Poster PS1-13-25

Preliminary data from a global multicohort Phase 2 randomized trial of pumitamig (PD-L1 × VEGF-A bsAb) + chemotherapy for 1L/2L+ locally advanced/metastatic TNBC

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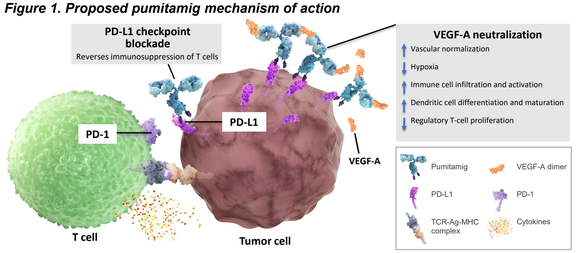
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Introduction

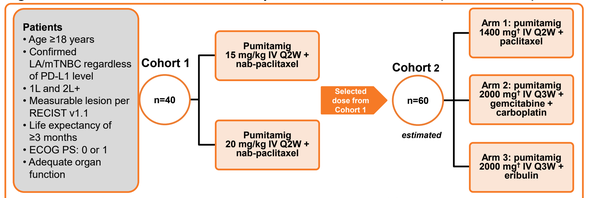
- Pumitamig (BNT327/BMS986545) is an investigational bispecific antibody designed to target both PD-L1 and VEGF-A[1] in the tumor and TME.
  - Binding to PD-L1 on tumor cells aims to restore effector T-cell function and to localize VEGF-A neutralization within the TME.
  - Neutralizing local VEGF can normalize tumor vasculature and reverse VEGF-induced immune suppression.
- Pumitamig + nab-paclitaxel showed encouraging activity in a Phase 1b/2 trial of 1L locally advanced or metastatic triple-negative breast cancer (LA/mTNBC) in China.[2]
- Herein we present the first pumitamig data from a global 1L/2L+ LA/mTNBC population (BNT327-02; NCT06449222).

Figure 1. Proposed pumitamig mechanism of action



Methods

Figure 2. Global Phase 2, randomized, open-label, multicohort trial (NCT06449222)



Primary endpoints: ORR, and best percentage change in tumor size per investigator (RECIST 1.1), early tumor shrinkage*; occurrence of TEAEs, AESIs, and treatment-emergent SAEs (NCI CTCAE v5.0); occurrence of dose interruption, dose reduction, and discontinuation of trial treatment due to AEs.
Secondary endpoints: PK (C_{max}, AUC_{tau}), and ADA; ORR (Cohort 2), DOR, DCR, TTR, and PFS per investigator (RECIST 1.1); OS; PFS, and OS rates.

*Early tumor shrinkage is defined as ≥10% decrease in the pretreatment sum of diameters at first posttreatment tumor scan in target lesions.
†Flat dose based on 20mg/kg Q2W dose

Results

Patients

- At cutoff (October 1, 2025), 74 patients with 1L/2L+ LA/mTNBC were enrolled; enrollment is completed in the dose selection Cohort 1 (15 mg/kg: n=19; 20 mg/kg: n=21) and ongoing in Cohort 2 (Arm 1: n=11; Arm 2: n=12; Arm 3: n=11).
- Median duration of treatment was 33.6 weeks (range: 2.0–49.0) with 25/40 patients still on treatment (Cohort 1) and 14.9 weeks (range: 2.0–27.4) with 31/34 patients on treatment (Cohort 2). Median follow-up was 33.6 weeks (range: 13.1–47.6) and 13.2 weeks (range: 2.4–27.1) in Cohort 1 and 2, respectively.

Results (continued)

Table 1. Baseline characteristics in 1L/2L+ LA/mTNBC

	Cohort 1			Cohort 2			
	Pumitamig 15 mg/kg + nab-paclitaxel	Pumitamig 20 mg/kg + nab-paclitaxel	Total	Pumitamig 1400 mg + paclitaxel	Pumitamig 2000 mg + gemcitabine + carboplatin	Pumitamig 2000 mg + eribulin	Total
Characteristic	N=19	N=21	N=40	N=11	N=12	N=11	N=34
Age, n	19	21	40	11	12	11	34
Years, median (min, max)	58.0 (37, 75)	55.0 (34, 74)	57.1 (34, 75)	44.3 (36, 74)	55.5 (32, 85)	56.5 (32, 79)	51.0 (32, 85)
ECOG PS, n (%)							
0	14 (73.7)	13 (61.9)	27 (67.5)	8 (72.7)	6 (50.0)	4 (36.4)	18 (52.9)
1	5 (26.3)	8 (38.1)	13 (32.5)	3 (27.3)	6 (50.0)	7 (63.6)	16 (47.1)
Prior systemic therapy, n (%)							
Yes	11 (57.9)	12 (57.1)	23 (57.5)	7 (63.6)*	6 (50.0)	11 (100)	24 (70.6)
Treatment setting, n (%)							
Early stage	10 (52.6)	12 (57.1)	22 (55.0)	6 (54.5)	5 (41.7)	9 (81.8)	20 (58.8)
Metastatic	1 (5.3)	-	1 (2.5)	1 (9.1)	1 (8.3)	2 (18.2)	4 (11.8)

