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PRESERVE-004/GOG-3081 (NCT05446298): A Phase 2 randomized dose optimization trial of gotistobart, a pH-sensitive anti-CTLA-4, in combination with pembrolizumab in platinum-resistant ovarian cancer

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15 September 2024 Barcelona, Spain

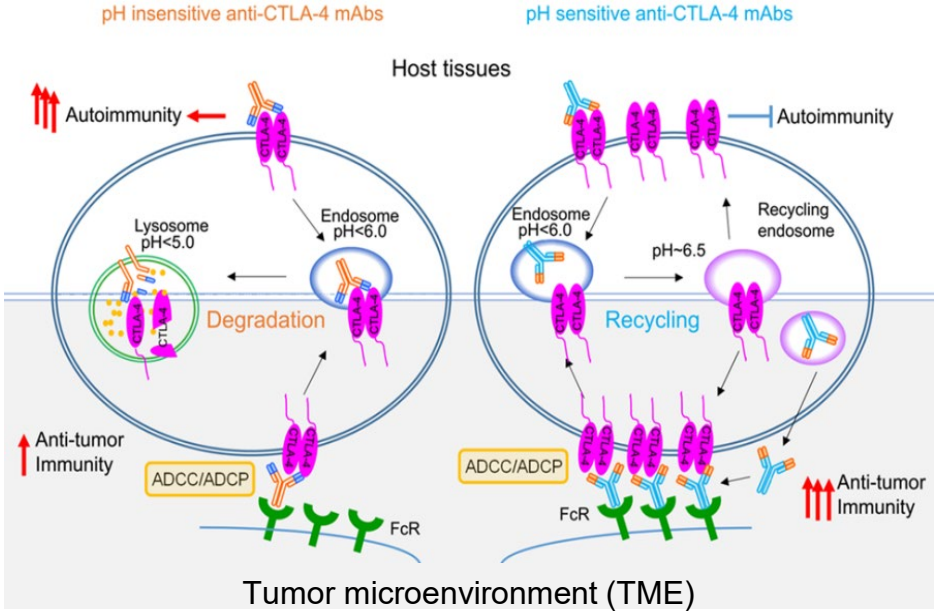
Declaration of interests

- Dr. Joyce N. Barlin reports the following disclosures:
  - Advisory board: Astra Zeneca, Clovis, Mersana, OncoC4, Immunogen, Eisai, Merck
  - Speaker's bureau: Astra Zeneca, Merck
  - Travel, accommodation, expenses for this meeting were provided by OncoC4.

- The PRESERVE-004/GOG-3081 (NCT05446298) study is sponsored by OncoC4 Inc. and is conducted in collaboration with BioNTech SE, Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and the GOG Foundation.

Gotistobart (BNT316/ONC-392)

Gotistobart is a pH-sensitive CTLA-4-preserving antibody.[1-4]



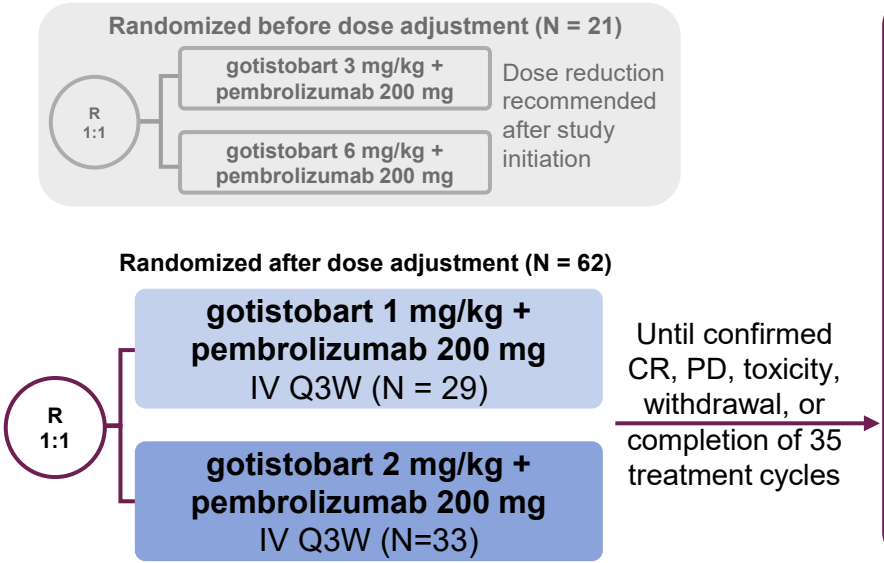
PRESERVE-004 aims to assess safety and efficacy of gotistobart + pembrolizumab in PROC.[5]

ADCC/ADCP, antibody dependent cellular cytotoxicity/phagocytosis; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; PROC, platinum-resistant ovarian cancer; TME, tumor microenvironment; Treg, regulatory T cell. 1. Zhang Y. et al., Cell Res. 2019:29(8) 609-627; 2. Kai H. et al., J Clin Oncol. 2023:41(suppl16: abstract 9024); 3. Liu Y, Zheng P. Trends in Pharmacol Sci. 2020: 41(1) 4-12; 4. Du K et al., Cell Res. 2018:28(4) 433-447. 5. ClinicalTrails.gov identifier: NCT05446298.

