Abstract 321: Phase 1 dose-expansion trial of intratumoral HER2- and HER3-primed dendritic cells injections for the treatment of early-stage TNBC and HR-low positive breast cancer: DecipHER trial.

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San Antonio Breast Cancer Symposium
December 9-12, 2025

Background

- Patients with breast cancers (BCs) harboring low expression of hormone receptors (HRs) and human epidermal growth factor receptor-2 (HER2) negative status have poor outcomes.[1]
- Results from the KEYNOTE-522 trial showed that activation of the immune system can improve outcomes of patients with these high-risk tumors.[2]
- Antigen-presenting cells (eg, dendritic cells [DCs]) are pivotal for robust cytotoxic responses due to broader activation of the adaptive immune system (ie, $CD4^+$ and $CD8^+$ Th1) against tumor-associated antigens (ie, HER2 or HER3).[3]

Methods

- This is phase dose-escalation, dose expansion phase 1 trial of DC intratumoral injections.
- Patients with clinical stage cT1cN1-2 or cT2-4cN0-2, HRs ≤20, HER2-negative BCs are eligible.
- Autologous DCs will be primed *ex vivo* against immunogenic peptides HER3 and HER2 Peptides (table 1).

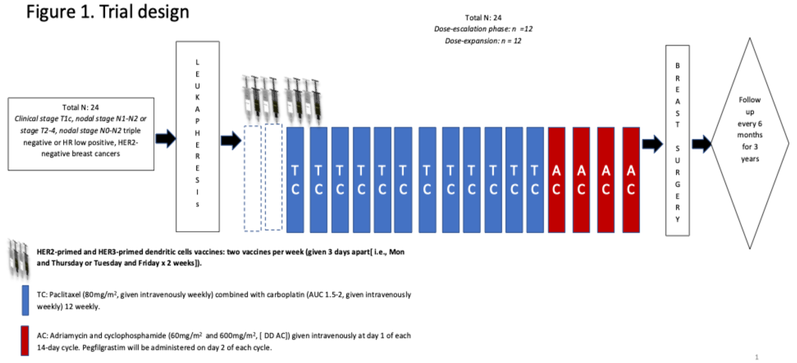
Table 1. HER3 and HER2 peptides

ECD HER3 Peptides	HER2 peptides (MHC Class II)
P81 (aa 401-415)	P42-56
P84 (aa 416-430)	P98-114
P91 (aa 451-465)	P328-345
ICD HER3 Peptides	P776-790
P38 (aa 850-864)	P927-941
P41 (aa 865-879)	P1166-1180
P52 (aa 920-934)	--
P86 (aa 1090-1114)	--
P89 (aa 1115-1129)	--

Methods

- Participants received alternating US-guided intratumoral HER2- and HER3-DC injections twice a week for 8 doses in total starting 2 weeks prior to neoadjuvant therapy with KEYNOTE 522 regimen (figure 1).
- The dose-escalation phase had 3 planned cohorts classic 3+3 design (ie, DL1-3 [10-20, 30-50, 80-100 million], n=12) and 12 additional patients were treated at the maximum tolerated dose (MTD) of 80-100 million cells.
- Primary endpoints were: the definition of maximum tolerated dose (MTD) of DC intratumoral injections
- Secondary endpoints included: absolute risk of adverse events (CTCAE version 5), complete pathological response rate (PCR) and recurrence-free survival.
- Per protocol; 6 pts treated at DL3 were added for analysis of PCR.
- The MTD had been previously estabilished at 80-100 million cells in the dose-escalation phase of the study.

Figure 1. Trial design



Results

- 12 patients were treated at the MTD between 06/2024 and 09/2024.
- The median age in years was 53.5 (32-76) and 16.7% of pts were black; 33.3% had HER2-low, 16.7% had grade 3, 22.2% had T3 and 61.1% had N1 BCs.
- All patients received all planned DCs.

Table 3. AEs at least possibly related to DCs (risk ≥10%)

Adverse event	Grade 1	Grade 2	Total
Fever	6 (50)	1 (8.3)	7 (58.3)
Chills	4 (33.3)	2 (16.7)	6 (50)
Pain	4 (33.3)	-	4 (33.3)
Headache	3 (25)	-	3 (25)
Fatigue	2 (16.7)	-	2 (16.7)
Nausea	2 (16.7)	-	2 (16.7)

- One immune-related AEs was observed, hypothyroidism (1 pt).
- None of the toxicities met the definition of DLT.
- Four pts had an SAE (i. bronchitis, ii. febrile neutropenia, iii. pulmonary embolism and iv. bilateral lower extremity weakness at weeks 13, 18, 22 and 14; respectively). One immune-related AEs was observed, hypothyroidism (1 pt).
- PCR (n=18) was observed in 77.8% of the pts and it was observed at higher frequency among pts with T2 vs T3 tumors (92.3 vs 50%).

Conclusions

Intratumoral DCs were well tolerated and showed preliminary efficacy and were well tolerated. This trial is ongoing to further assess the event-free survival of this novel treatment; correlative analyses will follow. The study is open at H. Lee Moffitt Cancer Center. Clinical trial information : NCT05504707

Acknowledgements

This study is funded by the SHULA'S foundation.

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