*Information on prior systemic therapy missing for 1 patient

Efficacy

- cORR was 61.5% and uORR was 71.8% (1L: 76.5%; 2L+: 68.2%) in Cohort 1. Mean best percentage change in tumor size was –42.6%, with 66.7% of patients achieving early tumor shrinkage in Cohort 1, respectively (**Table 2, Figures 3 and 4**).
- Among the 34 patients in Cohort 1 with centrally tested PD-L1 levels, 17 had a CPS ≥10 and 17 had a CPS <10. The uORR was 70.6% in both groups.
- PFS rates at 3, 6, and 9 months were 92.1%, 72.1%, and 59.3% in Cohort 1 overall, at 15 mg/kg 94.7%, 61.8%, and 61.8%, and at 20 mg/kg 89.5%, 81.3%, and 51.6%, respectively.
- Follow-up time in Cohort 2 (recruitment ongoing) is too short to evaluate on efficacy endpoints.
- Median PFS, median DOR, and median OS were not yet mature.

Table 2. Efficacy outcomes of evaluable patients in 1L/2L+ LA/mTNBC

	Cohort 1		
	Pumitamig 15 mg/kg + nab-paclitaxel	Pumitamig 20 mg/kg + nab-paclitaxel	Total
Endpoints	N=19	N=20	N=39
uBOR, n (%)			
Complete response (CR)	0	0	0
Partial response (PR)	12 (63.2)	16 (80.0)	28 (71.8)
Stable disease (SD)	7 (36.8)	2 (10.0)	9 (23.1)
Progressive disease (PD)	0	2 (10.0)	2 (5.1)
uORR (CR+PR), n (%) (95% CI)	12 (63.2) (38.4,83.7)	16 (80.0) (56.3,94.3)	28 (71.8) (55.1,85.0)
cORR (CR+PR), n (%) (95% CI)	10 (52.6) (28.9,75.6)	14 (70.0) (45.7,88.1)	24 (61.5) (44.6,76.6)
DCR (CR+PR+SD), n (%) (95% CI)	19 (100) (82.4,100)	17 (85.0) (62.1,96.8)	36 (92.3) (79.1,98.4)
Best percentage change, mean (%) (std dev)	-46.5 (34.2)	-39.3 (30.5)	-42.6 (32.1)
Early tumor shrinkage, n (%) 95% CI	11 (57.9) (33.5,79.7)	15 (75.0) (50.9,91.3)	26 (66.7) (49.8,80.9)

Figure 3. Percentage change in tumor size from baseline (evaluable response set) in 1L/2L+ LA/mTNBC with uBOR and line of treatment

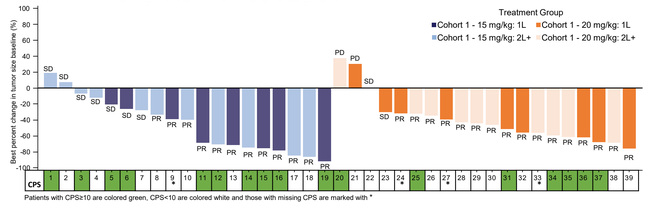
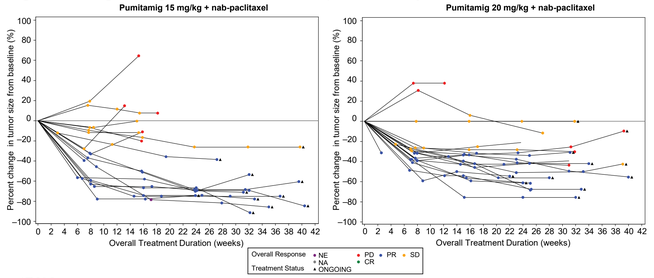


