Phase I/II study of neoadjuvant personalized vaccination with NECVAX-NEO1 in combination with pembrolizumab and chemotherapy in early-stage TNBC evaluating safety, immunogenicity, and clinical activity NCT06631092

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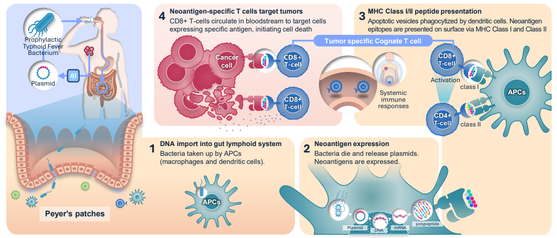
BACKGROUND and MECHANISM OF ACTION

NECVAX-NEO1 is an oral anticancer Salmonella-based vaccine encoding up to 15 patient and tumor-specific neoepitopes. Neoepitopes were identified, selected and ranked using NEC Immune Profiler (AI-based).

NECVAX-NEO1-05-DE (NCT6631092, EUCT 2024-512520-11-00) is an open-label, phase I/II multicenter clinical trial of NECVAX-NEO1 as add-on to first-line neoadjuvant anti-PD-1 monoclonal antibody therapy in patients with triple-negative breast cancer.

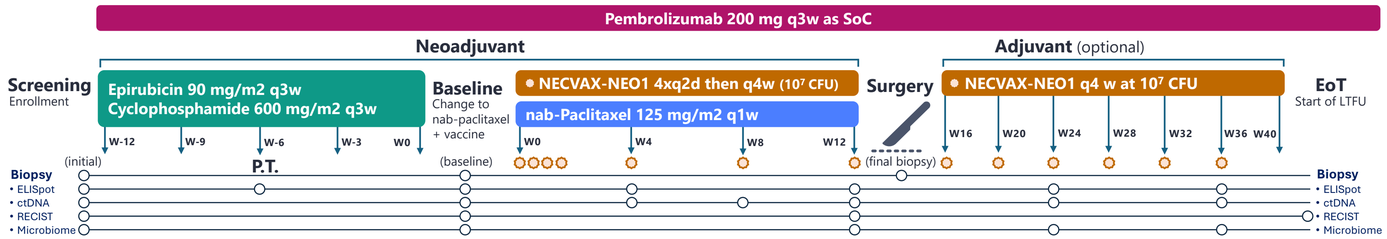
The **primary objective** is to assess safety and tolerability of NECVAX-NEO1, at the dose level of 10^7CFU, in addition PD-1 inhibitor therapy. **Secondary objectives** are clinical efficacy and anti-tumor activity of NECVAX-NEO1 (ctDNA levels).



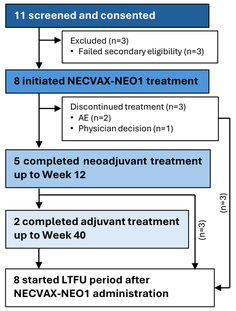
THE PATIENT JOURNEY

Inclusion
- Female and male aged >18 y.o. with ECOG ≤ 2.
- cT2-4 N0 or any N-positive (stage II-III) TNBC.
- Adequate renal, hepatic and bone marrow function.

Exclusion
- Prior transplantation.
- Previous malignant diseases, active infections, severe acute or chronic medical conditions.
- Pregnant women.
- Participation in other trials.

