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Balstilimab (anti-PD-1) in combination with zalifrelimab (anti-CTLA-4): Final results from a phase II study in patients (pts) with recurrent/metastatic (R/M) cervical cancer (CC)

D. O'Malley[1], M. Neffa[2], B.J. Monk[3], T. Melkadze[4], A. Kryzhanivska[5], I.V. Bulat[6], T. Meniawy[7], I. Bondarenko[8], W.I. Ortuzar Feliu[9], M. Ancukiewicz[9], I. Lugowska[10]

[1] Division of Gynecologic Oncology, The Ohio State University Wexner Medical Center and The James Comprehensive Cancer Center, Columbus, OH, USA, [2] Department of Surgery, Healthcare Regional Clinical Specialized Dispensary of the Radiation Protection, Kharkiv, Ukraine, [3] Department of Obstetrics and Gynecology, Arizona Oncology (US Oncology Network), Phoenix, AZ, USA, [4] Oncology, Research Institute of Clinical Medicine, Tbilisi, Georgia, [5] Gynecological Surgical Dept., Precarpathian Clinical Oncology Center, Ivano-Frankivsk, Ukraine, [6] Medical Oncology Department, Institute of Oncology-Chisinau, Chisinau, Moldova, [7] Medical Oncology, Linear Clinical Research, Nedlands, WA, Australia, [8] Oncology and Medical Radiology Department, Dnipropetrovsk City Multidisciplinary Clinical Hospital 4, Dnipro, Ukraine, [9] Clinical Development, Agenus Inc, Lexington, KY, USA[10] Department of Soft Tissue/Bone Sarcoma and Melanoma MSCMI, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background

Second-line treatment for R/M CC continues to present a major clinical challenge. Dual blockade of the PD-1 and CTLA-4 immune checkpoints is a validated therapeutic strategy for multiple malignancies. Here we present mature findings of a large single arm Phase II study evaluating the safety and antitumor activity of the anti-PD-1 antibody balstilimab (bal) plus the anti-CTLA-4 antibody zalifrelimab (zal) in pts with R/M CC.

Methods

Pts received bal 3 mg/kg Q2W in combination with zal 1 mg/kg Q6W for up to 2 years. The primary endpoint was objective response rate (ORR) assessed per RECIST 1.1 by independent review; secondary endpoints included safety, DOR, and survival.

Results

In total, 155 pts were treated with bal plus zal (safety population). Of these, 125 with measurable disease at baseline and one prior line of platinum-based therapy in the R/M setting constituted the efficacy-evaluable population, with outcomes presented in the table below. The median study follow-up was 19.4 months. The combination exhibited manageable tolerability and no new safety signals were identified. Grade ≥3 related AEs were seen in 33 pts (21.3%) with ALT elevation (3.2%), anemia, and diarrhea (1.9%) most frequently observed. Treatment discontinuations due to a related AE occurred in 15 pts (9.7%). Sixty-nine pts (44.5%) had immune-related AEs (12.6% grade ≥3); hypothyroidism (13.5%), hyperthyroidism, and diarrhea (each 7.1%) were the most common all grade events.Table: 724MO

Outcome	Balstilmab + Zalifrelimab (125) N (%)
ORR	32 (25.6)
CR	11 (8.8)
PR	21 (16.8)
DOR [range]	NR [9.3, NR]
6 month (%)	86.4
12 month (%)	66.7
ORR subsets	
PD-L1^{+} (n = 67)	22 (32.8)
PD-L1^{-} (n = 33)	3 (9.1)
Squamous cell carcinoma (n = 89)	29 (32.6)
Adenocarcinoma (n = 34)	3 (8.8)
OS estimates (%)	
6 months	69.0
12 months	52.7

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Conclusions

The combination regimen of bal plus zal demonstrated impressive response rates (including complete remissions), DOR, and

OS in patients with previously treated R/M CC. Clinical benefit was highest in patients with PD-L1^{+} tumors, with activity also seen in the PD-L1^{-} setting. The treatment regimen was well tolerated.

Clinical trial identification

NCT03495882.

Legal entity responsible for the study

Agenus Inc.

Funding

Agenus Inc.

Disclosure

D. O'Malley: Financial Interests, Personal, Advisory Role: Agenus; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: GSK/Tesaro; Financial Interests, Personal, Advisory Role: Immunogen; Financial Interests, Personal, Advisory Role: BBI; Financial Interests, Personal, Advisory Role: Ambry; Financial Interests, Personal, Advisory Role: Janssen; Financial Interests, Personal, Advisory Role: Abbvie; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: Regeneron; Financial Interests, Personal, Advisory Role: Novocure; Financial Interests, Personal, Advisory Role: Genentech/Roche; Financial Interests, Personal, Advisory Role: Iovance; Financial Interests, Personal, Advisory Role: Myriad Genetics; Financial Interests, Personal, Advisory Role: Eisai; Financial Interests, Personal, Advisory Role: Tarveda; Financial Interests, Personal, Advisory Role: Clovis; Financial Interests, Personal, Advisory Role: Merck; Financial Interests, Personal, Advisory Role: SeaGen; Financial Interests, Personal, Advisory Role: Rubis; Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Advisory Role: Mersana; Financial Interests, Personal, Advisory Role: Elevar; Financial Interests, Institutional, Sponsor/Funding: Agenus. B.J. Monk: Financial Interests, Personal, Advisory Role: Agenus; Financial Interests, Personal, Advisory Role: Akeso Bio; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: Genmab/Seattle Genetics; Financial Interests, Personal, Advisory Role: Iovance; Financial Interests, Personal, Advisory Role: Merck; Financial Interests, Personal, Advisory Role: Puma; Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Role: Merck; Financial Interests, Personal, Advisory Role: GSK/Tesaro; Financial Interests, Personal, Full or part-time Employment: US Oncology Network; Financial Interests, Leadership Role: GOG Foundation. W.I. Ortuzar Feliu: Financial Interests, Full or part-time Employment: Agenus. M. Ancukiewicz: Financial Interests, Ownership Interest: Agenus. All other authors have declared no conflicts of interest.