4th Cuneo City ImmunoTherapy Conference (CCITC)

Immunotherapy in Hematological Malignancies 2024

CUNEO
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Spazio Incontri Fondazione CRC

neoAntigens based vaccines in cancer prevention

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Organized by Prof. Massimo Massaia, SC Ematologia AO S.Croce e Carle, Cuneo - Italy and
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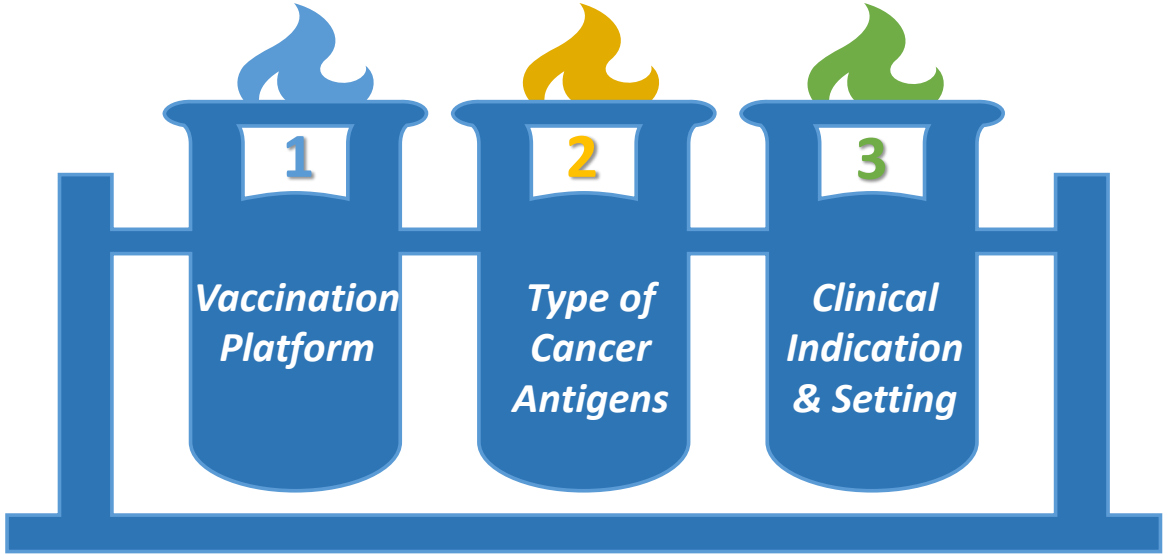
Disclosure of Elisa Scarselli

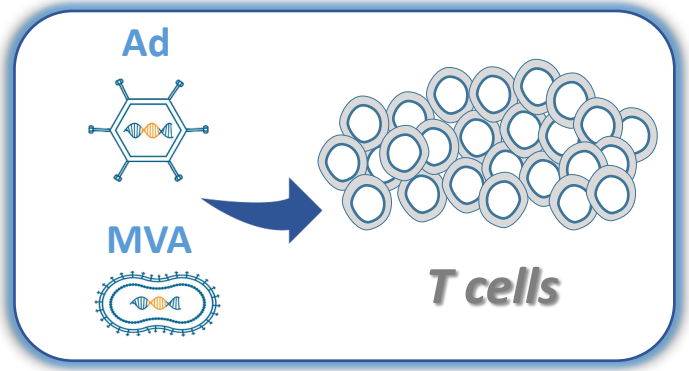
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Nouscom		Yes		Yes			

Key components for effective cancer vaccines

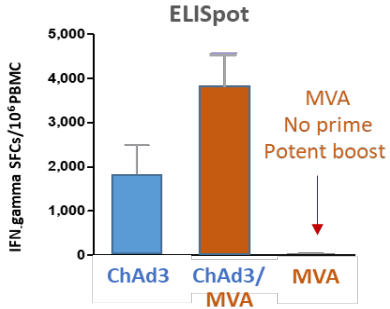


Vaccine platform: Viral vectored vaccines

1 **Heterologous Ad prime/MVA boost for a powerful T cell immunity**

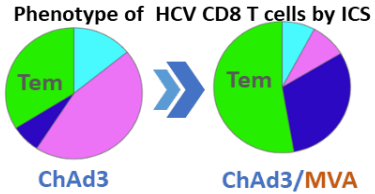


Increased magnitude of vaccine induced T cells



HCV Trial

High quality of T cells for a long lasting immunity

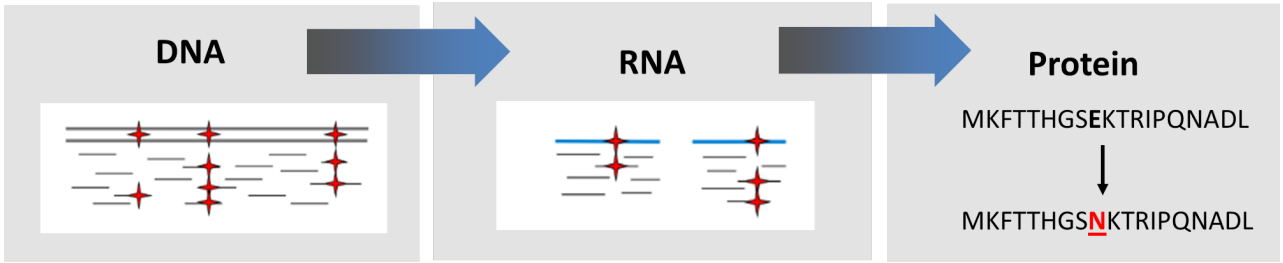


HCV Trial

T effector Memory (Tem)

