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Evaluation of the safety and efficacy of ivonescimab in combination with chemotherapy as first-line (1L) treatment for triple-negative breast cancer (TNBC): Updated findings from the open-label, phase II study

Quchang Ouyang[1], Xiaojia Wang[2], Can Tian[1], Xiying Shao[2], Jian Huang[2], Zhanhong Chen[2], Yongsheng Wang[3], Tao Sun[4], Tienan Yi[5], Xufang Yu[6], Zhongmin Wang[6], Baiyong Li[6], Yu Xia[6]

1.Hunan Provincial Tumor Hospital, Changsha, China;2. Zhejiang Cancer Hospital, Hangzhou, China; 3.Affiliated Cancer Hospital of Shandong First Medical University, Jinan, China; 4. Liaoning Cancer Hospital and Institute, Shenyang, China; 5. Xiangyang Central Hospital, Xiangyang, China;6.Akeso Biopharma, Inc., Zhongshan, China

BACKGROUND

- Locally advanced unresectable or metastatic TNBC is highly aggressive and has a poor prognosis, with limited treatment options relative to other types of breast cancer due to the lack of therapeutic targets[1,2]
- Standard-of-care IL treatment for locally advanced or metastatic TNBC is chemotherapy or chemotherapy in combination with a programmed cell death protein 1 (PD-1) inhibitor for tumors with a high combined positive score (CPS) for programmed death ligand 1 (PD-L1)[1-3]
- Ivonescimab, a tetrameric bispecific antibody targeting PD-1 and vascular endothelial growth factor (VEGF), has the potential to produce complementary and synergistic anti-tumor effects through both pathways via cooperative binding[4-6]
- Here, we update results (DCO July 15, 2025) from a phase II trial (NCT05227664) of ivonescimab in combination with paclitaxel or nab-paclitaxel in patients with locally advanced unresectable or metastatic TNBC

OBJECTIVE

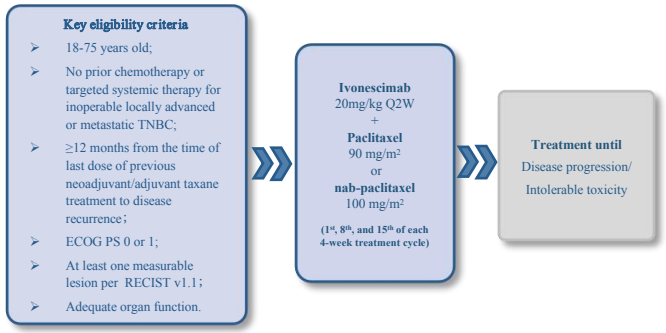
- To evaluate the safety and efficacy of ivonescimab in combination with chemotherapy in patients with locally advanced unresectable or metastatic TNBC who have not previously received systemic therapy

METHODS

Study Design

- In this open-label, multicenter, phase II trial, patients with locally advanced unresectable or metastatic TNBC were assigned to receive ivonescimab in combination with paclitaxel or nab-paclitaxel （**Figure 1**）.

Figure 1. Study design



ECOG PS, Eastern Cooperative Oncology Group performance status; Q2W, every 2 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1;

Outcomes

- The primary safety endpoints were incidence and severity of adverse events (AEs)
- The primary efficacy endpoint was objective response rate (ORR) based on RECIST v1.1
- Key secondary endpoints included disease control rate (DCR), duration of response (DOR), and progression-free survival (PFS) based on RECIST v1.1

RESULTS

Participants

- As of July 15, 2025, a total of 36 patients with locally advanced unresectable or metastatic TNBC were enrolled in the study
- All enrolled patients were women with a median age of 54.6 years (range, 35.4-73.3 years; **Table 1**)
- Of the enrolled patients, 50.0% had an ECOG PS score of 1, and 83.3% had a PD-L1 CPS of <10 at baseline
- 55.6% of patients previously received taxane-based neoadjuvant or adjuvant therapy
- The median duration of follow-up was 22.1 months (95% CI, 19.9-23.4)

Table 1. Baseline Characteristics

Characteristics	Total (N=36)
Age, median (range), years	54.6 (35.4, 73.3)
Sex, n (%)	
Men	0
Women	36(100)
ECOG PS, n (%)	
0	18 (50.0)
1	18 (50.0)
Number of metastatic sites, n (%)	
0-3	14 (38.9)
≥4	22 (61.1)
Brain metastases, n (%)	1 (2.8)
Liver metastases, n (%)	7 (19.4)
Disease status, n (%)	
Initial diagnosis metastatic	14 (38.9)
Recurrent/metastatic	22 (61.1)
Prior treatments for early-stage disease, n (%)	
Taxane	20 (55.6)
Endocrine therapy	6 (16.7)
CDK4/6 Inhibitor	2 (5.6)
Targeted therapy	1 (2.8)
PD-L1 expression (CPS),[a] n (%)	
PD-L1 CPS ≥10	6 (16.7)
PD-L1 CPS <10	30 (83.3)
PD-L1 CPS <1	18 (50.0)

CDK4/6, cyclin-dependent kinase 4/6; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death ligand 1.
a PD-L1 CPS assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay (Agilent).

