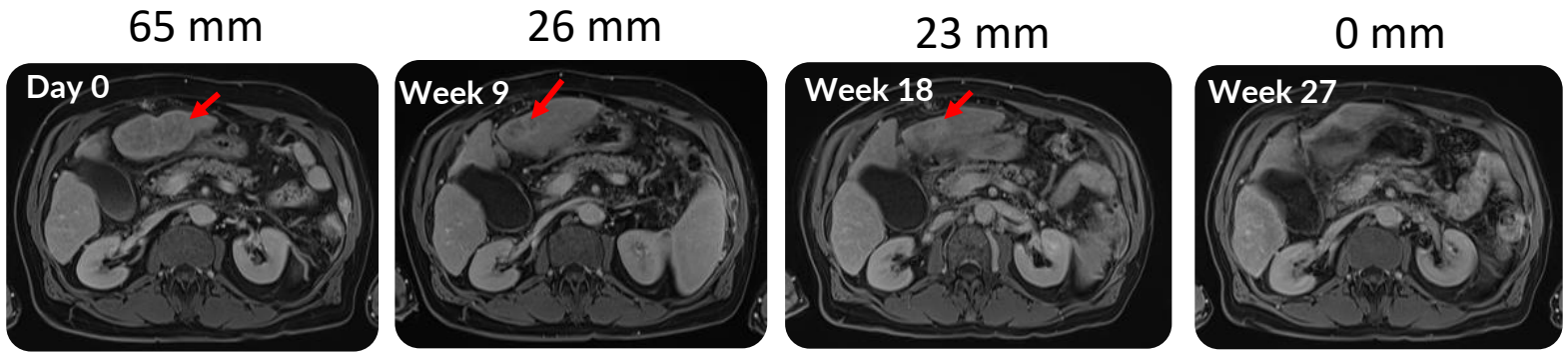
GNOS-PV02 (Sep2021)

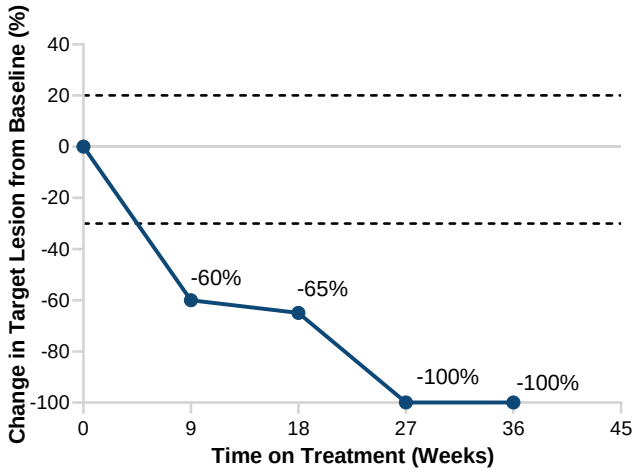
T2N0M0 (II) BCLC B

Beta-catenin mutation (CTNNB1 S45F)

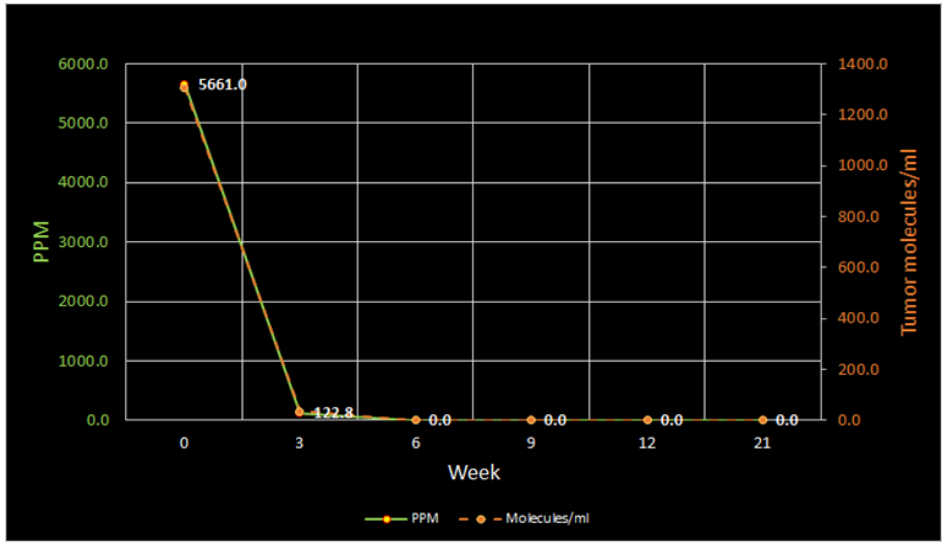
Neos: 40 (Targetable: 49)
PTCV doses: 9
Status: On study

