Exploratory phase II trial of camrelizumab (an anti-PD-1 antibody) combined with apatinib (a VEGFR-2 inhibitor) and chemotherapy as a neoadjuvant therapy for triple-negative breast cancer (NeoPanDa03): efficacy, safety and biomarker analysis

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Background

- Chemotherapy serves as the primary therapeutic approach for triple-negative breast cancer (TNBC), yet its efficacy remains unsatisfactory.
- We designed this single-arm phase II trial investigating neoadjuvant camrelizumab combined with apatinib and chemotherapy in early or locally advanced TNBC in order to evaluate the regimen's efficacy and safety profile, identify predictive biomarkers for treatment response, and search for the potential efficacy-enhancing strategies for non-pCR TNBC patients.

Method

- This study was a single-arm, open-label, single-center clinical trial (NCT05447702) involving patients with newly diagnosed stage II-III TNBC at West China Hospital.
- The overall design of the study is as follows.(Figure 1) The primary endpoint was defined as the total pathological complete response (tpCR) rate, whereas the secondary endpoints included the breast pathological complete response (bpCR), overall response rate(ORR), and incidence of treatment-related adverse events(AE).
- Pre- and post-neoadjuvant therapy serum and tissue samples were analyzed via Olink proteomics and RNA sequence to characterize the systemic response.

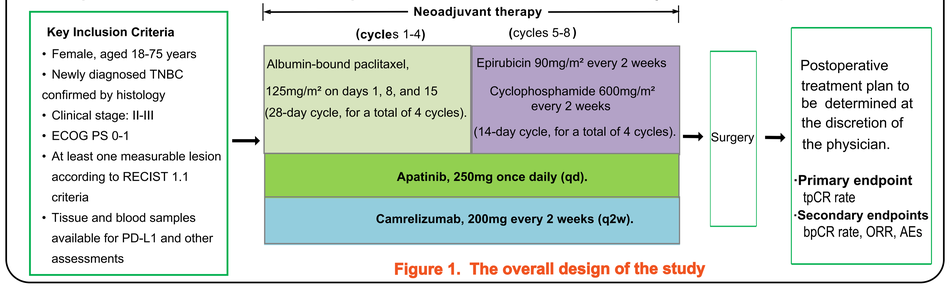


Figure 1. The overall design of the study

Results

Neoadjuvant therapy efficacy

- From June 2023 to April 2024, 35 patients were enrolled, of whom 1 patient withdrew due to adverse reaction intolerance. (Table 1)
- At treatment completion, the tpCR rate was 67.6% (23/34), and the bpCR rate was 70.6% (24/34). The ORR following neoadjuvant treatment reached 94.1% (32/34). The tpCR rate of the PD-L1 positive subgroup was greater than that of the PD-L1-negative subgroup.(Figure 2)

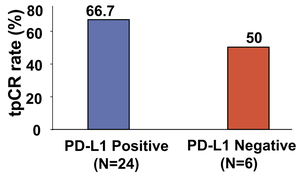


Figure 2. tpCR rate stratified by different PD-L1 expression levels.

Safety

- Elevated levels of alanine aminotransferase (38.2%) and aspartate aminotransferase (29.4%) were the most common grade 3-4 adverse events, with no significant toxicities or treatment-related deaths reported.

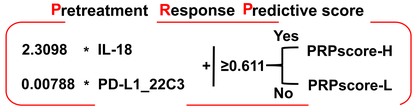


Figure 3. Formula of PRPscore rate of NAT

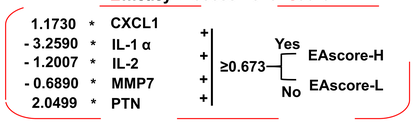


Figure 4. Formula of EAscore

	Total (n=34，%)
Age (years), median (IQR)	41(32,67)
≤40 year——n (%)	16(47.1)
HER2 status score, n (%)	
IHC 0-1	29 (85.3)
IHC 2+	5 (14.7)
Ki-67 level, n (%)	
≤30%	8 (23.5)
>30%	26 (76.5)
Clinical T stage, n (%)	
T1	1 (2.9)
T2	22 (64.7)
T3	10 (29.4)
T4	1 (2.9)
Clinical N stage, n (%)	
N0	7 (20.6)
N1	19 (55.9)
N2	2 (5.9)
N3	6 (17.6)
Overall clinical stage, n (%)	
Stage II	20 (58.8)
Stage III	14 (41.2)
PD-L1 status, n (%)a	
CPS≥1	24 (70.6)
CPS<1	6 (17.6)
Unknown	4 (11.8)

Table 1. Baseline patient characteristics

Biomarker analysis

- Genomic analysis revealed a significantly higher TP53 mutation rate in the pCR group (80% vs. 55.6%, P<0.05), while the non-pCR group exhibited a markedly elevated proportion of HRD-high patients (77.8% vs. 15.0%, P=0.01).
- Tumor microenvironment assessment confirmed reduced CD4+ T-cell infiltration (P=0.003) and enhanced fibroblast activation in non-pCR tumors.
- Comprehensive analysis of serum and tissue samples collected before and after neoadjuvant therapy via Olink and RNA sequencing revealed that the treatment induced a complex systemic immune response.
- These findings enabled the development of two novel scoring systems: a pretreatment response predictive score system for stratification and an efficacy assessment score system for treatment response evaluation. The PRPscore (baseline IL-18 + PD-L1 CPS) predicted pCR with an AUC of 0.823 (88% pCR rate in PRPscore-high group), (Figure 3) while the EAscore (post-treatment IL-1α/IL-2/PTN/CXCL1/MMP7) evaluated therapeutic response with an AUC of 0.93 (exhibiting 100% non-pCR in EAscore-low group). (Figure 4) The latter further implicated dysregulated IL-17 signaling as a potential therapeutic target.

Conclusion

- Camrelizumab and apatinib combined with chemotherapy have good clinical efficacy and good safety as neoadjuvant treatments for stage II-III TNBC, warranting further investigation and potential clinical application. The pioneering dual-score system (PRPscore + EAscore) enables personalized neoadjuvant therapy optimization.

The authors state that they have no conflicts of interest to report concerning publication of this abstract, or authorship.

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