

Next Generation Immune Checkpoint Inhibition With Botensilimab Plus Balstilimab in Recurrent Ovarian Cancer: Results by Platinum Sensitivity Status and 3-Year Overall Survival

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Background

- Treatment options for most patients with recurrent ovarian cancer are limited, with poor responses to conventional immune checkpoint inhibitors (ICI)¹⁻⁹
 - Single-agent PD-1/PD-L1 has demonstrated modest ORRs of 8%–10% and median PFS near 2 months, improving to 3.9 months when combined with the CTLA-4 inhibitor ipilimumab¹⁻³
 - Combinations of conventional ICI with chemotherapy or small molecules including PARPis and/or anti-angiogenic agents have not demonstrated clinically meaningful benefit^{1,4-9}
- Botensilimab (BOT), a multifunctional Fc-enhanced anti-CTLA-4 antibody, augments T-cell priming, reduces regulatory T cells, and activates antigen-presenting cells¹⁰
- BOT ± balstilimab (BAL; anti-PD-1 antibody pharmacologically comparable to approved PD-1 inhibitors) has shown activity in “cold” and ICI-refractory tumors, including recurrent ovarian cancer¹¹⁻¹⁸

Here, we report phase 1b (C-800-01 trial; NCT03860272) results with extended follow-up evaluating BOT+BAL in recurrent ovarian cancer by platinum sensitivity status, prior lines of therapy, and PARPi progression status

C-800-01 Study Design

NCT03860272 (C-800-01): First-in-Human, Phase 1b Trial of BOT±BAL in Patients with Advanced Solid Tumors

Key Ovarian Cohort Eligibility

- Recurrent ovarian cancer
- No standard therapy available or standard therapies previously failed

Study Endpoints

- Efficacy:** ORR per RECIST 1.1 by investigator, CBR, DCR, DOR, PFS, OS
- Safety:** AEs

Analyses

- Data Cutoff:** December 13, 2025
- Safety Population:** Patients who received ≥1 dose of study drug(s)
- Efficacy-Evaluable Population:** Patients with ≥1 post-baseline 6-week tumor imaging scan
 - Platinum Sensitive:** Disease progression or relapse >6 months after first-line or later platinum therapy
 - Platinum Refractory/Resistant:** Disease progression or relapse ≤6 months after first-line or later platinum therapy, including progression on or ≤1-month post–first-line platinum
 - Prior Line(s) of Therapy:** 1–3 prior lines vs ≥4 prior lines
 - PARPi Naïve:** Never received a PARPi
 - PARPi Progressed:** Radiographic disease progression while on PARPi maintenance or treatment

BOT Q6W

1 mg/kg or 2 mg/kg

Fc-enhanced
anti-CTLA-4
+

BAL Q2W

3 mg/kg

anti-PD-1

Results

Patient Characteristics

Table 1. Demographics and Baseline Disease Characteristics

		Overall N=44
Characteristic		
Age, years	Median (range)	66 (37–79)
Sex	Female	44 (100)
ECOG PS	1	22 (50)
Disease setting	Platinum sensitive ^a	12 (27)
	Platinum refractory/resistant ^b	32 (73)
Prior lines	Median (range)	4 (1–17)
	1–3	15 (34)
	≥4	29 (66)
PARPi experience	PARPi naïve	19 (43)
	PARPi exposed	25 (57)
	PARPi progressed ^c	21 (48)
Prior therapies	Platinum doublet	44 (100)
	Bevacizumab	34 (77)
	Radiotherapy	9 (20)
	PD-(L)1	6 (14)
Multiple metastatic sites	Mirvetuximab soravtansine-gynx	2 (5)
Liver metastases (visceral)		33 (75)
		6 (14)
Biomarkers, n/N (%)	BRCA-1/2 mutant	8/23 (35)
	PD-L1 positive (CPS ≥1%)	21/25 (84)
	MSS	41/41 (100)
	TMB >10 mut/Mb ^d	1/13 (8)
Histology	Elevated CA-125 (>35 U/mL)	29/39 (74)
	High-grade serous	36 (82)
	Clear cell (+1 mixed histology)	5 (11)
BOT dose	Carcinosarcoma	2 (5)
	Endometrioid adenocarcinoma	1 (2)
	BOT 1 mg/kg + BAL	21 (48)
	BOT 2 mg/kg + BAL	22 (50)
Safety population	Crossover ^e	1 (2)

n (%) unless otherwise stated.
^aDisease progression or relapse >6 months after first-line or later platinum therapy. ^bDisease progression or relapse ≤6 months after first-line or later platinum therapy, including progression on or ≤1-month post–first-line platinum. ^cRadiographic disease progression while on PARPi maintenance or treatment. ^dOne patient had a TMB >10 mut/Mb (TMB=11). ^eCrossover patient received 0.1 mg/kg BOT monotherapy Q3W and later received BOT 1 mg/kg Q6W + BAL.

