PS3-01

Evaluation of the Safety and Efficacy of Ivonescimab in Combination With Chemotherapy as First-Line Treatment for Triple-Negative Breast Cancer

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BACKGROUND

- Treatment options for advanced or metastatic triple-negative breast cancer (TNBC) are limited relative to other forms of breast cancer due to the lack of therapeutic targets[1,2]
- Standard-of-care first-line treatment for 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 is an investigational, tetrameric, bispecific antibody that targets PD-1 and vascular endothelial growth factor (VEGF) that has exhibited cooperative binding in vitro and could produce complementary and synergistic antitumor effects through both the PD-1 and the VEGF pathways[4-6]
- Here, we present results (through September 30, 2024) from a phase 2 trial (NCT05227664) of ivonescimab in combination with paclitaxel or nab-paclitaxel in patients with locally advanced unresectable or metastatic TNBC

OBJECTIVE

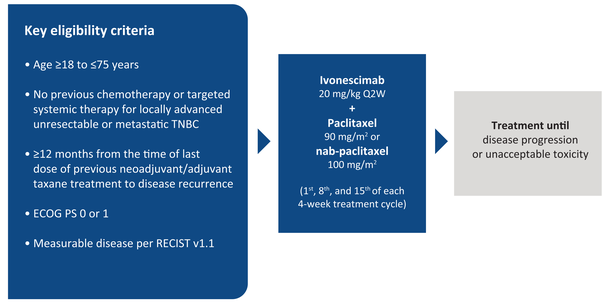
- To evaluate the safety and efficacy of ivonescimab in combination with chemotherapy in adults 18-75 years of age with locally advanced unresectable or metastatic TNBC who have not previously received systemic therapy

METHODS

Study Design

- In this open-label, multicenter, phase 2 trial, patients 18-75 years of age in China 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; TNBC, triple-negative breast cancer.

Outcomes

- The primary safety end points were incidence and severity of adverse events (AEs)
- The primary efficacy end point was objective response rate (ORR) based on Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST v1.1)
- Key secondary end points included disease control rate (DCR), duration of response (DOR), and progression-free survival (PFS) based on RECIST v1.1

RESULTS

Participants

- As of September 30, 2024, 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% and 50.0% had an Eastern Cooperative Oncology Group performance status score of 0 and 1, respectively, 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 11.8 months (95% CI, 10.9-12.8)

Table 1. Baseline Characteristics

Characteristic	All patients 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)
1	18 (50)
Number of metastatic sites, n (%)	
0-2	14 (38.9)
≥3	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.
Race/ethnicity demographic data were not collected.
[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%); 18 were grade ≥3 (50.0%; **Table 2**)
  - There were 0 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**)

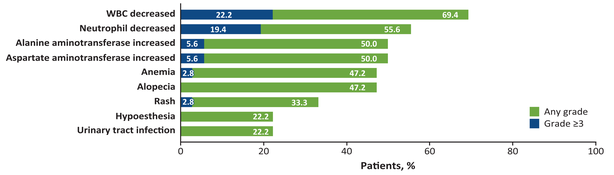
Table 2. Summary of Safety Results

Adverse event category	All patients N = 36
TRAE, n (%)	36 (100.0)
Grade ≥3	18 (50.0)
Serious TRAE	9 (25.0)
Leading to discontinuation	0
Leading to death	0

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

RESULTS

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



TRAE, treatment-related adverse event; WBC, white blood cell.

Efficacy

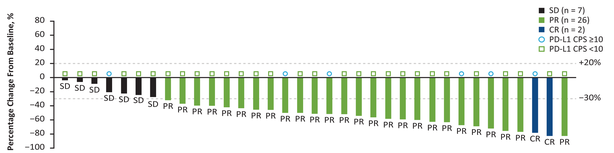
- At the time of data cutoff, 35 patients had ≥1 post baseline tumor assessment and were included in the efficacy analysis
- Overall, ORR was 80.0% (28/35), DCR was 100.0% (35/35), and median DOR was 7.49 months (95% CI, 5.32 to not evaluable [NE]) (**Table 3**)
  - When assessed by PD-L1 CPS category, 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 9.36 months (95% CI, 6.24-NE), with a 9-month PFS rate of 61.3%, which was similar among subgroups with CPS <10 and <1
- Individual patient-level responses at the time of data cutoff are shown in **Figures 3 and 4**

