PS3-08: Interim Overall Survival of Patients with Locally Advanced or Metastatic Triple-Negative Breast Cancer Treated with First-Line PM8002/BNT327 in Combination with Nab-Paclitaxel in a Phase Ib/II Study

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Introduction

PM8002/BNT327 is an investigational bispecific antibody containing two humanized VHHs against PD-L1 fused to the c-terminus of an anti-VEGF-A IgG, therefore targeting both PD-L1 and VEGF-A, designed to:

- **block the interaction of PD-L1/PD-1, thereby reversing the immunosuppressed, exhausted effector T cell phenotype and enhancing the cytotoxic T-lymphocyte–mediated immune response against tumor cells**
- **scavenge and neutralize VEGF-A released by tumor cells, thereby promoting blood vessel normalization**

We provide updated results including interim overall survival (OS) since initial reports at SABCS 2023 (Jiong Wu, et al, SABCS 2023 abstract PS08-06) and ESMO 2024 (Annals of Oncology (2024) 35 (suppl_2): S357-S405. 10.1016/annonc/annonc1579)

Method

Open-label, single-arm, multi-center, Phase Ib/II study of PM8002/BNT327 + nab-paclitaxel for 1L TNBC (NCT05918133) in China

Key Eligibility Criteria

- **Patients with locally advanced or metastatic TNBC who have not received prior systemic therapy for unresectable locally advanced or metastatic advanced TNBC**
- **Age ≥ 18 years**
- **ECOG PS 0-1**
- **Adequate organ function**

PM8002/BNT327 20mg/kg Q2W on Day 1, 15 of 28-day cycle
+
nab-paclitaxel 100mg/m² on Day 1, 8, 15 of 28-day cycle

until disease progression/ unacceptable toxicity

✓**Primary endpoints: objective response rate (ORR), safety (CTCAE 5.0)**
✓**Secondary endpoints: progression free survival (PFS), disease control rate (DCR), overall survival (OS)**

Results

Patients

- **42 Pts were enrolled by 11 Apr 2023 to assess the safety and efficacy of PM8002/BNT327 in combination with nab-paclitaxel (Table 1)**
- **As of the data cut-off date of 25 Oct 2024, 9 pts remained on treatment**
- **Median follow-up time was 19.5 months (95% CI: 18.0,20.6)**
- **Median duration of exposure was 10.0 months (range: 2.0, 23.3 months)**

Table 1. Baseline Characteristics

Patient Characteristics (n=42)	
Median age, years (Q1, Q3)	53.5 (41.0, 60.0)
Number of metastatic sites, n (%)	
0-2	17 (40.5)
≥ 3	25 (59.5)
Liver metastasis, n (%)	
Yes	16 (38.1)
No	26 (61.9)
Brain metastasis, n (%)	
Yes	2 (4.8)
No	40 (95.2)
Neo/adjuvant paclitaxel treatment, n (%)	
Yes	28 (66.7)
No	14 (33.3)

Efficacy

Antitumor activity observed (for subgroups by PD-L1 expression level see Table 2)

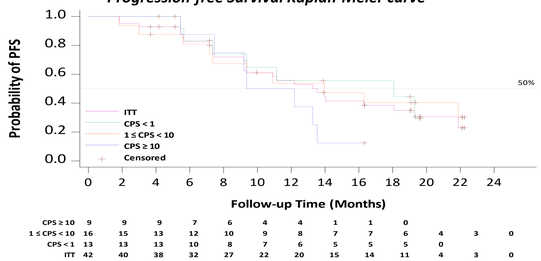
At the data cut-off date:

- **42 pts had at least 1 response evaluation**
- **Median PFS was 13.5 months (95% CI: 9.4, 19.3)**
- **After 15 subjects had died, matured 12-, 15- and 18-month OS rates were 80.8%, 78.1% and 69.7%, respectively; median OS was unmatured**

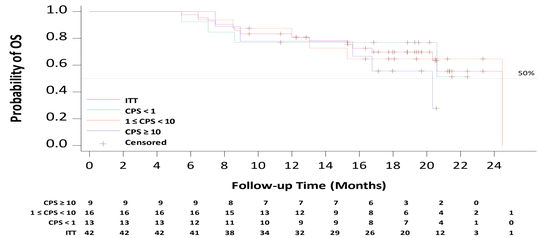
Table 2. Efficacy Outcomes of Evaluable Patients