- The median number of BOT and BAL doses received was 1 (range, 1–11) and 3 (range, 1–50), respectively

Safety

Table 3. Treatment-Related Immune-Mediated Adverse Events (in ≥5% of Patients)

		Overall N=44
n (%)	Any Grade	Grade ≥3
Any treatment-related imAE ^a	30 (68)	14 (32)
Gastrointestinal		
Diarrhea/colitis ^b	19 (43)	9 (20)
Dermatologic ^c	5 (11)	2 (5)
Endocrine		
Thyroid disorders ^d	4 (9)	0
Nervous system disorders ^e		
	3 (7)	1 (2)

Safety population.
^aimAEs were medically adjudicated and defined as related to treatment, thought to have an immune mechanism, determined by the investigator to be immune-related, and/or treated with systemic steroids (of any dose) and/or other immunosuppressants or with thyroid replacement hormones. imAEs were identified from a prespecified list of preferred terms. ^bDiarrhea/colitis (grouped term) included the preferred terms of immune-mediated enterocolitis, colitis, diarrhea, duodenitis, and enterocolitis. ^cDermatologic (grouped term) included the preferred terms of rash maculo-papular, immune-mediated dermatitis, lichen sclerosus, linear IgA disease, and rash erythematous. ^dThyroid events (grouped term) included the preferred terms of hypothyroidism and uncoded PT term (worsening Hashimoto's disease). ^eNervous system disorders (grouped term) included the preferred terms of peripheral sensory neuropathy, immune-mediated neuropathy, peripheral motor neuropathy, and uncoded PT term (autonomic neuropathy).

- There were no treatment-related deaths
- Visceral imAEs outside of the GI tract, including hepatic, pulmonary, cardiac, and adrenal insufficiency events, were rare, with each occurring in only 1 patient