Type of Cancer Antigens: neoAntigens (nAg)

2



Tumor-specific mutated peptides can be detected by the immune system as exogenous pathogens “non self”

nAg are potent immunogens with low risk of inducing autoimmunity

Selection of Clinical indication & Setting

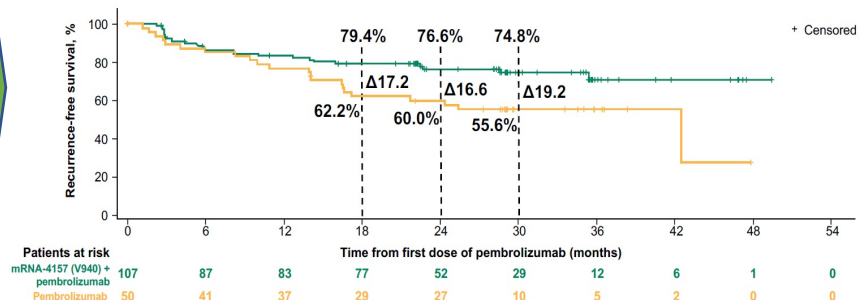
3

CPI responsiveness

Late Stage CPI responsive	Early Stage CPI responsive
Late Stage CPI non responsive	Early Stage CPI non responsive

Clinical Stage

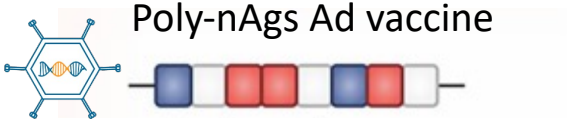
Clinical efficacy in **Adjuvant Melanoma**



RFS 3y follow-up data nAg mRNA vaccine + Pembro

Weber, ASCO 2024

Poly-nAgs vaccine synergizes with anti-PD-1 to cure established tumors

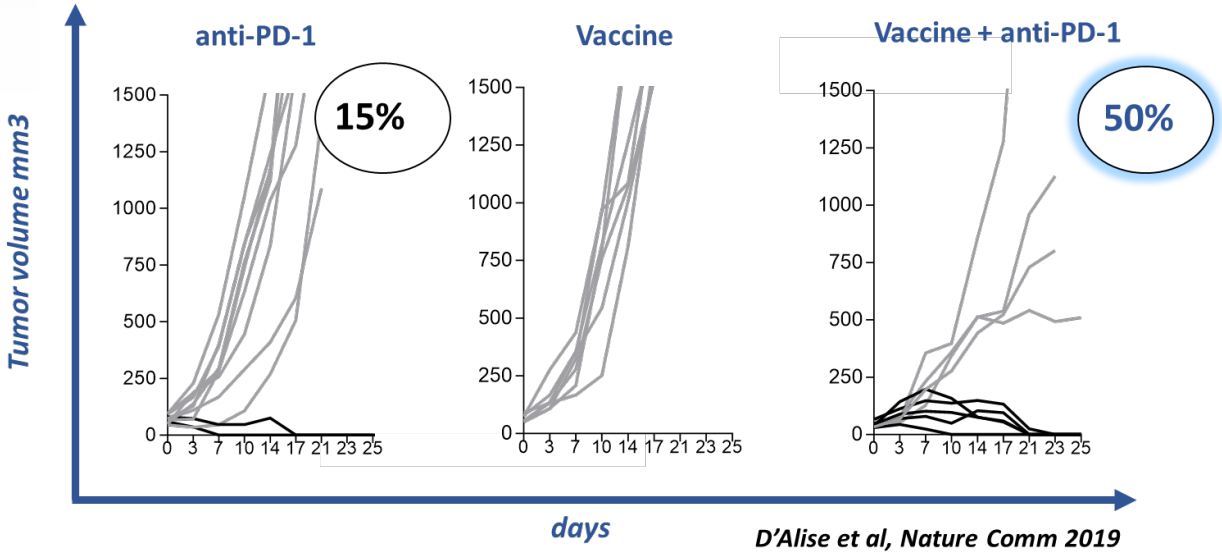


CT-26 or MC38 model

- Responsive to CPI

Established tumor setting

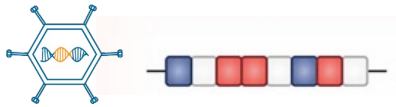
treatments initiation when tumors are ≈ 100 mm3



