Efficacy and safety of neoadjuvant disitamab vedotin (DV) in combination with toripalimab (Tor) and concurrent/sequential chemotherapy (chemo) in patients with HR-negative, HER2-low breast cancer: A randomized multicenter phase 2 study

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Background

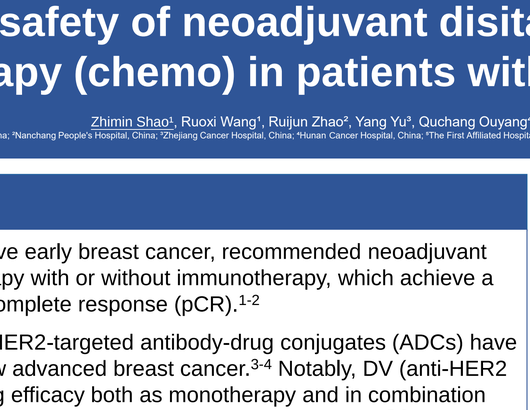
- For patients with triple-negative early breast cancer, recommended neoadjuvant regimens include chemotherapy with or without immunotherapy, which achieve a modest rate of pathological complete response (pCR).[1-2]
- Emerging data suggest that HER2-targeted antibody-drug conjugates (ADCs) have antitumor activity in HER2-low advanced breast cancer.[3-4] Notably, DV (anti-HER2 ADC) has shown encouraging efficacy both as monotherapy and in combination with Tor (PD-1 inhibitor) in patients with HER2-low advanced disease.[5-6]
- We evaluated neoadjuvant DV-containing regimens in patients with hormone receptor (HR)-negative HER2-low breast cancer in a randomized phase 2 trial (NCT06227117). The efficacy and safety results in the patients receiving DV plus Tor combined with concurrent/sequential chemotherapy are reported.

Methods

Study design

Key eligibility criteria:

- Previously untreated, invasive breast cancer of T1cN1-2M0 or T2-3N0-2M0 as per AJCC 8th edition
- Hormone receptor-negative
- Centrally confirmed HER2-low (defined as IHC 1+ or IHC 2+/ISH-);
- Patients who could tolerate and planned to undergo radical breast cancer surgery
- ECOG PS 0 or 1



Stratification factors

- PD-L1 status (positive or negative)
- Clinical stage (II or III)

Endpoints

- Primary: total pCR (tpCR, defined as ypT0/TisN0) rate
- Secondary: breast pCR (bpCR, defined as ypT0/Tis) rate, ORR, and safety

- Enrollment in group B was closed after 28 patinets had been randomized to this group, while enrollment in group A continued.
- Pathological response was assessed by local pathologists.

*DV dose cited here is based on calculations using bovine serum albumin (BSA)-based extinction coefficient (EC) implemented in China. Outside of China, DV dose calculation is based on DV EC which is equivalent to 1.07 (BSA-based EC) ÷ 1.41 (DV-based EC) X BSA-based EC dose. #Adjuvant treatment was determined by investigators after the surgery. Abbreviations: IHC, immunohistochemistry; ISH, in situ hybridization; ECOG PS, Eastern Cooperative Oncology Group Performance status; ORR, objective response rate.

Results

Patients and baseline characteristics

- As of data cutoff date (December 31, 2025), 40 patients were enrolled in group A and 28 in group B. All patients received assigned neoadjuvant treatment. 40 patients in group A and 27 in group B underwent surgery.

Table 1. Baseline characteristics

Baseline characteristics		Group A (N=40)	Group B (N=28)
Age, median (range), years		46.0 (29-69)	54.0 (36-68)
ECOG PS, n (%)	0	39 (97.5)	23 (82.1)
	1	1 (2.5)	5 (17.9)
Clinical stage, n (%)	II	25 (62.5)	16 (57.1)
	IIIA	15 (37.5)	12 (42.9)
HER2 status, n (%)	IHC 1+	29 (72.5)	19 (67.9)
	IHC 2+/ISH-	11 (27.5)	9 (32.1)
PD-L1 status, n (%)	CPS < 10	15 (37.5)	9 (32.1)
	10≤ CPS <20	8 (20.0)	8 (28.6)
	CPS ≥ 20	17 (42.5)	11 (39.3)