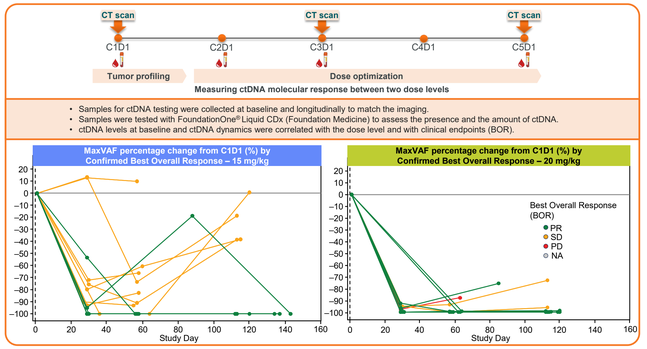
Figure 4. Change in target lesions from baseline (evaluable response set) in 1L/2L+ LA/mTNBC



ctDNA

- ctDNA dynamics at C3D1 was available for 17 patients in the 15 mg/kg group and 17 patients in the 20 mg/kg group in Cohort 1.
- Median ctDNA reduction (maxVAF) at C3D1 compared with baseline was 100% in both study arms, highlighting that pumitamig + nab-paclitaxel significantly reduces ctDNA levels.
- At C3D1, ctDNA clearance rate (100% decrease) was 52.9% (9/17) in the 15-mg/kg group and 70.6% (12/17) in the 20-mg/kg group, suggesting that the higher dose is more effective in inducing a ctDNA molecular response (**Figure 5**).
- Longitudinal ctDNA monitoring highlighted that distinct ctDNA kinetics between treatment arms further sustains the higher efficacy of the higher dose of 20 mg/kg:
  - Deeper and durable ctDNA reduction observed in patients receiving 20 mg/kg regardless of the BOR.
  - Although an initial ctDNA reduction was observed at the lower dose, ctDNA levels rebounded for most of the patients with SD as BOR.

Figure 5. ctDNA dynamics support dose optimization in 1L/2L+ LA/mTNBC



Safety

- Any-grade treatment-related TEAEs occurred in 97.5% and grade ≥3 treatment-related TEAEs in 42.5% of patients in Cohort 1 and in 88.2% and 38.2%, respectively, in Cohort 2. 3/40 patients (Cohort 1) discontinued pumitamig due to any TEAE, and 1 patient discontinued pumitamig due to pumitamig-related TEAEs (**Table 3**).

Safety (continued)

- Most common pumitamig-related TEAEs (occurring in ≥10% of overall population in either cohort) across both cohorts were fatigue (32.4%), nausea (17.6%), epistaxis (13.5%), hypertension (13.5%), diarrhea (12.2%), anemia (9.5%), and alanine aminotransferase increase (8.1%). Most of the commonly occuring TEAEs were low grade, with only hypertension (6.8%) and fatigue (2.7%) occurring at grade ≥3.
- 5/40 patients (Cohort 1) and 1/34 (Cohort 2) experienced TEAEs of special interest related to any treatment; serious TEAEs of special interest related to any treatment: 2/40 (Cohort 1), 1/34 (Cohort 2). Five patients experienced TEAEs of special interest related to pumitamig, which includes immune-mediated adrenal insufficiency, enterocolitis, and pancreatitis; pyrexia, infusion-related reaction, and rash maculo-papular.
- No pumitamig-related deaths and 1 paclitaxel-related death occurred.

Table 3. Safety summary (safety analysis set in 1L/2L+ LA/mTNBC)