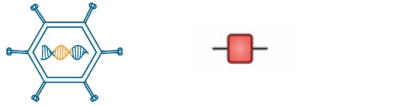
D'Alise et al, Nature Comm 2019

T cells against many nAgs are needed to cure established tumors

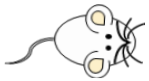
Poly nAgs Ad Vaccine



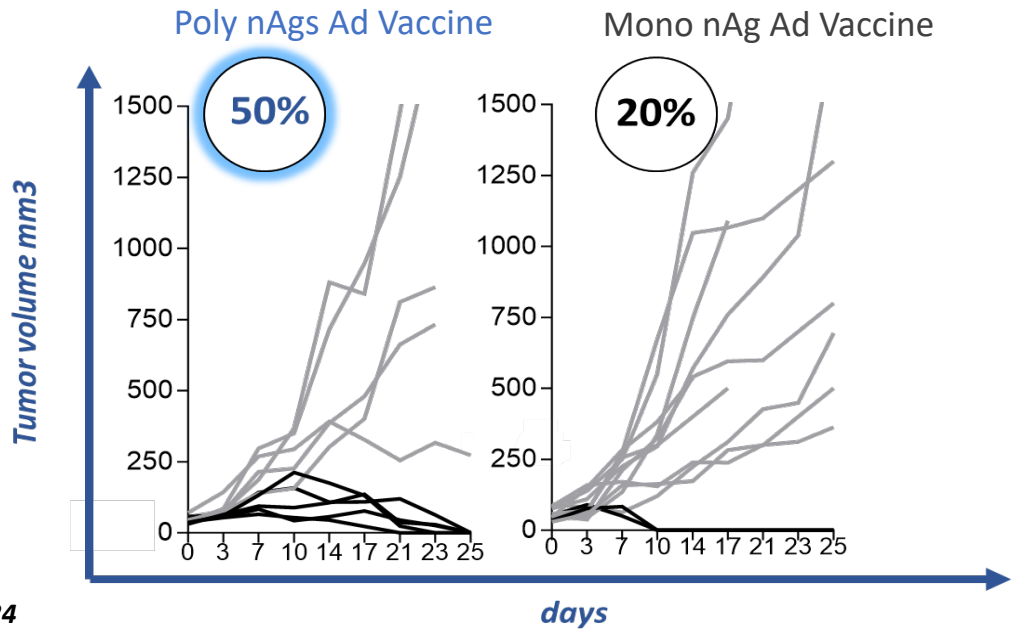
Mono nAg Ad Vaccine



CD4 & CD8 epitopes

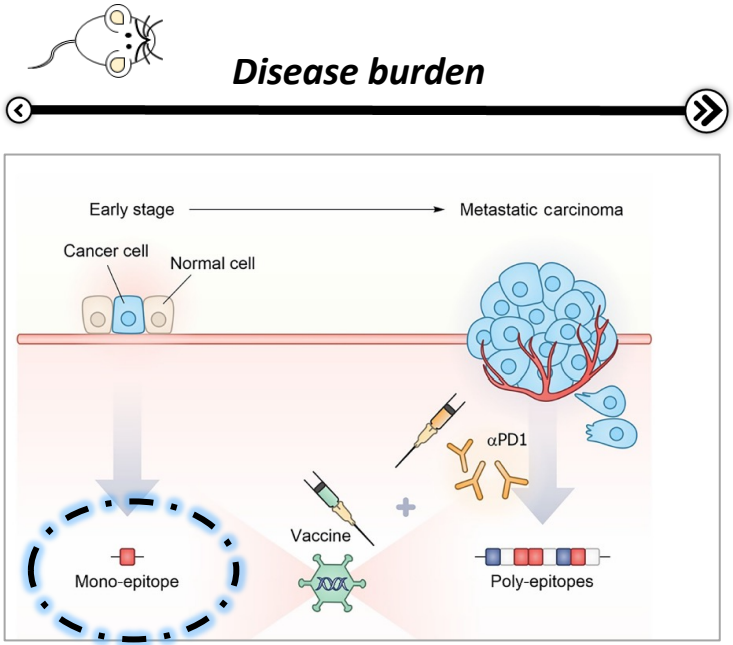


Vaccine + anti-PD-1 combo

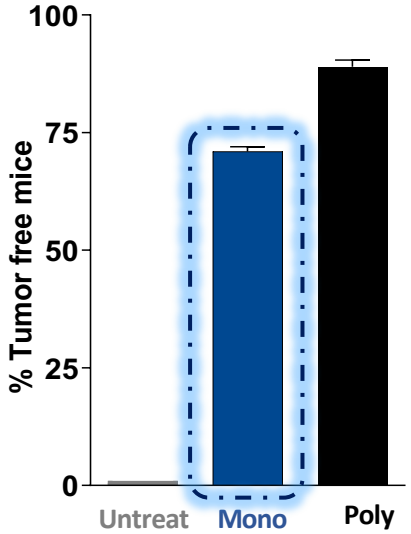


Garzia et al, Cancer Immunology Research 2024

T cells against a single nAg are sufficient to cure early tumors

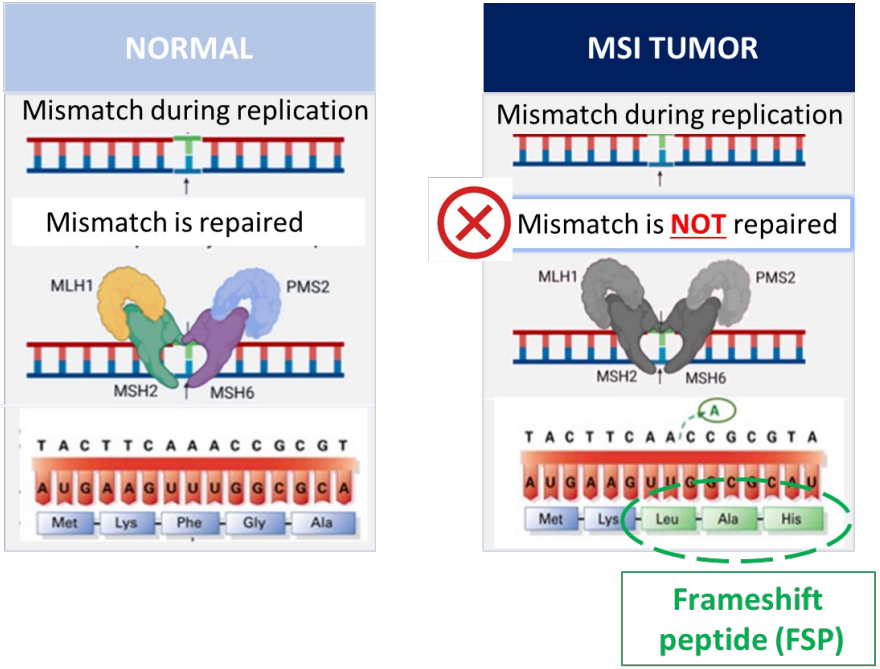


Vaccine stand alone



Garzia et al. Cancer Immun Res 2024

MSI tumors have shared and good quality nAgs



MSI tumors are caused by a defect in DNA mismatch repair system that leads to the accumulation of mutations (insertion/deletion) within microsatellite regions.

In coding regions, indels **cause a shift of the translational reading frame** resulting in **novel non-self frame shift peptide (FSP)**.