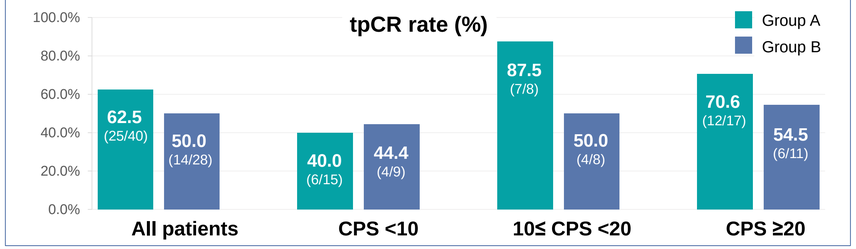
Efficacy

- Group A showed a numerically higher tpCR rate than group B (62.5% vs 50.0%).
- In group A, patients with CPS ≥10 had a higher tpCR rate over those with CPS <10.

Table 2. Efficacy summary

	Group A (N=40)	Group B (N=28)
tpCR (ypT0/TisN0), n (%; 95% CI)	25 (62.5; 45.8-77.3)	14 (50.0; 30.6-69.4)
bpCR (ypT0/Tis), n (%; 95% CI)	26 (65.0; 48.3-79.4)	15 (53.6; 33.9-72.5)
RCB Score*		
0	21 (52.5)	5 (19.2)
I	5 (12.5)	2 (7.7)
II	1 (2.5)	4 (15.4)
III	2 (5.0)	3 (11.5)
NA	11 (27.5)	12 (46.2)
ORR, n (%; 95% CI)	37 (92.5; 79.6-98.4)	21 (75.0; 55.1-89.3)

All data analyses were performed based on the intention-to-treat patients, unless otherwise indicated. *Assessed in patients who underwent surgery after neoadjuvant treatment without receiving new anti-tumor treatment during the neoadjuvant stage (group A: N=40; group B: N=26). NA, not assessed.



Safety

- Treatment-related adverse events (TRAEs) of grade 3-4 occurred in 29 (72.5%) patients in group A and in 23 (82.1%) patients in group B.
- No grade 5 TRAEs occurred in either group.

Table 3. Summary of adverse events

n (%)	Group A (N=40)	Group B (N=28)
TRAEs of any grade	40 (100)	28 (100)
Leading to treatment discontinuation	3 (7.5)	5 (17.9)
irAE	3 (7.5)	7 (25.0)
The most common TRAEs of any grade		
Alanine aminotransferase increased	37 (92.5)	24 (85.7)
White blood cell count decreased	37 (92.5)	24 (85.7)
Aspartate aminotransferase increased	36 (90.0)	25 (89.3)
Nausea	36 (90.0)	12 (42.9)
Neutrophil count decreased	36 (90.0)	24 (85.7)
Anaemia	32 (80.0)	17 (60.7)
Asthenia	30 (75.0)	18 (64.3)
Platelet count decreased	28 (70.0)	5 (17.9)
Vomiting	25 (62.5)	9 (32.1)
Hypertriglyceridaemia	23 (57.5)	14 (50.0)
Decreased appetite	22 (55.0)	12 (42.9)
Hypercholesterolaemia	22 (55.0)	12 (42.9)
Alopecia	16 (40.0)	15 (53.6)

TRAE was defined as an adverse event attributed to any study treatment; irAE: immune-related adverse event.

Conclusions

- Neoadjuvant treatment of DV + Tor + carboplatin showed numerically better efficacy in patients with previously untreated, HR-negative, HER2-low, early breast cancer.
  - tpCR rate: 62.5% (95% CI: 45.8-77.3).
  - bpCR rate: 65.0% (95% CI: 48.3-79.4).
- Both treatment regimens showed manageable safety profiles.

References

1. Bianchini G, et al. Nat Rev Clin Oncol 2022; 19:91-113.
2. Mittendorf EA, et al. Lancet 2020; 396:090-1100.
3. Modi S, et al. N Engl J Med 2022; 387:9-20.
4. Bardia A, et al. N Engl J Med 2024; 391:2110-2122.
5. Wang J, et al. Cancer Commun 2024; 44:833–851.
6. Wang Y, et al. EClinicalMedicine 2024; 68:102415.

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