Phase 2, randomized, open-label, multicenter study of gotistobart + pembrolizumab in PROC[1]

Patients with platinum-resistant, high-grade serous ovarian cancer

- Adult patients (≥ 18 yrs old)
- Prior hysterectomy and salpingo-oophorectomy
- ≥1 systemic platinum-based therapy
- Platinum-resistant
- RECIST 1.1 measurable lesions
- ECOG score 0-1



Primary endpoint
- ORR by investigator per RECIST 1.1
- Safety per TRAEs, TRSAEs, and irAEs

Secondary endpoints
- DoR, DCR, BOR, PFS, OS

Exploratory endpoints
- PK and ER
- TRAE-related study discontinuation

CR, complete response; PD, progressive disease; BOR, best overall response; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; irAEs, immunotherapy-related adverse effects; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; Q3W, once every 3 weeks; R, randomization; RECIST, response evaluation criteria in solid tumors; SAEs, severe adverse events; TRAE, treatment-related adverse events; TRSAEs, treatment-related serious adverse event. 1. ClinicalTrails.gov identifier: NCT05446298.

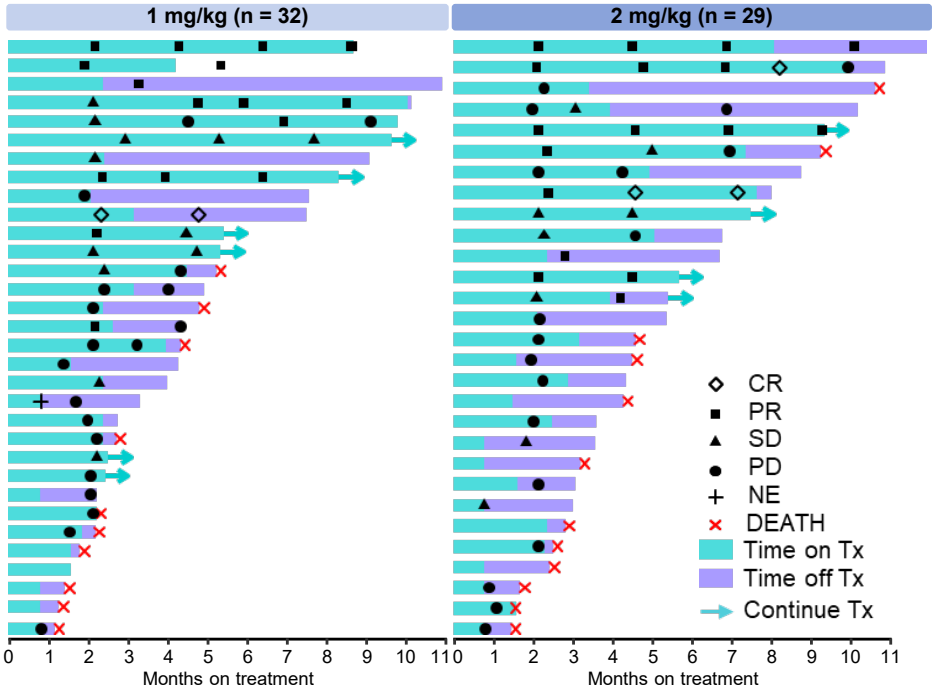
Baseline disease characteristics and study drug exposure

	gotistobart + pembrolizumab 200mg	
Characteristic	**1 mg/kg (n = 33)**	**2 mg/kg (n = 29)**
Age – median (range), years	65.2 (10.25)	63.5 (8.46)
Race – n (%) White/ Black/ Asian/ Other	27 (81.8)/ 1 (3.0)/ 1 (3.0)/ 3 (9.1)	25 (86.2)/ 2 (6.9)/ 1 (3.4)/ 1 (3.4)
ECOG performance-status score – n (%) 0 1	 19 (57.6) 14 (42.4)	 15 (51.7) 14 (48.3)
Primary cancer diagnosis n (%) High-grade serous ovarian cancer Primary peritoneal cancer Fallopian tube cancer	 28 (84.8) 3 (9.1) 2 (6.1)	 25 (86.2) 2 (6.9) 2 (6.9)
Metastatic disease at enrolment, n (%)	24 (72.7)	25 (86.2)
Prior cancer regimens – median (range)	4.0 (2–9)	3.0 (1–8)
BEV-naïve, n (%)	6 (18.2)	12 (41.4)
Study drug exposure		
Treatment duration, mean months (SD)	3.03 (2.43)	3.18 (2.45)
Gotistobart cycles, median (range)	3.0 (1–12)	3.0 (1–12)
Gotistobart dose intensity, % (range)	98.4 (56.6–106.9)	98.4 (56.7–105.1)

