RaPiDS (GOG-3028): A Randomized Phase II Study of Balstilimab (AGEN2034) as Monotherapy or in Combination with Zalifrelimab (AGEN1884) in Second-Line Cervical Cancer

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Background
- While targeting the programmed death 1 (PD-1)/programmed death ligand 1 (PD-L1) immune checkpoint pathway has provided an important advance for the treatment of patients with advanced cervical cancer,1 opportunities exist to improve current outcomes.2 Amongst these, dual blockade of PD-1 and cytotoxic T lymphocyte-associated protein 4 (CTLA-4) represents an attractive therapeutic approach, given that this is an effective strategy in other tumor types.3
- Balstilimab (AGEN2034, anti-PD-1) demonstrated meaningful and durable single-agent activity in previously-treated patients with metastatic, persistent, or recurrent cervical cancer in a large phase II trial (NCT03104699).4 Notably, responses were observed in PD-L1+ patients as well as those with PD-L1 tumor expression. Responses also occurred in patients whose tumors were of squamous cell carcinoma or adenocarcinoma origin.
- Balstilimab plus zalifrelimab (AGEN1884; anti-CTLA-4) was evaluated in a parallel, independent study in a similarly selected patient population (NCT03495882). The combination provided improved clinical benefit over monotherapy, as evidenced by higher relative response rates and longer duration of response irrespective of PD-L1 tumor status or histology.5
- Taken together, these findings demonstrate that both single-agent balstilimab and the balstilimab/zalifrelimab combination are effective and well tolerated as second-line treatment for advanced/metastatic cervical cancer and may represent promising new options for patients in this disease setting.

Mechanism of Action

Introduction of ADCC and ADCP of Tregs
Suppression of DC production
Prevention of tumor resistance to apoptosis
Restoration of CD8+ T cell mediated killing of tumor cells
Restoration of CD8 signaling

Study Design
- RaPiDS is a Randomized Phase II study assessing the safety and efficacy of balstilimab (anti-PD-1), both as monotherapy and in combination with zalifrelimab (anti-CTLA-4), in patients with cervical cancer who relapsed after platinum-based therapy for advanced (recurrent/persistent/metastatic) disease (second-line).
- A planned total of 200 patients will be randomized 1:1 to:
  - Arm 1: Balstilimab 300 mg administered IV on Day 1 of a 3-week cycle (Q3W)
  - Arm 2: Balstilimab 300 mg Q3W plus zalifrelimab 1 mg/kg administered IV on Day 1 of a 6-week cycle (Q6W)
- Patients may receive treatment for up to 24 months (or until confirmed progression, unacceptable toxicity, or withdrawal from the trial).

Trial Endpoints

Primary
- Objective response rate (ORR) determined by an Independent Radiology Review Committee (IRRC) according to RECIST v1.1.

Key Secondary
- Safety and tolerability of balstilimab as monotherapy or in combination with zalifrelimab
- Duration of response, stable disease, and disease control rate (per IRRC and investigator, RECIST v1.1)
- Progression-free survival, defined as time from first dose to first documentation of disease progression (or death within 12 weeks of last tumor assessment)
- Median overall survival, defined as time from first dose to death from any cause
- Quality of life outcomes using the Functional Assessment of Cancer Therapy – Cervical Cancer Trial Outcome Index (FACT-Cx) and Brief Pain Inventory (BPI)

Key Inclusion Criteria
- Women ≥ 18 years of age
- Histologically or cytologically confirmed diagnosis of squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix
- Has cervical cancer that has relapsed after a platinum-based (first-line) regimen for advanced (recurrent, unresectable, or metastatic) disease
- Measurable disease i.e., at least 1 target lesion to assess response, per RECIST v1.1.
- ECOG performance status of 0 or 1
- Have adequate hematologic, renal, and hepatic function

Key Exclusion Criteria
- Diagnosis of clear cell carcinoma, minimal deviation adenocarcinoma, gastric type adenocarcinoma, or mesonephric carcinoma
- Prior treatment with an immune checkpoint inhibitor
- More than 1 systemic treatment regimen for advanced cervical cancer
- Known severe hypersensitivity reactions to fully human monoclonal antibodies
- Active, or history of, autoimmune disease requiring immunosuppressive systemic treatment within 2 years of start of trial treatment
- Received systemic corticosteroid therapy in ≥ 3 days prior to 1st dose of trial treatment

Enrollment & Key Eligibility
- 200 patients with recurrent/persistent/metastatic cervical cancer
- One prior platinum-based regimen for advanced disease
- Randomized, non-comparative, blinded phase II trial design

Balstilimab 300 mg Q3W + Placebo

Balstilimab 300 mg Q3W + Zalifrelimab 1 mg/kg Q6W

1:1 Randomization

Additional Information

The trial is open and enrolling at centers in the US. This study is registered at Clinicaltrials.gov NCT03894215