Those mutations affect a limited number of genes and are, therefore, **shared** among patients.

NOUS-209: an off-the-shelf neoantigens vaccine for MSI

Bioinformatic analysis of mutations in hundreds MSI tumors from TCGA database

MSI tumors

Colorectal Gastric Endometrial

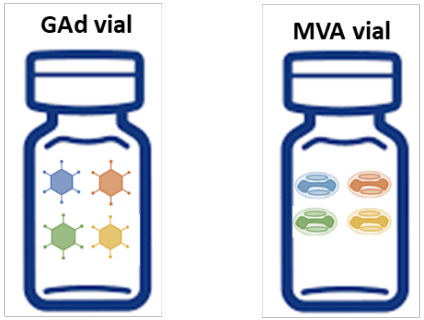
Leoni et al.2020

Selection shared FSP by proprietary algorithm

209 FSP were selected and assembled into **4 artificial genes**

FSPs

NOUS-209 Vaccine



Ph1 Study of NOUS-209 anti-PD-1 Combo in metastatic MSI patients

Population

n=20

Anti-PD-1 naive MSI GI
1L/2L mCRC
1L/2L gastric/GEJ

Primary Endpoint: safety and RP2D

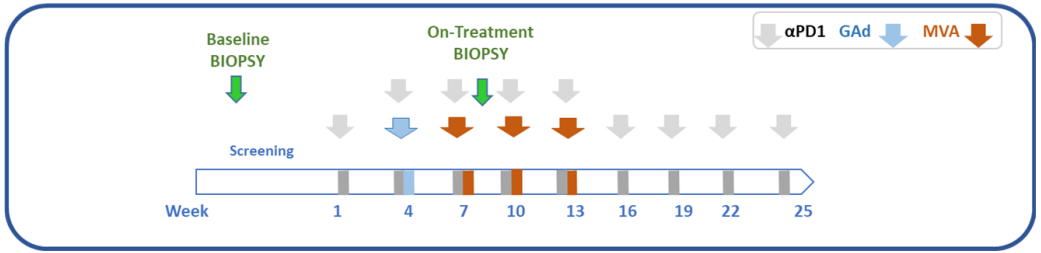
- ✓ Clean safety profile, similar to Pembro monotherapy

Secondary Endpoint: Immunogenicity

- ✓ Potent and broad long lasting immune response

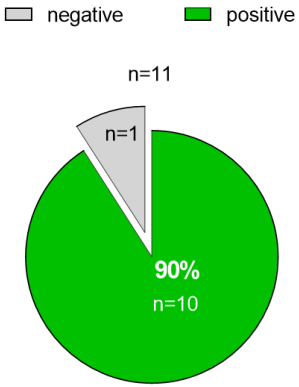
Exploratory Endpoints: Efficacy (RECIST 1.1) & biomarkers