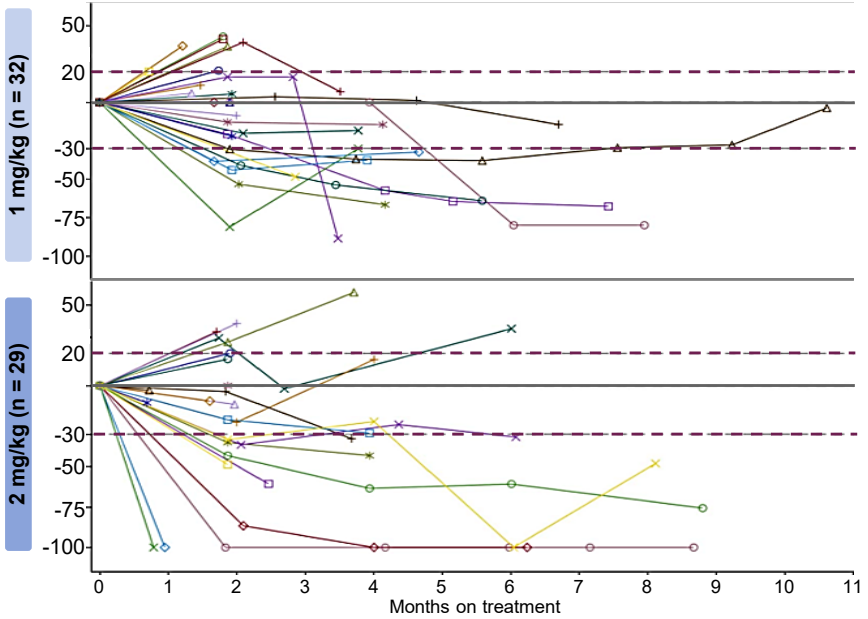
Data cut off: July 19, 2024

BEV, Bevacizumab; ECOG, Eastern Cooperative Oncology Group; n, number; SD, standard deviation.

Antitumor activity



	gotistobart + pembrolizumab 200mg	
	1 mg/kg (n = 32)	2 mg/kg (n = 29)
ORR (unconfirmed) % (n)	**25.0% (8)**	**27.6% (8)**
95% CI	11.5–43.4	12.7–47.2
Complete response[a,b]	3.1% (1)	6.9% (2)
Partial response[a]	21.9% (7)	20.7% (6)
Stable disease	21.9% (7)	13.8% (4)
Progressive disease	40.6% (13)	44.8% (13)
No post-baseline assessment[c]	12.5% (4)	13.8% (4)



Data cut off: July 19, 2024. CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease. [a]Includes both confirmed and unconfirmed responses (3 unconfirmed responders in each treatment group); [b]One out of 3 unconfirmed responders are still on treatment, for both treatment groups; [c]Patients died or discontinued from study without any post-baseline scan.

