Background
AGEN2034 (balstilimab) is a novel fully human monoclonal immunoglobulin G4 (IgG4) antibody, designed to block PD-1 with high affinity. The objective of this dose escalation study was to assess the safety, MTD, pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of AGEN2034 monotherapy in patients with advanced refractory malignancies.

Methods
Between April 2017 - April 2019 50 patients with advanced solid tumors were enrolled in a phase 1 dose escalation study. The primary safety endpoint was dose limiting toxicity (DLT). The study population is subsets of patients with heavily pretreated recurrent epithelial ovarian cancer and a subset of patients with heavily pretreated recurrent cervical cancer. The study population is subset of patients with heavily pretreated recurrent epithelial ovarian cancer was defined as patients who have received prior platinum-based treatment and have at least 12 weeks of disease progression after the last prior treatment. The study population is subset of patients with heavily pretreated recurrent cervical cancer was defined as patients who have received prior cervical cancer treatment and have at least 12 weeks of disease progression after the last prior treatment.

Results
The primary endpoint was dose limiting toxicity (DLT). The most common DLT was fatigue (4/12 patients). The most common serious adverse events were fatigue (6 patients) and nausea (2 patients). The recommendation for phase II was 10 mg/kg q3w.

Conclusion
In total efficacy and safety, PK and PD data suggest that 3mg/kg Q2W is the recommended phase II dose for the treatment of advanced ovarian cancer patients.

Eligibility criteria
- Patients with histologically or cytologically confirmed metastatic or locally advanced malignancy for whom no standard of care treatment is available
- No prior treatment with PD-1, PD-L1 or CTLA-4 antagonists
- Have objective evidence of disease diagnosed by local site investigator
- Must have received prior platinum-based therapy
- Patients with any histologically or cytologically confirmed metastatic or locally advanced malignancy for whom no standard of care treatment is available
- No prior treatment with PD-1, PD-L1 or CTLA-4 antagonists
- Have objective evidence of disease diagnosed by local site investigator
- Must have received prior platinum-based therapy
- Patients from the C-700 Phase 1 doseescalation study with PD-L2+ ovarian tumors were excluded from the study population.

Figure 1. Mechanism of Action of AGEN2034
Figure 2. Study design - dose escalation
Figure 3. Objective response rate (ORR) determined by investigator per RECIST v1.1
Figure 4. Spider plot of percent change in target lesion, ovarian cancer patients in dose escalation phase
Figure 5. Pharmacodynamic immune response to AGEN2034 in ovarian cancer subset

Table 1. Baseline characteristics

Table 2. Drug-related treatment-emergent adverse events reported by investigator

Table 3. Immune–related adverse event reported by the investigator

Table 4. Treatment overview–emergent adverse events

Safety and Tolerability

Table 1. Baseline characteristics

Table 2. Drug-related treatment-emergent adverse events reported by investigator

Table 3. Immune–related adverse event reported by the investigator

Table 4. Treatment overview–emergent adverse events

Conclusions
AGEN2034 is generally well tolerated. PD-L2+ ovarian cancer patients with heavily pretreated recurrent epithelial ovarian cancer and PD-L2+ ovarian tumors were excluded from the study population.

The activity noted in ovarian cancer warrants additional investigation. Given the lack of effective therapy and survival benefits for patients with recurrent ovarian cancer, results reported here acclimate the role of the immune checkpoint inhibitors in this patient population.

Safety and efficacy of AGEN2034 suggest that 3mg/kg Q2W is the recommended phase II dose for the treatment of advanced ovarian cancer patients.