Efficacy and safety of balstilimab with or without zalifrelimab in recurrent cervical cancer: Results from the global phase 2 RaPiDs trial (GOG-3028)

Poster # 1164P

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Background

- Patients with recurrent and/or metastatic cervical cancer have a poor prognosis, and effective second-line treatments for advanced relapsed disease are lacking[1]
  - Immunotherapy represents a promising therapeutic approach in this setting[2]
  - PD-(L)1 and CTLA-4 inhibitors are agents of interest
- Balstilimab (BAL; anti–PD-1 monoclonal antibody) showed single-agent clinical activity and tolerability in previously-treated patients with metastatic, persistent, or recurrent cervical cancer[3,4]
- Zalifrelimab (ZAL; anti–CTLA-4 monoclonal antibody) potentiated the activity of BAL in advanced cervical cancer, leading to activity irrespective of PD-L1 status or histology[4]
- We present findings from the phase 2 RaPiDS trial evaluating BAL ± ZAL in patients with advanced cervical cancer and progression after first-line platinum-based chemotherapy[5,6]

RaPiDS Study Design (N=212)

NCT03894215 (GOG-3028/C-750-01): A 2-Arm, **Ra**ndomized, Non-comparative, **P**hase 2 Trial of BAL (anti–**PD**-1) as a Monotherapy or Combination Therapy with ZAL (anti–CTLA-4) or with Placebo in Women with Recurrent Cervical Cancer (**S**econd Line); **RaPiDS** Trial[5,6]

Key Eligibility

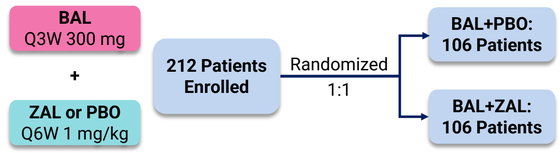
- Recurrent/persistent/metastatic cervical cancer
- One prior platinum-based regimen

Study Endpoints

- Primary: ORR by BICR per RECIST v1.1
- Secondary: TEAEs, DOR[a], DCR[a], PFS[a], and OS

[a]By BICR and investigator per RECIST v1.1

Treatment *(up to 2 years)*



Data Collection

Data cutoff date: 16-SEP-2024

- PD-L1 expression analysis prior to treatment
- Imaging every 6 weeks for up to 2 years
- Intent-to-treat population: All randomized patients with measurable disease at baseline (demographics and overall efficacy endpoints)
- Safety population: All randomized patients who received ≥1 dose of study drug (safety endpoints)

Results

Patient Characteristics

Characteristic		BAL+PBO n=106	BAL+ZAL n=106
Age	Median (range)	46 (25–79)	50 (25–80)
Race, n (%)	White	69 (65)	69 (65)
	Black or African American	6 (6)	7 (7)
	Asian	2 (2)	5 (5)
	Other/not reported	29 (27)	25 (24)
Ethnicity, n (%)	Hispanic or Latino	56 (53)	59 (56)[a]
ECOG PS, n (%)[b]	0	46 (43)	49 (46)
	1	58 (55)	56 (53)
	3	1 (1)	0
Tumor histology, n (%)	Squamous cell carcinoma	75 (71)	66 (62)
	Adenocarcinoma	20 (19)	34 (32)
	Adenosquamous	9 (9)	4 (4)
PD-L1 status, n (%)	Positive	68 (65)	54 (51)
	Negative	25 (24)	40 (38)
	Unknown	12 (11)	12 (11)
Central pelvic recurrence, n (%)	**Yes**	18 (17)	17 (16)
Prior therapies, n (%)	Radiotherapy	90 (85)	91 (86)
	Platinum	106 (100)	106 (100)
	Taxane	98 (93)	91 (86)
	Bevacizumab	41 (39)	41 (39)
Metastases at screening, n (%)	Lungs	38 (36)	38 (36)
	Distant lymph nodes	36 (34)	37 (35)
	Liver	17 (16)	18 (17)
	Bone	8 (8)	9 (9)

Table 1. Demographics and Baseline Characteristics. [a]Two patients in the BAL+ZAL arm did not report ethnicity. [b]One patient in each treatment arm was missing ECOG PS data.