SAEs: 2, unrelated to study treatment
AEs related to PTCV/pIL12/EP: 2, both Grade 1





ctDNA Analysis



See abstract # 692: ctDNA analysis for monitoring tumor progression/regression

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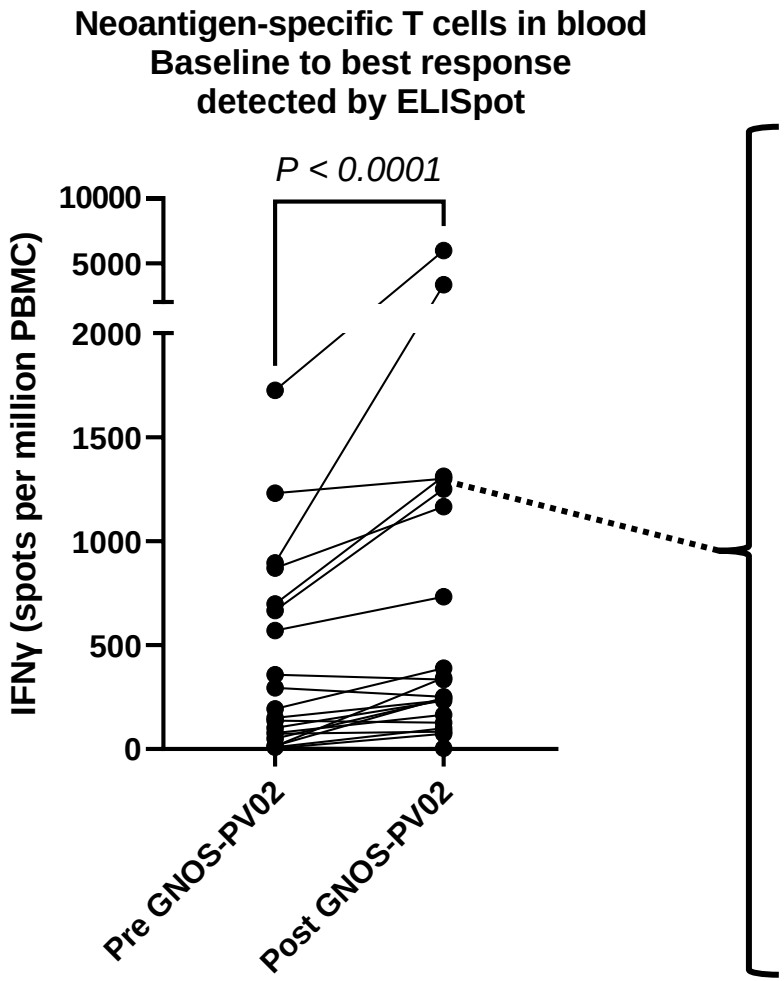
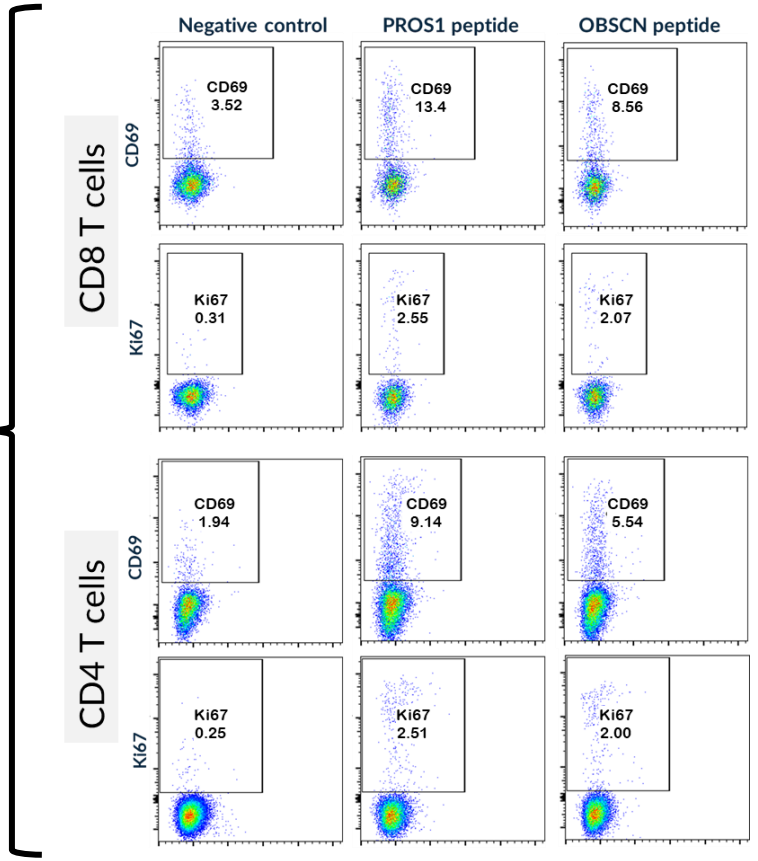
IMMUNE MONITORING SUMMARY: GNOS-PV02 VACCINATION ELICITED STRONG PTCV-SPECIFIC T CELL RESPONSE IN ALL EVALUATED PATIENTS (n = 22)





