ASCO 2024
#5524

Efficacy and Safety of PM8002/BNT327, a Bispecific Antibody Targeting PD-L1 and VEGF-A, as a Monotherapy in Patients with Solid Tumors: Advanced Cervical Cancer and Platinum-Resistant Recurrent Ovarian Cancer Cohorts

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Background

- PM8002/BNT327 is an investigational bispecific antibody targeting both PD-L1 and VEGF-A. It contains two humanized VHHs against PD-L1 fused to the c-terminus of an anti-VEGF-A IgG (see right).
- Results from a Phase I dose-escalation and dose-expansion study showed that PM8002 was well-tolerated in patients with solid tumors from 1 mg/kg to 45 mg/kg (SITC2022 (abstract #725) and ASCO2023 (abstract #2536)).
- Here, we present the results of cervical cancer (CC) and platinum-resistant recurrent ovarian cancer (PROC) cohorts from an ongoing Ib/IIa trial in China (PM8002-A001).

Methods

- Patients with CC (≤2 prior treatment lines) or PROC (≤1 prior treatment line after platinum resistance) were enrolled into this Ib/IIa study. Tumor responses were evaluated every 6 weeks during the first year, then every 12 weeks.
  - The primary endpoint was objective response rate (ORR) per RECIST1.1.
  - The secondary endpoints were disease control rate (DCR), progression-free survival (PFS) and safety.
- Trial Registration: NCT05918445.
- This study was approved by the Ethics Committee for Drug Clinical Trials, Shanghai East Hospital and Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College.

Study Design

Key Eligibility Criteria
- Advanced or metastatic CC (≤2 prior treatment lines) and PROC (≤1 prior treatment line after platinum resistance)
- Age 18-75 years
- ECOG score 0-1
- Adequate organ function
- No evidence of significant bleeding and coagulation disorder or other significant bleeding risk

20 mg/kg Q2W n =73
30 mg/kg Q2W n =1
30 mg/kg Q3W n =7
45 mg/kg Q3W n =6
→ Cohort1: CC n=48 Corhot2: PROC n =39
→ Disease progression or intolerable toxicity

Results

Patient Enrollment

- As of March 15, 2024, 48 patients with advanced CC and 39 patients with PROC have been enrolled (Table 1).
- 52.1% of patients with CC and 51.3% with PROC had ECOG scores of 1.
- 64.6% of patients with CC received 1 prior anti-cancer therapy, 31.2% received 2 therapies and 4.2% received 3 therapies. 59.0% of PROC patients received 1 prior treatment after platinum resistance.
- 36.2% of patients with CC were PD-L1 positive (CPS≥1), and 18.6% of patients were PD-L1 negative (CPS<1).
- Median follow-up time in patients with CC and PROC was 13.8 months and 14.8 months, respectively.

Table 1. Baseline Characteristics

Characteristics	CC (n=48)	PROC (n=39)
Median age, years (Q1, Q3)	54.0 (45.5,61.0)	54.0 (50.0,59.0)
ECOG PS, n (%)		
0	23 (47.9)	19 (48.7)
1	25 (52.1)	20 (51.3)
PD-L1 CPS, n (%)		
<1%	9 (18.8)	-
1-10%	8 (16.7)	-
≥10%	13 (27.1)	-
NE	18 (37.5)	-
No. of metastatic sites, n (%)		
0-2	33 (68.8)	13 (33.3)
≥3	15 (31.3)	26 (66.7)
Lines of prior anti-cancer therapies, n (%)		
0	0 (0)	16 (41.0)*
1	31 (64.6)	23 (59.0)*
2	15 (31.3)	0 (0)*
≥3	2 (4.2)	0 (0)*

*No. of therapies after platinum resistance for PROC

Safety Observations

- Any-grade treatment-related adverse events (TRAEs) occurred in 95.4% of patients (83/87) with ≥ Grade 3 TRAEs of 36.8% (32/87).
- Any-grade immune-related adverse events (irAEs) occurred in 56.3% (49/87) of patients with ≥ Grade 3 irAEs of 8.0% (7/87).
- Serious adverse events (SAEs) were observed in 33.3% (29/87) of patients.
- 14.9% (13/87) of patients discontinued PM8002 treatment due to TRAEs.
- Most common TRAEs (≥15.0%) were proteinuria, hypertension, hypothyroidism, anemia, thrombopenia, white blood cell count decrease and hypoalbuminaemia.