Efficacy

Efficacy Endpoint	BICR		Investigator Assessed	
	BAL+PBO n=106	BAL+ZAL n=106	BAL+PBO n=106	BAL+ZAL n=106
Confirmed ORR, % n, 95% CI	**26%** 27, 18–35	**24%** 25, 17–33	**15%** 16, 10–23	**24%** 25, 17–33
CR, n (%)	9 (9)	8 (8)	5 (5)	5 (5)
PR, n (%)	18 (17)	17 (16)	11 (10)	20 (19)
SD, n (%)	39 (37)	45 (43)	49 (46)	40 (38)
PD, n (%)	34 (32)	30 (28)	34 (32)	36 (34)
NE/no data, n (%)	6 (6)	6 (6)	7 (7)	5 (5)
DCR, % n, 95% CI	62% 66, 53–71	66% 70, 57–74	61% 65, 52–70	60% 64, 51–69
Median DOR, months (95% CI)	NR (5.6–NR)	23.2 (11.0–NR)	NR (NR–NR)	23.2 (6.9–29.0)
18-month DOR, % (95% CI)	61 (36–78)	64 (36–83)	80 (51–93)	58 (35–76)
Median PFS, months (95% CI)	4.1 (2.8–5.2)	4.2 (2.8–5.6)	2.9 (2.7–4.2)	4.1 (2.8–4.8)
18-month PFS, % (95% CI)	21 (13–31)	24 (15–34)	18 (10–26)	18 (11–26)

Table 2. Efficacy by BICR and Investigator.

Efficacy, Continued

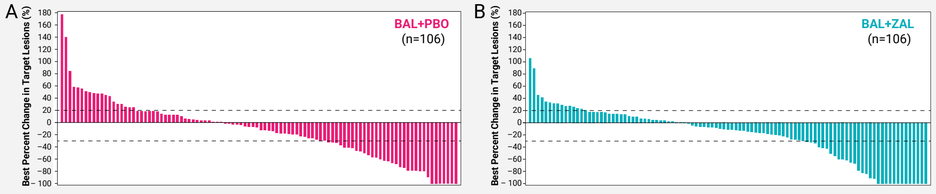
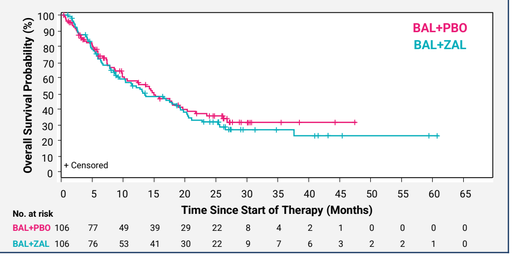


Figure 1. Best Overall Response per BICR in Patients Treated with (A) BAL+PBO or (B) BAL+ZAL.

Efficacy Endpoint	BAL+PBO n=106	BAL+ZAL n=106
Median OS, months, 95% CI	15.0 9.9–20.4	13.5 9.0–19.3
18-month OS, % 95% CI	44 33–54	43 33–53
Median follow-up, months, range	9.9 0.5–51.6	10.9 0.5–61.9

Table 3 and Figure 2. Overall Survival.



Efficacy: PD-L1 Status Subgroups[a]

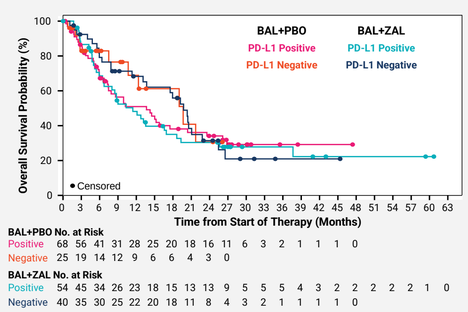
Efficacy Endpoint	PD-L1 Positive		PD-L1 Negative	
	BAL+PBO n=68	BAL+ZAL n=54	BAL+PBO n=25	BAL+ZAL n=40
BICR				
Confirmed ORR, % n, 95% CI	25% 17, 17–38	24% 13, 15–38	20% 5, 9–41	23% 9, 13–38
CR, n (%)	6 (9)	6 (11)	1 (4)	1 (3)
PR, n (%)	11 (16)	7 (13)	4 (16)	8 (20)
Median DOR, months (95% CI)	NR (4.3–NR)	22.8 (4.4–NR)	5.6 (2.8–NR)	23.2 (2.8–NR)
Median PFS, months (95% CI)	3.4 (1.4–5.1)	2.8 (1.5–5.6)	3.0 (1.4–5.8)	5.5 (4.0–10.9)
Investigator Assessed				
Confirmed ORR, % n, 95% CI	15% 10, 9–27	26% 14, 17–40	8% 2, 2–27	20% 8, 11–36
CR, n (%)	3 (4)	3 (6)	1 (4)	1 (3)
PR, n (%)	7 (10)	11 (20)	1 (4)	7 (18)
Median DOR, months (95% CI)	NR (2.4–NR)	26.3 (4.2–NR)	NR (NR–NR)	23.2 (2.9–NR)
Median PFS, months (95% CI)	2.8 (1.4–4.2)	2.9 (1.7–4.2)	3.5 (1.4–6.9)	4.3 (2.8–5.6)

Table 4. Efficacy by PD-L1 Status.