GNOS-PV02 + pIL12 Vaccination elicits:

- Neoantigen-reactive T cells
- Both $CD8^+$ and $CD4^+$
- $IFN\gamma^+/CD69^+/CD137^+/Ki67^+$

See abstract # 691: PTCV induced immune pressure and evidence for clonal escape

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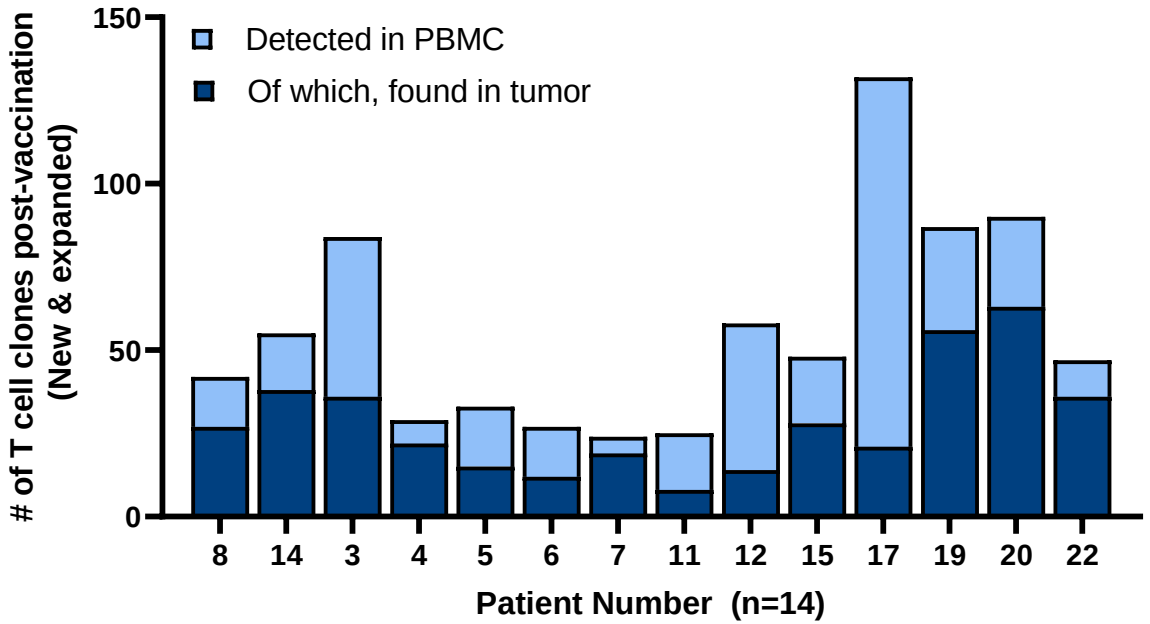
GNOS-PV02 VACCINATION INDUCES NEW & EXPANDED T CELLS WHICH TRAFFIC TO TUMOR (TILs) IN 100% (14 of 14) OF ASSAYED PATIENTS