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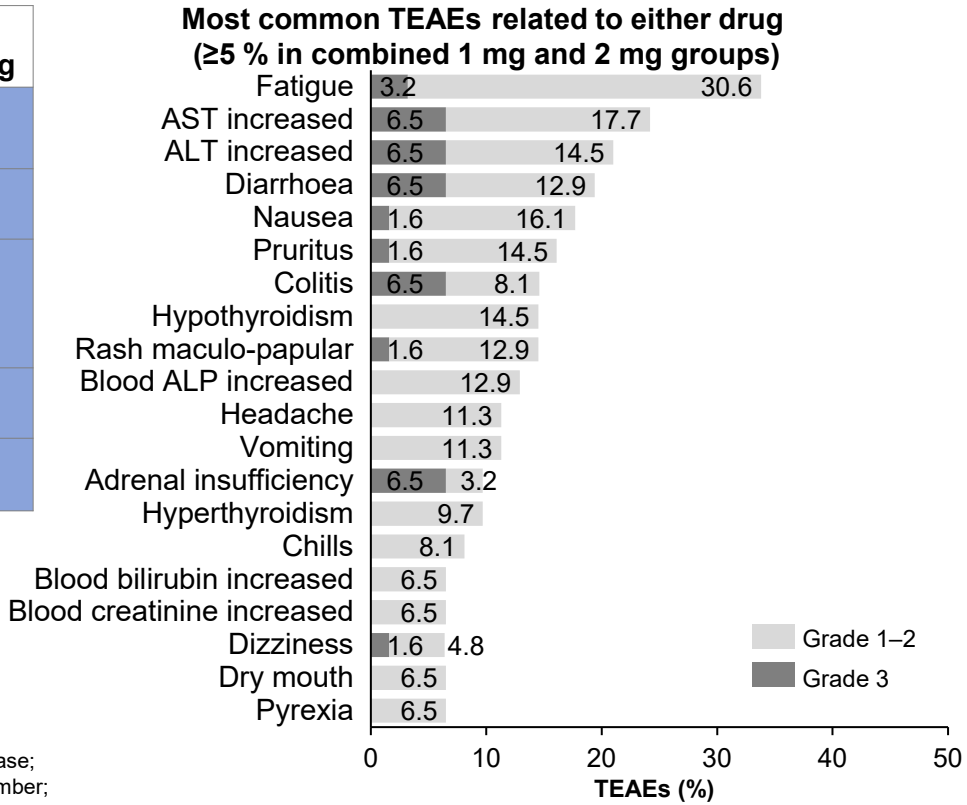
Summary of safety

	gotistobart + pembrolizumab 200 mg	
	1 mg/kg N = 33	**2 mg/kg** N = 29
TEAEs, n (%)	33 (100.0)	28 (96.6)
Grade ≥ 3, n (%)	25 (75.8)	25 (86.2)
TEAEs related to either drug, n (%)	27 (81.8)	23 (79.3)
Grade ≥ 3, n (%)	15 (45.5)	12 (41.4)
Serious TEAEs	18 (54.5)	21 (72.4)
irAE All grades, n (%)	15 (45.5)	18 (62.1)
Grade ≥ 3, n (%)	8 (24.2)	11 (37.9)
TEAEs leading to gotistobart discontinuation	7 (21.2)	8 (27.6)



Data cut off: July 19, 2024

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; TEAE, treatment emergent adverse event; irAE, immune-related adverse event; N, number; SD, standard deviation.

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Conclusions

- Early results from PRESERVE-004 demonstrate that gotistobart + pembrolizumab in PROC has a manageable tolerability profile at both dose levels, with no new safety signals.
- Preliminary results for efficacy are encouraging.
- The final dose selection will be based on the totality of safety, efficacy, and pharmacology.
- If confirmed by further pre-planned analyses, the combination of gotistobart + pembrolizumab in PROC may be explored in a randomized setting.

PROC, platinum-resistant ovarian cancer.

Acknowledgments

- The authors would like to thank the patients and their families, and the staff, research coordinators and investigators at each participating institution.
- Principle investigators of the PRESERVE-004/GOG-3081 study:

Joyce N. Barlin, Women's Cancer Care Associates, Albany, NY, United States; **Peter C. Lim**, Center of Hope, Reno, NV, United States; **Jessica Thomes Pepin**, Minnesota Oncology, Woodbury, MN, United States; **Elizabeth E. Hopp**, Medical College of Wisconsin, Milwaukee, WI, United States; **Noelle G. Cloven**, Texas Oncology, Fort Worth, TX, United States; **Christine Lee**, Texas Oncology, Woodlands, TX, United States; **Helen D. Eshed**, Texas Oncology, Austin, TX, United States; **Destin Black**, Willis-Knighton Cancer Center, Shreveport, LA, United States; **Hope M. Cottrill**, Baptist Health Lexington, Lexington, KY, United States; **Lauren Hand**, Baptist Health Jacksonville, Jacksonville, FL, United States; **David M. O'Malley**, The Ohio State University and the James Comprehensive Cancer Center, Columbus, OH, United States; **Linus T. Chuang**, Nuvance Health, Danbury, CT, United States; **Lyndsay Willmott**, HonorHealth Cancer Care, Phoenix, AZ, United States; **Amanda Podolski**, Icahn School of Medicine, Mount Sinai, NY, United States; **Sudarshan Sharma**, UChicago Medicine Advent Health Hinsdale Cancer Institute, IL, United States; **Charles Anderson**, Willamette Valley Cancer Institute and Research Center – Eugene, OR, United States; **Mary Gordinier**, Norton Cancer Institute - St. Matthews, KY, United States; **Bradley J. Monk**, Florida Cancer Specialists, West Palm Beach, FL, United States

- The authors thank the extended OncoC4 and BioNTech teams: Qiong Wang for statistical analysis, Lili Pan for translational analysis, Stephen Georgiou for medical writing support.