Efficacy Endpoint	PD-L1 Positive		PD-L1 Negative	
	BAL+PBO n=68	BAL+ZAL n=54	BAL+PBO n=25	BAL+ZAL n=40
Median OS, months, 95% CI	**13.7** 7.4–20.4	**11.4** 6.6–16.9	**19.7** 10.7–NR	**19.7** 13.1–22.8
18-month OS, % 95% CI	38 26–50	35 22–48	61 34–80	56 38–70

Table 5 and Figure 4. Overall Survival by PD-L1 Status.

[a]Among all randomized patients with post-baseline tumor assessment ≥87 days from randomization prior to data cutoff and who had ≥1 record in BICR adjudication accepted target lesion at screening.



Safety

n (%)	BAL+PBO n=105	BAL+ZAL n=106	Overall n=211
Any Grade ≥3 TRAE			
Related to ZAL or PBO	16 (15)	24 (23)	40 (19)
Related to BAL	16 (15)	23 (22)	39 (19)
Any AE leading to discontinuation			
ZAL or PBO	12 (11)	13 (12)	25 (12)
BAL	12 (11)	14 (13)	26 (12)
Immune-mediated TRAEs (>5%)			
Hyperthyroidism	7 (7)	2 (2)	9 (4)
Hypothyroidism	5 (5)	16 (15)	21 (10)
Diarrhea	13 (12)	16 (15)	29 (14)
Pruritis	3 (3)	9 (9)	12 (6)
Grade ≥3 immune-mediated TRAEs			
Related to ZAL or PBO	3 (3)	11 (10)	14 (7)
Related to BAL	3 (3)	11 (10)	14 (7)

Table 6. Safety Overview.

- No new safety signals
- No treatment-related deaths (grade 5)

CONCLUSIONS

- In this randomized, blinded, 2-arm, non-comparative phase 2 trial enrolling patients with recurrent/metastatic cervical cancer regardless of PD-L1 status, anti-tumor responses and survival signals were observed with BAL+PBO and BAL+ZAL highlighting meaningful clinical activity
- Investigator-assessed ORR was numerically higher with BAL+ZAL than BAL+PBO, but discordance between investigator and BICR assessments limits conclusions about ZAL's incremental benefit
- Median overall survival for PD-L1–negative patients showed improvement compared with PD-L1–positive patients across both arms
- For CTLA-4/PD-1 doublet therapy, BAL+ZAL showed higher rates of grade ≥3 treatment-related and immune-mediated AEs than BAL+PBO; however, no new safety signals were observed in line with prior experience[3,4]

These data support continued development of balstilimab for treatment of recurrent/metastatic cervical cancer irrespective of PD-L1 status

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Abbreviations: AE, adverse event; BAL, balstilimab; BICR, blinded independent review committee; BOT, botensilimab; CR, complete response; CTLA-4, cytotoxic T-lymphocyte associated protein-4; DCR, disease control rate (CR, PR, or SD ≥6 weeks); DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; GOG, Gynecologic Oncology Group; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PBO, placebo; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival; PR, partial response; PS, performance status; Q[X]W, every X weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; TEAEs, treatment-emergent adverse events; TRAEs, treatment-related adverse events; ZAL, zalifrelimab.

References: **1.** Boussios, S et al. *Crit Rev Oncol Hematol*. 2016; 108:164–174. **2.** Liu, Y et al. *Front Pharmacol*. 2019; 10:65. **3.** O'Malley, et al. *Gynecol Oncol*; 2021; 163:274–280. **4.** O'Malley, et al. *J Clin Oncol*; 2021; 40:762–771. **5.** O'Malley, et al. *Future Oncol*; 2021; 17:3433–3443. **6.** ClinicalTrials.gov identifier: NCT03894215. Updated February 20, 2025. Accessed August 7, 2025. https://clinicaltrials.gov/ct2/show/NCT03894215.

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