- ✓ Preliminary efficacy data correlating with Vaccine MoA



NOUS-209 induces durable T cell responses

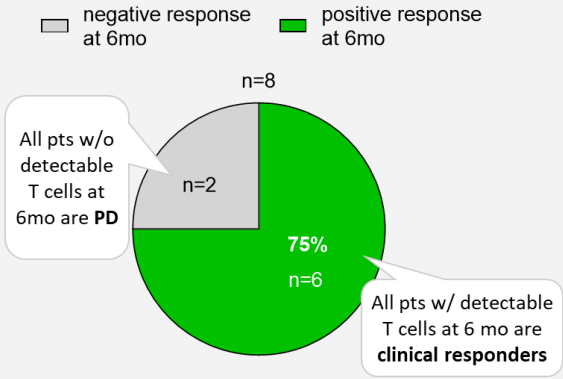
Pts with positive T cell response at peak



Ex-vivo ELISpot

T cell response detected in 90% of pts at RP2D

Pts with positive T cell response at 6 months

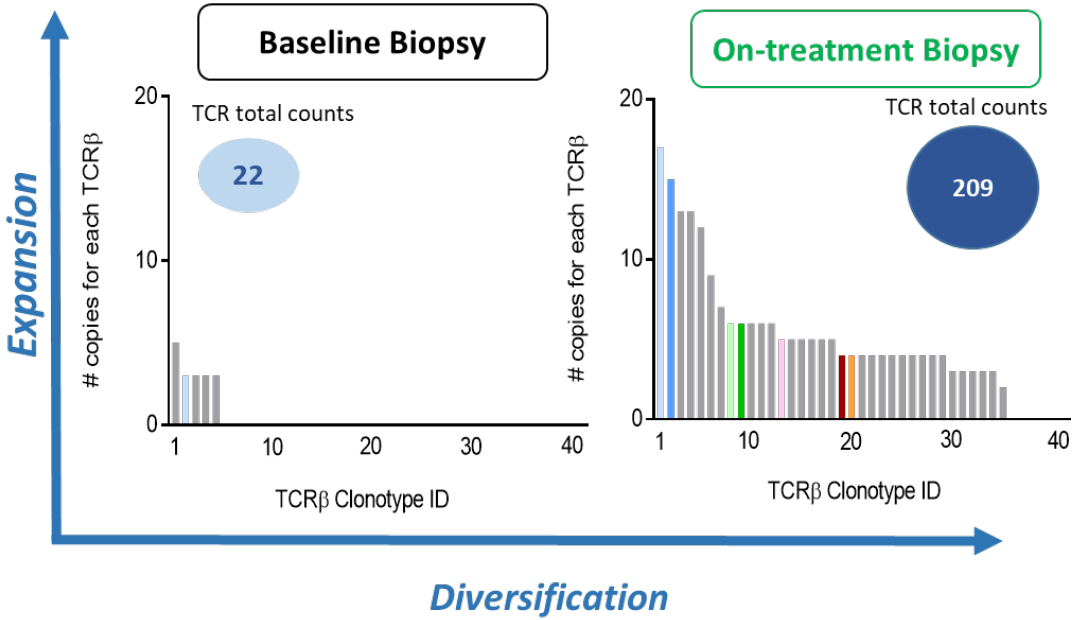


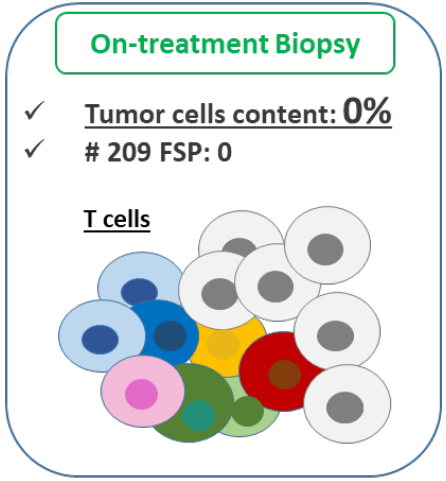
Ex-vivo ELISpot

75% of evaluable pts have long lasting T cells response

Efficacy Biomarker: Vaccine induced TCRs expand in the tumor

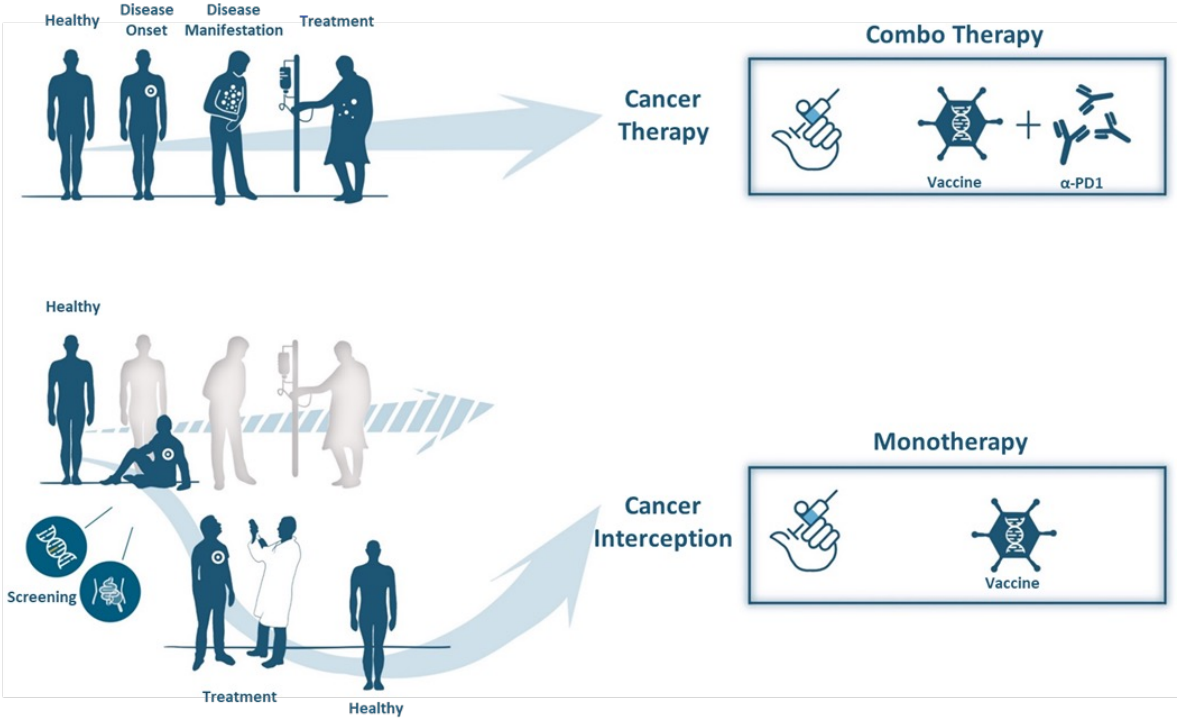
F24 nAg specific TCR identified by NGS of IVS T cell culture from pt1 are tracked in tumor & shown as colored bars