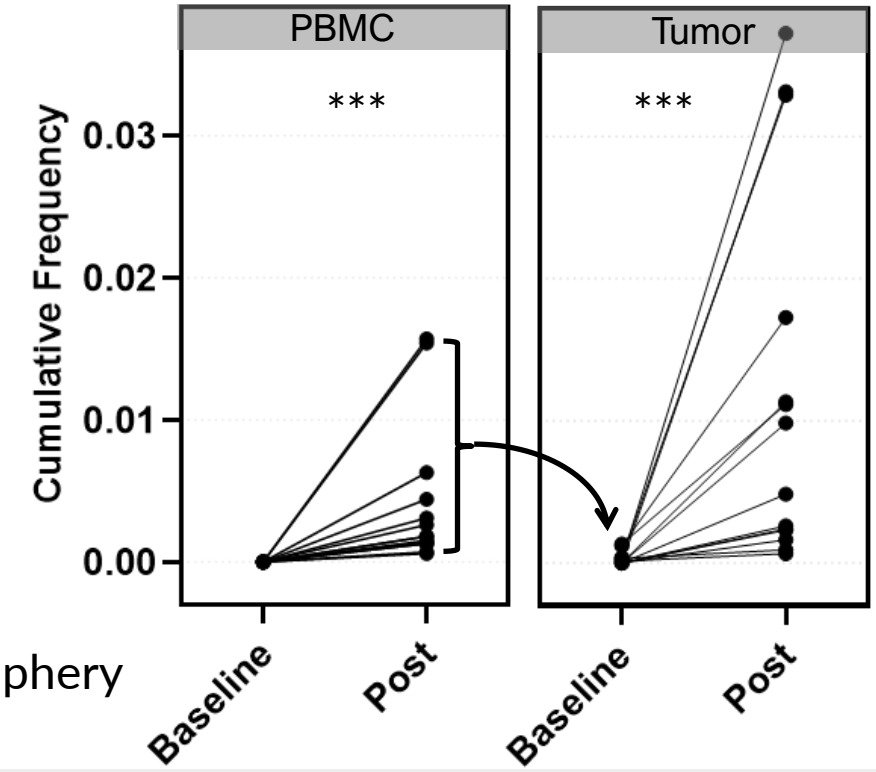
Post-vaccination new & expanded T cell clones detected in each patient

Number of clones ← → **Cumulative frequency**



T cell clones with increased frequency in the periphery...

... are then newly detected in high frequency in the tumor



In all patients, post-vaccination:

(1) An increase is seen in new & expanded T cell clones in the periphery

(2) These new & expanded clones traffic to the tumor (TILs)

****, p < 0.001, Wilcoxon matched-pairs signed-rank*

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SUMMARY: PTCV + PEMBROLIZUMAB 2L IN ADVANCED HCC

- GNOS-PV02 is safe and exceptionally well tolerated
- GNOS-PV02 is effective in patients with advanced HCC who have been previously treated with TKI
  - All patients developed tumor-specific CD4 and CD8 T-cells in PBMCs and within tumor tissue, confirming trafficking (TILs)
  - Overall response rate in 7/23 (30%) which is improved compared to historical results of PD1 (L1) monotherapy
  - 3 patients remain cancer-free

NEXT STEPS: PTCV + PEMBROLIZUMAB 2L IN ADVANCED HCC

- Current study has now been expanded to 36 patients with the additional 12 already consented
- Improved vaccine manufacturing should accelerate "needle to needle" timing to enable use in both 1L & 2L settings
- Phase 2b study in 2L HCC patients post bevacizumab/atezolizumab
- Creating path to achieve FDA registration in HCC
- Future PTCVs could be combined with other immunotherapies and molecular targeted therapies for 1L and 2L therapy of HCC and other cancers

ACKNOWLEDGEMENTS

We would like to thank all of the patients, families and caregivers who participated in this study, along with the investigators and site staff that continue to support this important study

We would like to thank the staff at Geneos Therapeutics, and the Wistar Institute

ADDITIONAL ABSTRACTS WITH MOA DATA

- SITC Oral Presentation 1174: Personalized DNA neoantigen vaccine (GNOS-PV02) in combination with plasmid IL-12 and pembrolizumab as second-line (2L) treatment for advanced hepatocellular carcinoma (HCC) (Edward Gane – Presenter)

- SITC Poster 692 (10-11Nov22): Circulating tumor DNA analysis of advanced HCC patients treated with neoantigen targeted personalized cancer DNA vaccine in combination with IL-12 and anti-PD1 (Jian Yan – Presenter)

- SITC Poster 691 (10-11Nov22): Immune pressure in an advanced hepatocellular cancer patient following treatment with personalized neoantigen DNA vaccine (GNOS-PV02) in combination with plasmid IL-12 (pIL12) and anti-PD1 (pembrolizumab) (Mark Yarchoan – Presenter)