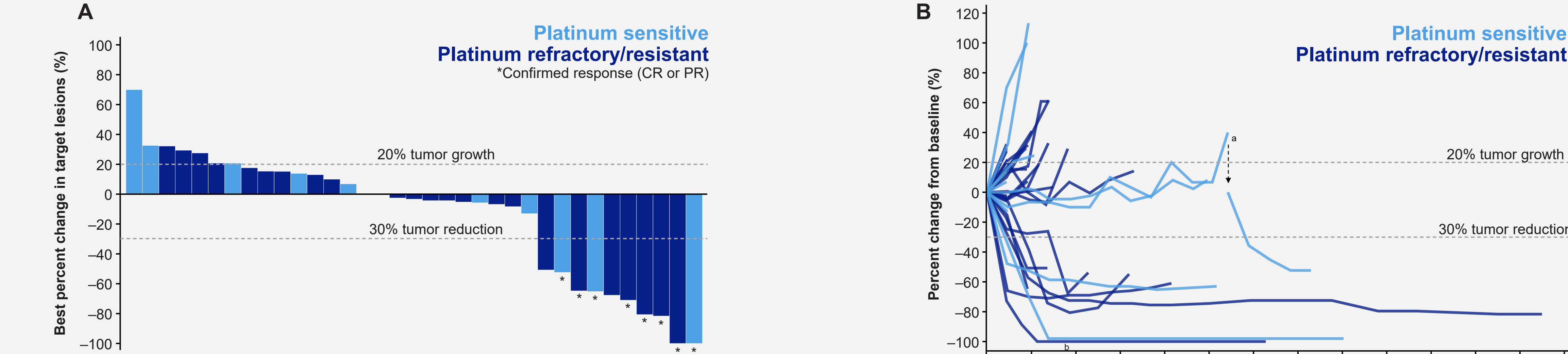
Efficacy

Table 2. Efficacy Overview by Subgroup and Overall

	Platinum Sensitive n=10	Platinum Refractory/ Resistant n=25	1–3 Prior Lines n=12	≥4 Prior Lines n=23	PARPi Naïve n=16	PARPi Progressed n=17	Overall n=35
ORR, n (%) 95% CI	3 (30) 7–65	5 (20) 7–41	4 (33) 10–65	4 (17) 5–39	6 (38) 15–65	2 (12) 2–36	8 (23) 10–40
CR	0	1 (4)	1 (8)	0	1 (6)	0	1 (3)
PR	3 (30)	4 (16)	3 (25)	4 (17)	5 (31)	2 (12)	7 (20)
Median DOR, mo (95% CI)	4.2 (2.8–NE)	11.0 (6.8–NE)	8.3 (4.2–NE)	12.3 (2.8–NE)	8.3 (2.8–NE)	12.3 (NE–NE)	9.7 (2.8–NE)
DCR at ≥6 wks, n (%) 95% CI	5 (50) 19–81	16 (64) 43–82	7 (58) 28–85	14 (61) 39–80	12 (75) 48–93	8 (47) 23–72	21 (60) 42–76
CBR at ≥24 wks, n (%) 95% CI	4 (40) 12–74	7 (28) 12–49	4 (33) 10–65	7 (30) 13–53	7 (44) 20–70	4 (24) 7–50	11 (31) 17–49
Median PFS, mo (95% CI)	2.1 (1.3–5.6)	3.2 (1.3–6.8)	3.4 (1.3–9.6)	2.8 (1.3–6.8)	4.1 (1.8–9.9)	1.4 (1.3–6.8)	2.8 (1.4–5.5)
12-mo PFS, % (95% CI)	20 (3–48)	11 (2–29)	8 (1–31)	18 (5–39)	14 (2–35)	20 (4–43)	14 (5–29)
Median OS, mo (95% CI)	12.9 (2.4–NE)	14.8 (10.5–NE)	14.8 (9.9–NE)	13.9 (10.5–NE)	14.8 (10.0–NE)	NR (8.8–NR)	14.8 (12.1–NE)
24-mo OS, % (95% CI)	45 (11–75)	47 (23–68)	43 (11–72)	48 (23–69)	42 (15–68)	61 (29–82)	48 (27–65)
36-mo OS, % (95% CI)	45 (11–75)	47 (23–68)	NE ^a	48 (23–69)	NE ^a	61 (29–82)	48 (27–65)
Follow-up, mo							
Median (range)	11.0 (2.0–36.6)	10.9 (1.3–38.7)	11.5 (1.3–34.3)	10.9 (2.0–38.7)	12.5 (1.3–34.3)	9.2 (2.0–38.7)	10.9 (1.3–38.7)
Median reverse KM (95% CI)	25.2 (2.0–NE)	21.3 (10.9–33.4)	14.6 (3.6–NE)	25.2 (6.9–34.2)	21.3 (10.9–NE)	27.7 (5.6–34.2)	25.2 (10.9–33.4)

Efficacy-evaluable population.
^aLandmark beyond follow-up time.

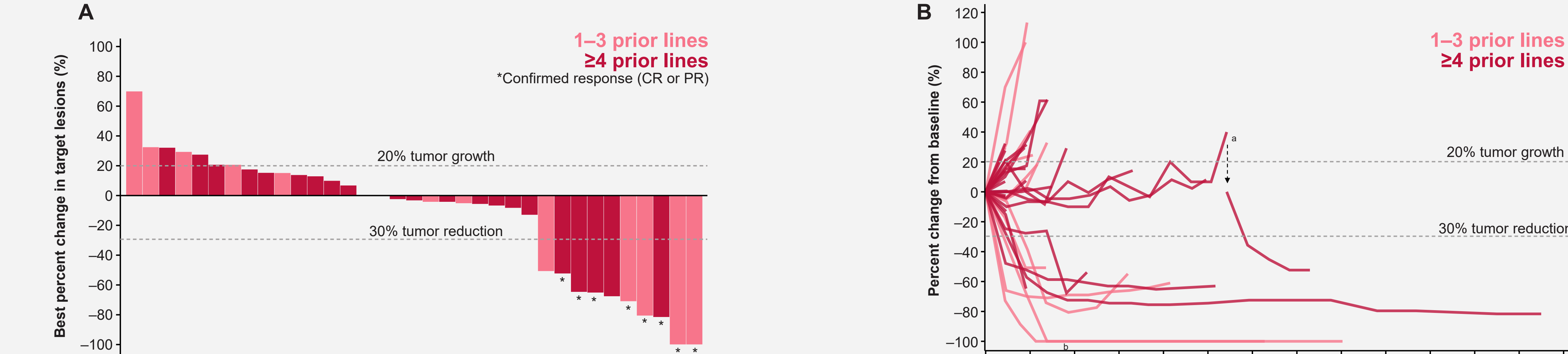
Figure 1. (A) Best Overall Response and (B) Response Over Time by Platinum Sensitivity Status



Efficacy-evaluable population; patients with percent change from baseline in tumor measurement.
^aDenotes the crossover patient: showing initial BOT monotherapy treatment baseline (0.1 mg/kg of BOT) with the line break representing baseline once the combination was started (BOT 1 mg/kg + BAL).
^bThe patient received radiation around 24 weeks to a solitary escape lesion with no subsequent evidence of disease.