Colored cells: F24 specif TCR

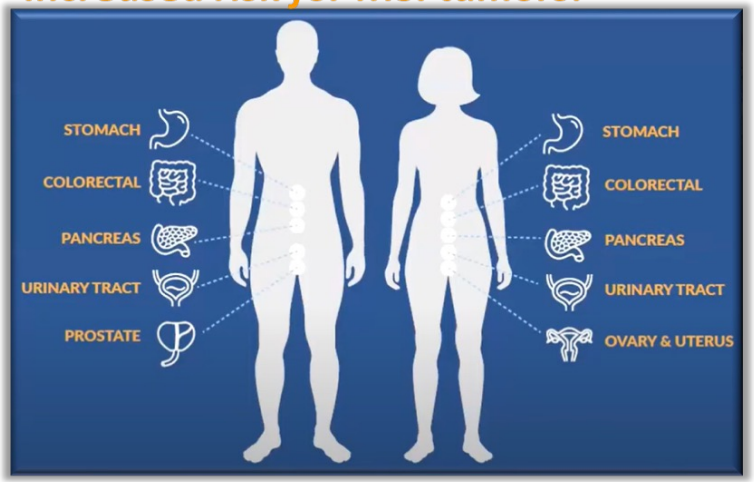
Cancer interception concept & treatment requirements



Lynch Syndrome: high unmet medical need

- **Genetic condition, inherited germline mutations in MMR genes**
- Population prevalence estimate: **1 in 300**
  - ➢**~1 M carriers in US, vastly underdiagnosed**

Increased risk for MSI tumors:

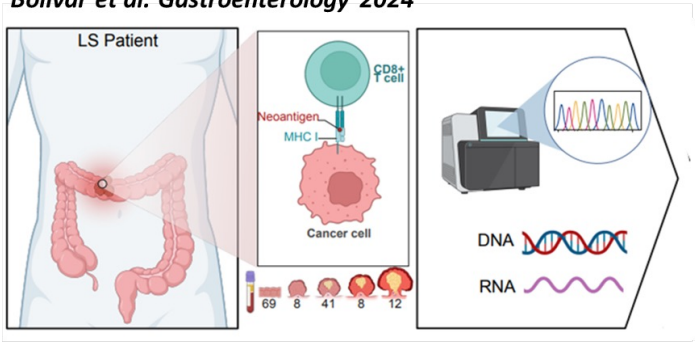


LS-related tumors	Life-time risk
✓Colorectal Cancer	(52-82%)
✓Endometrial Cancer	(25-60%)
✓Gastric Cancer	(6-13%)
✓Ovarian Cancer	(4-12%)
✓Urinary Tract Tumors	(1-4%)
✓Small Bowel	(3-6%)
✓CNS – GBM	(1-3%)

Gruber, Gene Reviews (2012) Hampel and de la Chapelle, CAPR (2011);