Tables 2 & 3. Overview of Treatment-Related Adverse Events

Categories	n (%)
All TRAEs	83 (95.4)
≥3 TRAEs	32 (36.8)
SAEs	29 (33.3)
irAEs	49 (56.3)
≥3 irAEs	7 (8.0)
TRAEs leading to discontinuation	13 (14.9)

Parameter	Grade, n (%)			
TRAEs ≥ 15%	**All**	**3**	**4**	**5**
Proteinuria	32 (36.8)	4 (4.6)	0	0
Hypertension	26 (29.9)	8 (9.2)	0	0
Hypothyroidism	21 (24.1)	0	0	0
Anemia	18 (20.7)	1 (1.1)	0	0
Thrombopenia	18 (20.7)	0	0	0
WBC count decrease	17 (19.5)	1 (1.1)	0	0
Hypoalbuminaemia	17(19.5)	0	0	0

Efficacy Signals

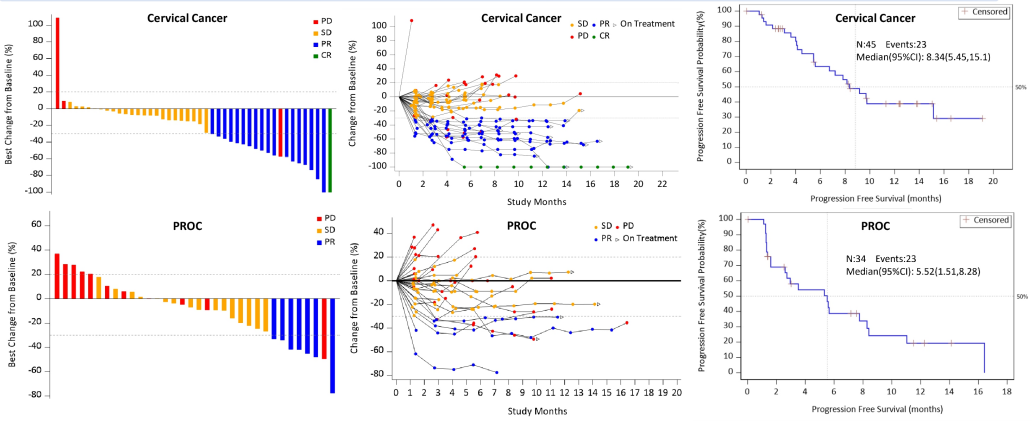
- Among 45 evaluable patients with cervical cancer:
  - 1 complete response (CR), 18 partial responses (PR) and 23 stable diseases (SD). were observed; ORR of 42.2% (19/45) and DCR of 93.3% (42/45).
  - ORR of CC patients with PD-L1-positive tumors (CPS≥1) was 52.4% (11/21).
  - Median PFS (mPFS) was 8.3 months.
- Among 34 evaluable PROC patients: 7 PRs and 16 SDs were observed with an ORR of 20.6% (7/34) and DCR of 67.7% (23/34). The mPFS was 5.5 months.

Table 4. Efficacy Outcome of Evaluable Patients

Parameter	CC	PROC
Efficacy evaluable patients, n	45	36
On treatment, n	12	4
Median duration of exposure, m (min, max)	6.3 (0.5,19.1)	3.8 (0.03,17.7)
ORR, n/% (95% CI)	42.2 (27.7,57.9)	20.6 (8.7,37.9)
DCR, n/% (95% CI)	93.3 (81.7,98.6)	67.7 (49.5,82.6)
Median PFS, months (95% CI)	8.3 (5.5,15.2)	5.5 (1.6,8.3)
Median OS, months (95% CI)	- (14.6, -)	11.6 (8.7, -)
Median DOR, months (95% CI)	- (3.02,-)	9.6 (2.6, -)
6 month PFS rate, n/% (95% CI)	63.4 (46.0,76.6)	38.7 (21.1,56.0)
12 month PFS rate, n/% (95% CI)	38.8 (22.7,54.7)	19.3 (6.5,37.3)
6 month OS rate, n/% (95% CI)	86.7 (72.7,93.8)	87.9 (70.9,95.3)
12 month OS rate, n/% (95% CI)	74.7 (58.9,85.2)	49.6 (31.2,65.6)

At data cut-off, 12 patients with CC and 4 with PROC are still on treatment.

Figure 1. Waterfall/Spider Plots and Kaplan-Meier Curves (PFS)



Conclusions

PM8002/BNT327 showed preliminary antitumor activity as a monotherapy in previously treated patients with PROC or advanced cervical cancer.

Acknowledgements

This study was sponsored by Biotheus Inc and PM8002/BNT327 is being jointly developed by Biotheus and BioNTech. The authors would like to thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers.

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