- Efficacy benefit was seen in patients with platinum-sensitive disease (ORR, 30%) and platinum-refractory/resistant disease (ORR, 20%)

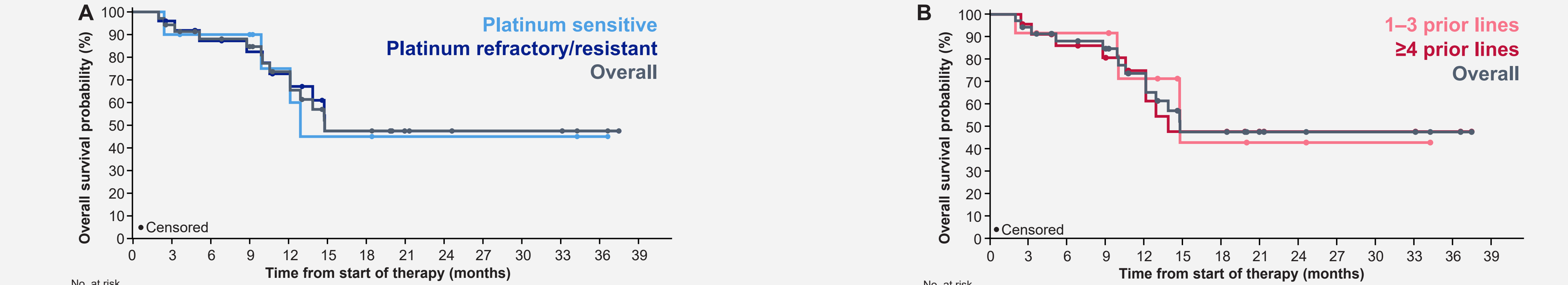
Figure 2. (A) Best Overall Response and (B) Response Over Time by Number of Prior Lines



Efficacy-evaluable population; patients with percent change from baseline in tumor measurement.
^aDenotes the crossover patient: showing initial BOT monotherapy treatment baseline (0.1 mg/kg of BOT) with the line break representing baseline once the combination was started (BOT 1 mg/kg + BAL).
^bThe patient received radiation around 24 weeks to a solitary escape lesion with no subsequent evidence of disease.

- Efficacy benefit was seen in patients with 1–3 prior lines (ORR, 33%) and ≥4 prior lines (ORR, 17%)

Figure 3. Overall Survival by (A) Platinum Sensitivity Status and (B) Number of Prior Therapy Lines



Efficacy-evaluable population.

- At last follow-up in the safety population, 11 patients (25%) were alive and off all therapy, including 6 responders

Conclusions

- BOT+BAL demonstrated durable clinical activity** in heavily pretreated recurrent ovarian cancer, with an **ORR of 23%, median DOR of 9.7 months, and median OS of 14.8 months**
- The OS curve plateaued beyond 2 years, with **identical 2- and 3-year OS rates of 48%**, indicating **long-term, durable survival** in a subset of patients
- Responses and long-term survival** were observed across **platinum sensitivity groups** (ORR, 30% sensitive vs 20% refractory/resistant; 3-year OS, 45% vs 47%) and in **heavily pretreated patients** (ORR, 17% with ≥4 prior lines; 3-year OS, 48%)
- Safety remained consistent with the known BOT+BAL profile, with **no new safety signals or treatment-related deaths**

Consistent with BOT's differentiated, Fc-enhanced immunologic mechanism, these durable responses and long-term survival support continued evaluation of BOT+BAL in recurrent ovarian cancer, a disease where conventional ICI has shown limited clinical benefit

Abbreviations: AEs, adverse events; BAL, balstilimab; BOT, botensilimab; BRCA, breast cancer gene; CA-125, cancer antigen 125; CBR, clinical benefit rate; CI, confidence interval; CPS, combined positive score; CR, complete response; CTLA-4, cytotoxic T-lymphocyte associated protein 4; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; Fc, fragment crystallizable; GI, gastrointestinal; ICI, immune checkpoint inhibitor; IgA, immunoglobulin A; imAE, immune-mediated adverse event; KM, Kaplan-Meier; mo, months; MSS, microsatellite-stable; mut/Mb, mutations per megabase; NE, not estimable; No., number; NR, not reached; ORR, objective response rate; OS, overall survival; PARPi, poly(ADP-ribose) polymerase inhibitor; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PR, partial response; PT, preferred term; RECIST, Response Evaluation Criteria in Solid Tumors; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; TMB, tumor mutational burden; wks, weeks.

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