Pre-cancers lesions in Lynch Carriers display NOUS-209 nAgs

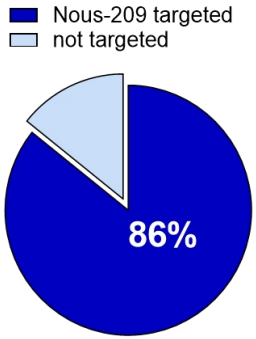
Bolivar et al. Gastroenterology 2024



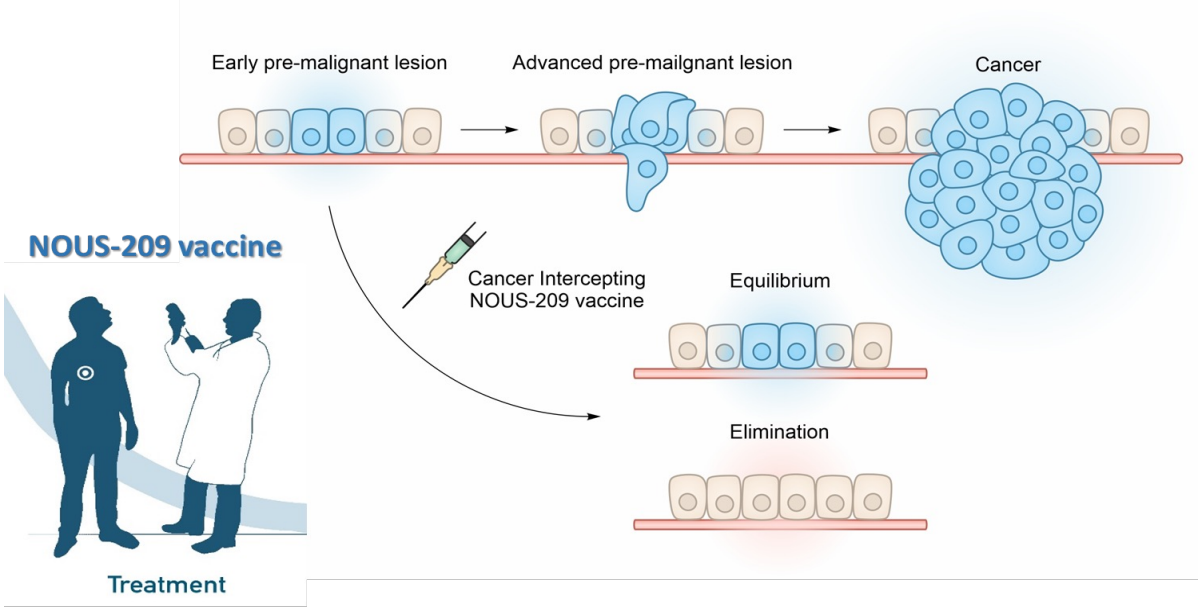
Exome and RNA seq. data from **pre-cancer lesions** in 43 Lynch Carriers

MSI pre-cancer lesions display shared FSPs

86% of LS pts (Bolivar et al dataset) targeted by Nous-209 vaccine



NOUS-209 vaccine to intercept cancer in Lynch carriers



Adapted from Finn, Nature reviews 2017

Phase Ib Clinical Trial of NOUS-209 in Lynch Syndrome carriers

Population

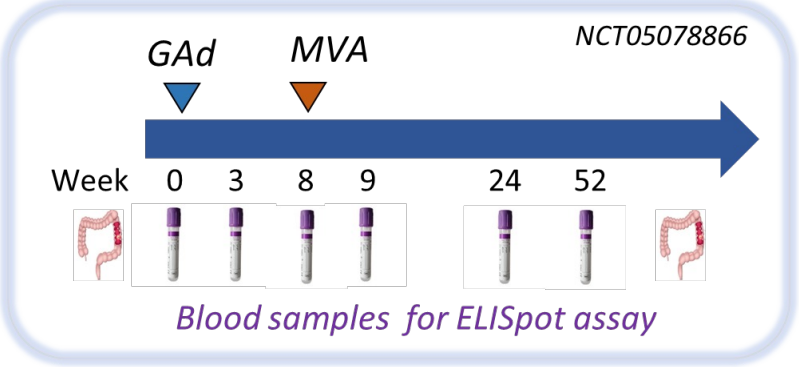
LS carriers (all comers)
N=45

- **Primary Endpoint**: safety & immunogenicity
- **Secondary:** TCR repertoire (blood, CRC normal mucosa, TIL, others)

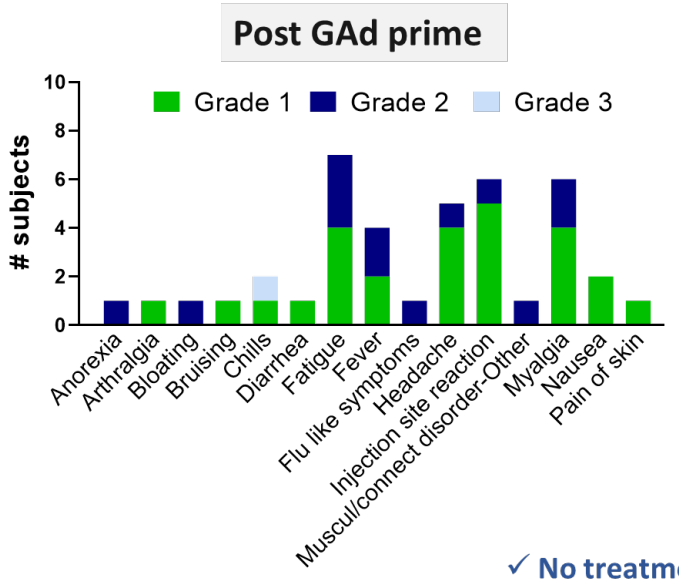
Clinical Sites:
- MD Anderson Cancer Center (**PI: Eduardo Vilar-Sanchez)**
- University of Puerto Rico (PI: Maria R. Cruz-Correa)
- Fox Chase Cancer Center (PI: Michael J. Hall)
- City of Hope Comprehensive Cancer Center (PI: Gregory E. Idos)