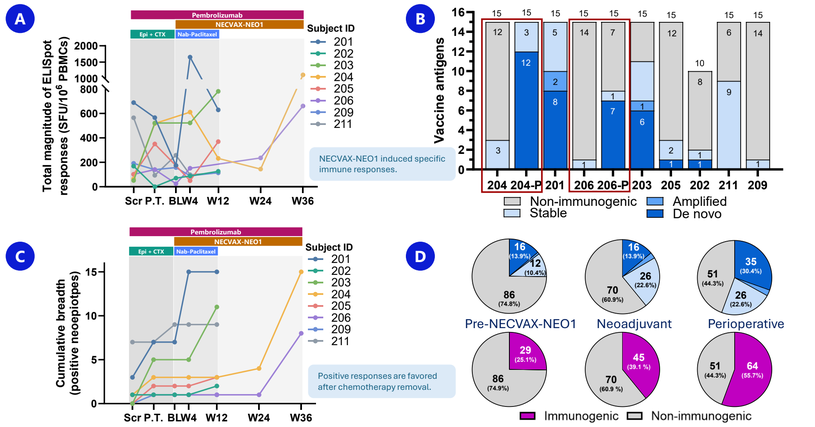


1. PATIENT DISPOSITION



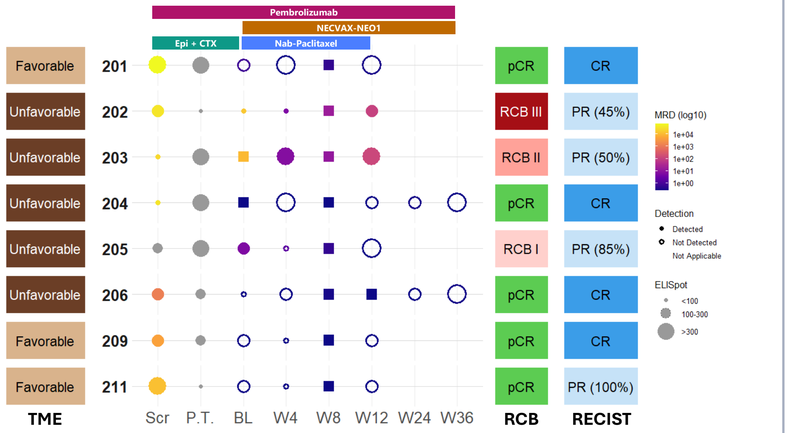
Characteristics at Screening		Characteristics at Screening	
n	8	Disease Stage	
Age (years)		Primary Tumor (T)	
mean (SD)	46.1 (10.6)	cT2	7
median (IQR)	45 (13.8)	cT3	1
Sex		Regional Lymph Node (N)	
Male	0	cN0	4
Female	8	cN1	4
Weight (kg		Metastasis	
mean (SD)	79.5 (14.8)	M0	8
median (IQR)	76.5 (12.0)	Diagnosis	
Height (cm)		IIA	2
mean (SD)	167.0 (9.9)	IIB	5
median (IQR)	168.0 (8.0)	IIIA	1
ECOG status			
0	8		

2. IMMUNE RESPONSE (IFN-γ ELISpot)



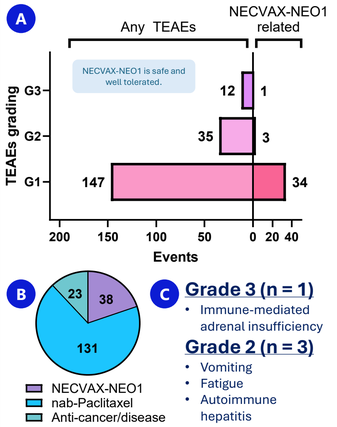
Longitudinal neoepitope-specific immune responses assessed by IFN-γ ELISpot. (A) Total magnitude of ELISpot responses (SFU/10^6 PBMC) per subject and visit. Grey shading indicates the different chemotherapy periods. (B) Classification of neoepitope-specific responses per subject as de novo, amplified, stable, or non-immunogenic. Subjects labelled "P" include the perioperative period. (C) Cumulative breadth of ELISpot responses per subject and visit. (D) Number of responses by response category for the entire cohort (upper panel) and total number of positive responses across treatment phases (lower panel).