Variable	ITT	PD-L1 CPS<1	PD-L1 1≤CPS<10	PD-L1 CPS≥10	NOT DONE
Population (n)	42	13	16	9	4
CR	1 (2.4)	0	1 (6.3)	0	0
PR	32 (76.2)	10 (76.9)	10 (62.5)	9 (100)	3 (75.0)
SD	7 (16.7)	3 (23.1)	4 (25.0)	0	0
PD	2 (4.8)	0	1 (6.3)	0	1 (25.0)
ORR %	78.6	76.9	68.8	100	75.0
(95% CI)	(63.2, 89.7)	(46.2, 95.0)	(41.3, 89.0)	(66.4, 100)	(19.4, 99.4)
cORR %	73.8	76.9	56.3	100	75.0
(95% CI)	(58.0, 86.1)	(46.2, 95.0)	(29.9, 80.3)	(66.4, 100)	(19.4, 99.4)
DCR %	95.2	100	93.8	100	75.0
(95% CI)	(83.8, 99.4)	(75.3, 100)	(69.8, 99.8)	(66.4, 100)	(19.4, 99.4)
mPFS	13.5	18.1	14.0	10.8	14.0
(Mo), (95%CI)	(9.4, 19.3)	(5.7, --)	(7.2, --)	(5.5, 13.5)	(1.8, --)
12-mo OS rate%	80.8	76.9	80.8	77.8	100
(95%CI)	(65.3, 89.9)	(44.2 ,91.9)	(51.4, 93.4)	(36.5, 93.9)	(100, 100)
15-mo OS rate%	78.1	76.9	72.7	77.8	100
(95%CI)	(62.1, 88.0)	(44.2, 91.9)	(42.0, 88.9)	(36.5, 93.9)	(100, 100)
18-mo OS rate%	69.7	76.9	64.6	55.6	100
(95%CI)	(52.7, 81.6)	(44.2, 91.9)	(34.1, 83.8)	(20.4, 80.5)	(100, 100)

Progression-free Survival Kaplan-Meier curve



Overall Survival Kaplan-Meier curve



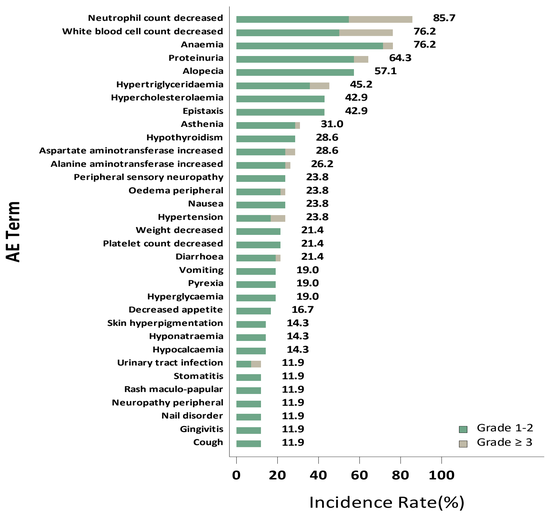
Safety

- **Any-grade and grade ≥3 TRAEs of the combination regimen occurred in 100% and 59.5% pts, respectively. No Grade 5 TRAEs were observed**
- **TRAEs leading to treatment discontinuation occurred in 9.5% pts**
- **The most common immune-related adverse events (irAEs) included hyperthyroidism, hypothyroidism and rash**
- **The most common AEs typically associated with VEGF inhibition were hypertension and proteinuria, which were mostly Grade 1 or 2**

Table 3. Overview of TRAEs of the combination regimen

Safety Overview	N=42 n (%)
All TRAEs	42 (100)
Grade 3-4 TRAEs	25 (59.5)
SAEs	10 (23.8)
TRAE leading to dose interruption	27 (64.3)
TRAE leading to dose reduction	6 (14.3)
TRAEs leading to treatment discontinuation	4 (9.5)
irAE	13 (31.0)
Grade 3-4 irAE	4 (9.5)

TRAE in ≥ 10% of patients



Febrile neutropenia was reported in 4 patients (9.5%; Grade 3 [n=2] and Grade 4 [n=2]). Other Grade 3 TRAEs occurring in 2 patients: gamma glutamyl transferase increased, pancreatitis, acute pancreatitis and in 1 patient: blood alkaline phosphatase increased, dermatitis, abdominal distension, oral mucosa erosion, pharyngitis.

Conclusions

- ✓ **In pts with LA/mTNBC, first-line therapy with PM8002/BNT327 combined with nab-paclitaxel showed clinically meaningful survival outcomes and antitumor activity regardless of PD-L1 status**
- ✓ **A manageable safety profile was observed, with no new safety signals beyond those typically described for nab-paclitaxel and anti-PD-1/PD-L1 and anti-VEGF monotherapies**
- ✓ **A randomised Phase III clinical trial (NCT06419621) in first-line TNBC is ongoing in China as well as a global Phase II trial (NCT06449222)**

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