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

	All patients N = 35[a]	PD-L1 CPS ≥10 n = 6	PD-L1 CPS <10 n = 29	PD-L1 CPS <1 n = 17
ORR, % (95% CI)	80.0 (63.1-91.1)	83.3 (35.9-99.6)	79.3 (60.3-92.0)	88.2 (63.6-98.5)
BOR, n (%)				
CR	2 (5.7)	1 (16.7)	1 (3.4)	0
PR	26 (74.3)	4 (66.7)	22 (75.9)	15 (88.2)
SD	7 (20.0)	1 (16.7)	6 (20.7)	2 (11.8)
DCR, % (95% CI)	100.0 (90.0-100.0)	100.0 (54.1-100.0)	100.0 (88.1-100.0)	100 (80.5-100.0)
DOR				
Median, months (95% CI)	7.49 (5.32-NE)	NR (3.58-NE)	7.49 (3.91-NE)	7.49 (3.45-NE)
6-month DOR rate, % (95% CI)	72.2 (45.4-87.4)	80.0 (20.4-96.9)	70.0 (38.2-87.6)	64.2 (30.2-84.8)
PFS				
Median, months (95% CI)	9.36 (6.24-NE)	NR (5.36-NE)	9.30 (5.55-NE)	9.30 (5.26-NE)
6-month PFS rate, % (95% CI)	73.8 (52.7-86.6)	83.3 (27.3-97.5)	71.2 (46.6-86.0)	70.0 (38.2-87.6)
9-month PFS rate, % (95% CI)	61.3 (39.7-77.1)	66.7 (19.5-90.4)	59.8 (35.0-77.7)	61.3 (30.0-81.9)

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.
[a]35 patients with ≥1 post baseline tumor assessment were included

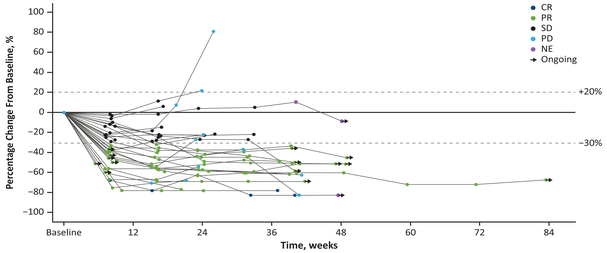
Figure 3. Best Percentage Change From Baseline in Sum of Tumor Diameters (full analysis set, N = 35)



CPS, combined positive score; CR, complete response; PD-L1, programmed death ligand 1; PR, partial response; SD, stable disease.

RESULTS

Figure 4. Percentage Change From Baseline in Sum of Tumor Diameters Over Time (full analysis set, N = 35)



CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

CONCLUSIONS

- Ivonescimab in combination with chemotherapy had a manageable safety profile and promising antitumor activity in patients with locally advanced unresectable or metastatic TNBC
  - This updated analysis, which included additional participants enrolled after the previous data cut, showed improved ORR in the overall population
- Results of this analysis support further evaluation of ivonescimab in combination with chemotherapy as a first-line treatment for TNBC

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REFERENCES

1. Li Y et al. *J Hematol Oncol*. 2022;15(1):121.
2. Zagami P, Carey LA. *NPJ Breast Cancer*. 2022;8(1):95.
3. American Cancer Society. Treatment of triple-negative breast cancer. Accessed October 10, 2024. https://www.cancer.org/cancer/types/breast-cancer/treatment/treatment-of-triple-negative.html.
4. Zhao Y et al. *EClinicalMedicine*. 2023;62:102106.
5. Wang L et al. *J Thorac Oncol*. 2024;19:465-474.
6. Frentzas S et al. *J Immunother Cancer*. 2024;12:e008037.
7. Ouyang Q et al. Presented at: the European Society for Medical Oncology, September 16, 2024; Barcelona, Spain.

DISCLOSURES

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