3. SUMMARY OF PATIENT-LEVEL RESPONSES



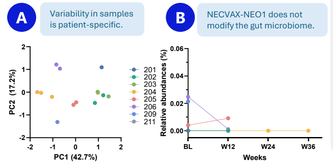
Patient-level longitudinal immune, molecular, and clinical response. Each row represents an individual patient and each column a study visit. Circle size indicates ELISpot response magnitude (SFU/10^6 PBMC), and circle color indicates ctDNA level. Filled and open circles indicate detectable and undetectable ctDNA, respectively; grey circles indicate missing ctDNA measurements, and squares indicate missing ELISpot measurements. Pathological response at surgery is shown as pCR (green) or RCB I–III (red scale). RECIST response at week 12 is shown as PR (light blue) or CR (dark blue), with percentage reduction from screening in parentheses. TME status at screening is classified as favorable (antitumoral) or unfavorable (pro-tumoral), as defined in Panel 6C.

4. SAFETY



Safety profile. (A) Number of treatment-emergent adverse events (TEAEs) by grade, classified as related or unrelated to NECVAX-NEO1. (B) Total number of TEAEs related to NECVAX-NEO1, nab-paclitaxel, or other anticancer therapies. (C) Grade 2 and 3 TEAEs considered related to NECVAX-NEO1.

5. GUT MICROBIOME

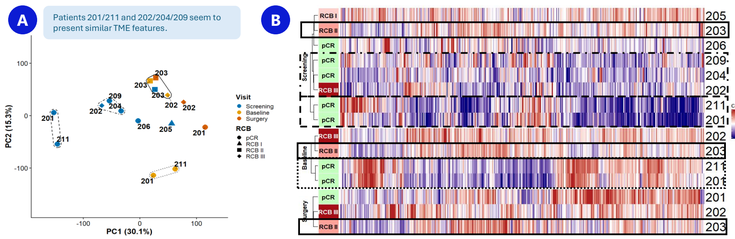


Intestinal microbiome composition.

(A) PCA of bacterial species after 70% prevalence filtering and batch normalization, showing sample distribution across study timepoints.

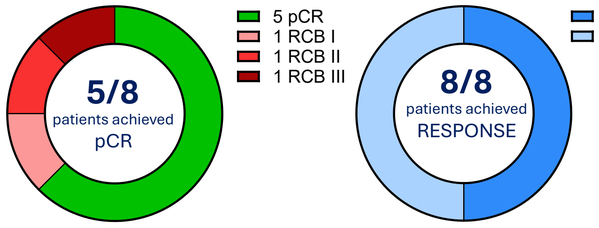
(B) Relative abundance of *Salmonella enterica* across study timepoints.

6. TME CHANGES AND PATIENT CLUSTERING

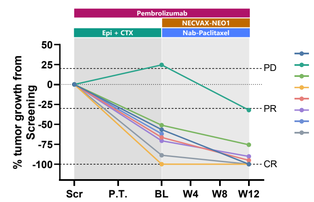


Tumor microenvironment changes. (A) Principal Component of Analysis (PCA) of whole-transcriptome expression, showing sample clustering by patient, visit, and pathological response. (B) Heatmap of the top 5,000 genes discriminating pCR from non-pCR samples, selected by unadjusted Wilcoxon p-values; expression is shown as z-scores. (C) Functional TME composition scores per patient and visit, with contributions weighted by cell-population abundance and functional score. White diamond indicates the net TME score. Positive and negative values indicate favorable and unfavorable profiles, respectively.

7. CLINICAL RESPONSE



8. RECIST 1.1 ANALYSIS



RECIST 1.1 assessment. Radiographic changes in target lesions (%) for each patient. PD, progressive disease; PR, partial response; CR, complete response.

KEY CONCLUSIONS

- ✓ NECVAX-NEO1 was safe and well tolerated.
- ✓ Chemotherapy induced an early immune response.
- ✓ NECVAX-NEO1 induced specific immune responses.
- ✓ Responses increased after chemotherapy is stopped.
- ✓ All patients achieved CR or PR (ORR = 100%).
- ✓ Immune active TME at Screening predicted a favorable outcome.

NEXT

- → Study extended to 28 patients.
- → Dose increased to 10^8 CFU.
- → Change to KEYNOTE 522 SoC.

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