Safety

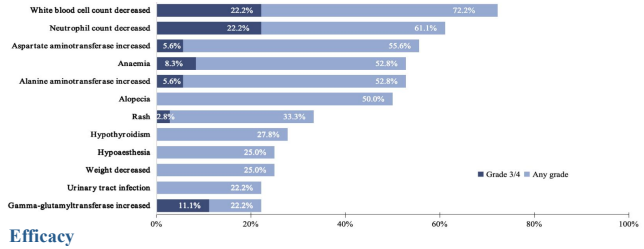
- Treatment-related adverse events (TRAEs) were reported in 36 patients (100.0%); 21 were grade ≥3 (58.3%; **Table 2**)
  - There were no TRAEs that led to treatment discontinuation or death
  - Overall, the most common TRAEs were decreased white blood cell count and decreased neutrophil count, most of which were grade <3 (**Figure 2**)

Table 2. Summary of Safety Results

Safety Overview	Total N=36
TRAE, n (%)	36 (100.0)
CTCAE Grade ≥3	21 (58.3)
Serious TRAE	10 (27.8)
Leading to Treatment Discontinuation	0
Leading to Death	0
irAE	
CTCAE Grade ≥3	4 (11.1)
Leading to Treatment Discontinuation	0

TRAE, treatment-related adverse event; irAE, immune-related adverse event.

Figure 2. Most Common TRAEs With an Incidence Rate of ≥20%



Efficacy

- At the time of data cutoff, 35 patients had ≥1 post baseline tumor assessment and were included in the efficacy analysis
- Overall, ORR was 80.0% (28/35), DCR was 100.0% (35/35), and median DOR was 12.2 months (95% CI, 7.4 to not evaluable [NE]) (**Table 3**)
  - When assessed by PD-L1 CPS category, the ORRs in the CPS ≥10 and CPS <10 subgroups were 83.3% (5/6) and 79.3% (23/29), respectively
- Overall, the median PFS was 15.2 months (95% CI, 8.4-22.3), with a 12-month PFS rate of 56.3%, , which was similar among subgroups with CPS <10 and ≥10
- Individual patient-level responses and PFS are shown in **Figures 3 and 4**
- The OS data are not mature yet

Table 3. Summary of Efficacy Results Overall and in Key Subgroups

	All patients (N=35*)	PD-L1 CPS≥10 (N=6)	PD-L1 CPS<10 (N=29)	PD-L1 CPS≥1 (N=18)
ORR, % (95%CI)	80 (63.1,91.6)	83.3(35.9, 99.6)	79.3(60.3, 92.0)	72.2(46.5, 90.3)
BOR, n (%)				
CR	2 (5.7)	1 (16.7)	1 (3.4)	2 (11.1)
PR	26 (74.3)	4 (66.7)	22 (75.9)	11 (61.1)
SD	7 (20.0)	1 (16.7)	6 (20.7)	5 (27.8)
DCR, % (95%CI)	100(90.0, 100)	100(54.1, 100)	100(88.1, 100)	100(81.5, 100)
DOR				
Median, months (95%CI)	12.2 (7.4, NE)	12.2 (3.6, NE)	9.9 (7.4, NE)	12.2 (7.4, NE)
6m DOR rate, % (95% CI)	79.9 (58.1, 91.1)	80.0 (20.4, 96.9)	79.8 (54.6, 91.9)	91.7 (53.9, 98.8)
PFS				
Median, months (95% CI)	15.2 (8.4, 22.3)	15.9 (5.36, NE)	13.04 (8.4, NE)	15.9 (6.2, NE)
9m PFS rate, % (95% CI)	68.4 (49.1, 81.7)	66.7 (19.5, 90.4)	69.1 (47.3, 83.3)	70.8 (43.5, 86.7)
12m PFS rate, % (95% CI)	56.3 (36.4, 72.2)	66.7 (19.5, 90.4)	54.3 (32.2, 72.0)	63.8 (36.1, 82.0)

BOR, best overall response; CPS, combined positive score; CR, complete response; DCR, disease control rate; DOR, duration of response; NE, not evaluable; NR, not reached; ORR, objective response rate; PD-L1, programmed death ligand 1; PFS, progression-free survival; PR, partial response; SD, stable disease.
*35 patients with ≥1 post baseline tumor assessment were included

Figure 3. Best Percentage Change From Baseline (full analysis set, N = 35)

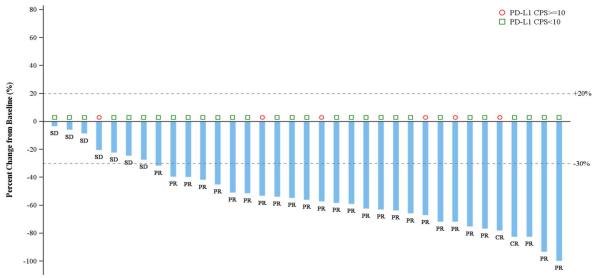
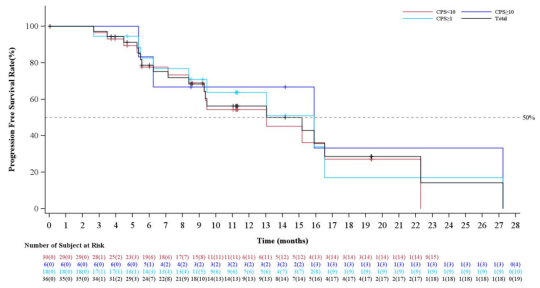


Figure 4.Progression-free Survival



CONCLUSIONS

- Ivonescimab in combination with chemotherapy had a manageable safety profile, with no new safety signals observed .
- The combination of Ivonescimab and chemotherapy showed promising ORR and prolonged PFS in patients with locally advanced unresectable or metastatic TNBC across all PD-L1 subgroups .
- A phase III study of ivonescimab combined with chemotherapy as first-line treatment for TNBC is ongoing (NCT06767527).

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DISCLOSURES

- All authors have no conflicts of interest to disclose.

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