	Cohort 1						Cohort 2							
	Pumitamig 15 mg/kg + nab-paclitaxel		Pumitamig 20 mg/kg + nab-paclitaxel		Total		Pumitamig 1400 mg + paclitaxel		Pumitamig 2000 mg + gemcitabine + carboplatin		Pumitamig 2000 mg + eribulin		Total	
	N=19		N=21		N=40		N=11		N=12		N=11		N=34	
Patients with, n (%)	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TEAE	19 (100)	13 (68.4)	21 (100)	14 (66.7)	40 (100)	27 (67.5)	8 (72.7)	3 (27.3)	12 (100)	8 (66.7)	11 (100)	2 (18.2)	31 (91.2)	13 (38.2)
Treatment-related (any treatment)	19 (100)	8 (42.1)	20 (95.2)	9 (42.9)	39 (97.5)	17 (42.5)	8 (72.7)	3 (27.3)	12 (100)	8 (66.7)	10 (90.9)	2 (18.2)	30 (88.2)	13 (38.2)
Any TESAE	7 (36.8)	6 (31.6)	10 (47.6)	9 (42.9)	17 (42.5)	15 (37.5)	2 (18.2)	2 (18.2)	1 (8.3)	1 (8.3)	2 (18.2)	0	5 (14.7)	3 (8.8)
Treatment-related (any treatment)	4 (21.1)	3 (15.8)	4 (19.0)	3 (14.3)	8 (20.0)	6 (15.0)	2 (18.2)	2 (18.2)	0	0	2 (18.2)	0	4 (11.8)	2 (5.9)
Any TEirAE	4 (21.1)	2 (10.5)	4 (19.0)	0	8 (20.0)	2 (5.0)	2 (18.2)	1 (9.1)	0	0	0	0	2 (5.9)	1 (2.9)
Any TEAE leading to dose interruption of any treatment	6 (31.6)	5 (26.3)	10 (47.6)	5 (23.8)	16 (40.0)	10 (25.0)	5 (45.5)	3 (27.3)	5 (41.7)	3 (25.0)	3 (27.3)	0	13 (38.2)	6 (17.6)
Any TEAE leading to dose reduction of CT	4 (21.1)	3 (15.8)	7 (33.3)	1 (4.8)	11 (27.5)	4 (10.0)	1 (9.1)	1 (9.1)	3 (25.0)	3 (25.0)	2 (18.2)	0	6 (17.6)	4 (11.8)
Any TEAE leading to discontinuation of any treatment	0	0	3 (14.3)	3 (14.3)	3 (7.5)	3 (7.5)	0	0	1 (8.3)	1 (8.3)	0	0	1 (2.9)	1 (2.9)
Any TEAE leading to discontinuation of pumitamig	0	0	3 (14.3)	3 (14.3)	3 (7.5)	3 (7.5)	0	0	0	0	0	0	0	0

Conclusions

- **Pumitamig in combination with chemotherapy shows encouraging efficacy and a manageable safety profile in 1L/2L+ LA/mTNBC, consistent with data from a prior Chinese trial in 1L LA/mTNBC.[2]**
  - Although efficacy was seen independent of CPS levels, the benefit is particularly meaningful in patients with CPS <10, potentially addressing a current unmet need.
  - No new safety signals were seen compared with the previously characterized safety profile of pumitamig.
- **ctDNA dynamics show a higher molecular response and a deeper and durable ctDNA reduction rate for patients receiving 20 mg/kg, potentially indicating better long-term outcome.**
- **Based on these global 1L/2L+ data, 20 mg/kg pumitamig was selected as the dose for Cohort 2 (as flat dose equivalent) and for further development of pumitamig in LA/mTNBC.**
  - The ongoing global ROSETTA Breast-01 Phase 3 trial (NCT07173751) is investigating the efficacy and safety of pumitamig plus chemotherapy in 1L LA/mTNBC with CPS <10 at 1500 mg Q2W or 2000 mg Q3W* as the equivalent to the 20-mg/kg Q2W dose tested in this trial.†

* 1200 mg Q2W or 1500 mg Q3W in patients with a body weight <50 kg

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Abbreviations: 1L, first-line; 2L, second-line; ADA, antidrug antibody; AE, adverse event; AESI, adverse event of special interest; Ag, antigen; AJCC, American Joint Committee on Cancer; AUC_{tau}, area under the plasma concentration-time curve from time zero to the end of the dosing interval; BOR, best overall response; bsAb, bispecific antibody; C, Cycle; CDx, companion diagnostic; C_{max}, maximal concentration; cORR, cancer objective response rate; CPS, combined positive score; CT, computed tomography; ctDNA, circulating tumor DNA; D, Day; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; LA, locally advanced; maxVAF, maximum somatic variant allele fraction; MHC, major histocompatibility complex; mTNBC, metastatic tripe-negative breast cancer; NA, not available; nab, nanoparticle albumin-bound; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NE, not evaluable; ORR, objective response rate; OS, overall survival; PD-1, programmed death protein-1; PD-L1, programmed death ligand-1; PFS, progression-free survival; PK, pharmacokinetics; Q2W, every 2 weeks; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SAE, serious adverse event; SD, stable disease; TCR, T-cell receptor; TEAE, treatment-emergent adverse event; TEirAE, treatment-emergent immune-related adverse event; TESAE, treatment-emergent serious adverse event; TME, tumor microenvironment; TTR, time to response; uBOR, unconfirmed best overall response; uORR, unconfirmed objective response rate; VEGF, vascular endothelial growth factor.

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1. Miao X, et al. *Cancer Res*. 2025;85(8 suppl 1):Abstract 6061
2. Wu J, et al. *Clin Cancer Res*. 2025;31(12):Abstract PS3-08

†ROSETTA Breast-01 TiP Schmid P et al; Abstract 2177
Friday, December 12, 2025, 12:30 pm - 2:00 pm

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