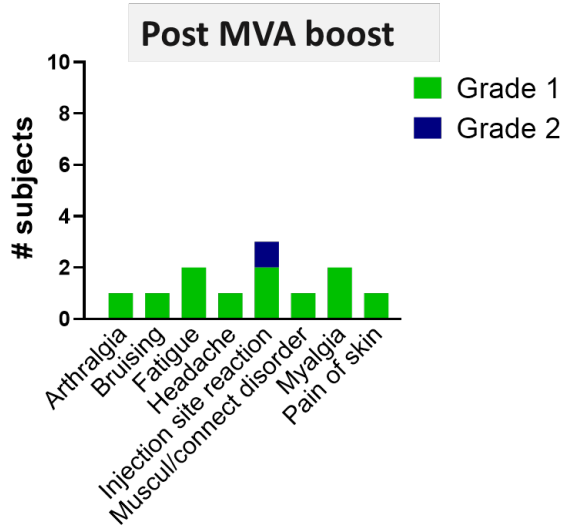
NIH NATIONAL CANCER INSTITUTE
funded by the NCI DCP CP-CTNet network, grant UG1CA242609

Treatment schema



NOUS-209 is safe and well tolerated in LS carriers

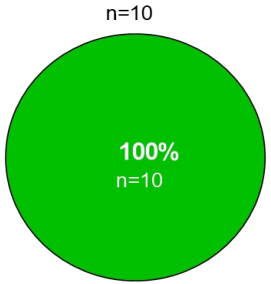




✓ No treatment-related SAEs
✓ Safe and well tolerated

NOUS-209 elicits immune response in all vaccinated volunteers

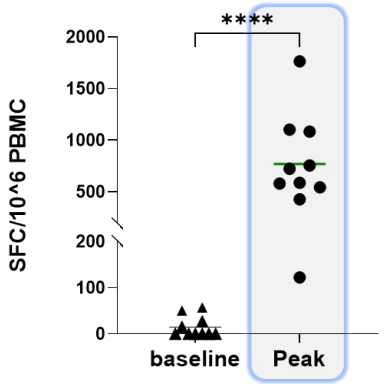
LS carriers with positive T cell response



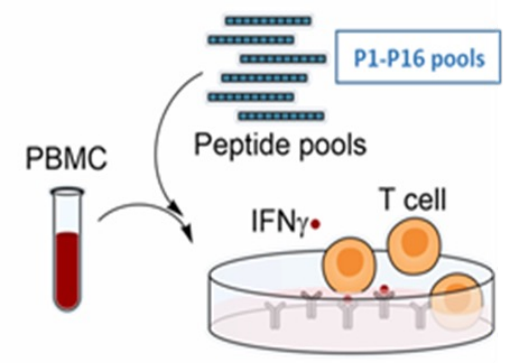
Ex-vivo IFNγ ELISpot

Positive T cell response detected in 100% of subjects post vaccination

Ex-vivo IFN-γ ELISpot (N=10)

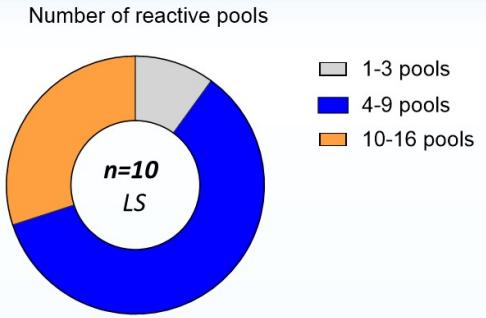


NOUS-209 induces broad immune response against multiple nAgs



Immunogenicity measured by ex-vivo ELISpot on PBMCs using **16 peptide pools covering the 209 FSPs.**
Each pool covers multiple FSPs

Breadth immune response



- ✓ 10% pts showed reactivity against 1 to 3 pools
- ✓ **60%** of pts showed reactivity against 4 to 9 pools
- ✓ **30%** of pts showed reactivity against 10 to 16 pools

Key learnings from Nous209 phase-I trials

Safety

- Monotherapy is safe and well tolerated in LS
- Vaccine anti-PD-1 combo has a clean profile similar to anti-PD-1 alone

Immunogenicity

- Vaccine induced immune response in nearly all patients
- Induced T cell responses recognize multiple neoantigens
- Induction of both CD4 and CD8 T cells
- Vaccine induced T cells are long lasting

Clinical efficacy in line with the MoA

- Expansion and Diversification of TIL in pts with clinical response
- Successful tracking of vaccine induced T cells trafficking in the tumor

Thank you!

I would like to thank the patients, their families as well as investigators for their participation in the trials