response and 26 (25.0%) partial responses (Table). Median DOR was 4.7 months (95% CI: 3.8–8.3). Median PFS was 2.8 months (95% CI: 2.6–3.9). Treatment-emergent adverse events (TEAEs) were experienced by 100% of patients and included most commonly diarrhea ($n = 73$, 67.0%), anemia ($n = 72$, 66.1%), and nausea ($n = 71$, 65.1%). Grade ≥ 3 TEAEs occurred in 75 (68.8%) patients (Table). TEAEs of neutropenia occurred in 30 (27.5%) patients, including 23 (21.1%) patients with grade ≥ 3 neutropenia; 2 (1.8%) patients experienced febrile neutropenia (both grade 3). Sepsis occurred in 7 (6.4%) patients, including 1 (0.9%) patient with grade 3, 4 (3.7%) patients with grade 4, and 2 (1.8%) patients with grade 5 sepsis. Discontinuation of adavosertib due to TEAEs occurred in 19 (17.4%) patients; TEAEs led to death in 4 (3.7%) patients (due to respiratory failure, cardiac disorder, biliary sepsis, and sepsis [all $n = 1$]).

Conclusions

Adavosertib showed antitumor activity in patients with advanced recurrent/persistent USC. Severe neutropenia and sepsis were observed with the recommended phase II monotherapy dose of adavosertib used in this study.

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A phase I study of tremelimumab, durvalumab, and hypofractionated radiotherapy for metastatic gynecologic cancers (040)

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Objectives

The efficacy of anti-PD-L1/PD-1 therapies has been demonstrated in women with metastatic cervical cancer. The impact and safety of dual checkpoint inhibitors combined with hypofractionated radiotherapy (RT) in women with metastatic gynecologic cancers remain an open question. We conducted a phase I study of durvalumab (anti-PD-L1) and tremelimumab (anti-CTLA-4) in conjunction with hypofractionated RT to confirm the safety and tolerability of this combination and early response rates in women with metastatic gynecologic malignancies.

Methods

Patients with metastatic cervical, vulvar, or vaginal cancer with at least one prior systemic platinum-based regimen and at least 2 sites of disease were enrolled in this prospective, IRB-approved study. Patients who had prior immune-based therapies were not eligible. Patients received durvalumab (1500 mg) and tremelimumab (75 mg) intravenously every 4 weeks for 4 cycles starting on day 1, followed by 4 cycles of durvalumab (1500 mg) every 4 weeks. Hypofractionated RT (8 Gy × 3) was delivered to up to one metastatic site on days 3–7. Treatment was stopped for disease progression or toxicity development. The response was assessed every 8 weeks on CT imaging using immune-related (IR) RECIST criteria, and toxicity was assessed using CTCAEv4.03. Tumor PDL1 status was obtained locally as part of the standard of care.

Results

A total of 18 patients were included in the analysis (16 with cervical cancer and 2 with vaginal cancer). The mean age was 43.9 years (range: 25–63). Six patients (33.3%) were PD-L1 low, and 12 (66.7%) were PD-L1 high (defined as a combined positive score ≥ 1). All patients experienced at least 1 adverse event. The most frequent adverse events were gastrointestinal side effects (71), metabolism/nutrition disorders (70), or fatigue (15). Ten (55%) patients experienced a total of 21 serious adverse events. There were 3 IR adverse events in 2 patients: 1 with grade 2 hypothyroidism and 1 with grade 3 dermatitis and conjunctivitis. Three (16%) patients with cervical cancer had an overall partial (1, PR) or complete response (2, CR) to treatment by IR RECIST, all of whom had PDL1 high tumors. Overall, the clinical benefit rate (CBR), which included patients with stable disease, CR, or PR, was 55.6% ($n = 10$): 4 (66.7%) PD-L1 low and 6 (50%) PD-L1 high. CBR in patients without prior pelvic RT was 100% ($n = 5/5$) and 38.5% ($n = 5/13$) with prior radiotherapy. The CBR for patients who had one prior line of therapy was 57.1% versus 50% in patients who had 2 prior lines of therapy. Median overall survival was 8.3 months (95% CI: 6.2–16.2 months). Tw patients remain without evidence of disease 35 and 30 months post-therapy initiation.

Conclusions

The combination of durvalumab and tremelimumab with radiotherapy was well-tolerated overall and consistent with previously reported studies. Clinical benefit was observed with this regimen despite multiple prior lines of systemic therapy, prior pelvic radiotherapy, and PDL1 low tumors. Objective responses were observed only in patients with high PD-L1 tumors.

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Botensilimab, a novel innate/adaptive immune activator, plus balstilimab (anti-PD-1) in patients with recurrent platinum refractory/resistant ovarian cancer (041)

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Objectives

Botensilimab (BOT) promotes optimized T-cell priming, activation, and memory formation by strengthening antigen-presenting cell/T-cell co-engagement. As a fragment crystallizable (Fc)-enhanced next-generation anticytotoxic T-lymphocyte antigen 4 (CTLA-4) antibody, BOT also promotes intratumoral Treg depletion to improve potency while mitigating difficult-to-treat side effects associated with first-generation CTLA-4 therapy. Results from an expanded phase IA/B study (NCT03860272) in patients with recurrent platinum-resistant/refractory ovarian cancer treated with BOT plus balstilimab (BAL; anti-programmed cell death protein 1 [PD-1]) are presented.

Methods

Patients received BOT 1 or 2 mg/kg q6w + BAL 3 mg/kg every 2 weeks. Crossover to combination treatment from BOT monotherapy (rescue) is permitted. Endpoints include incidence of adverse events (AE), objective response rate (ORR; unconfirmed responses included), disease control rate (DCR; the best overall response of either stable disease [SD] or a complete [CR] or partial response [PR]), duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Enrollment is ongoing.

Results

Seventeen patients were evaluated for safety and efficacy (treated as of April 7, 2022, with ≥1 q6w tumor imaging assessment), including one rescue patient; data cutoff August 10, 2022. Patients were heavily pretreated, and the median number of prior lines of therapy was 4 (range: 2–7). The most common histology type was high-grade serous. The median duration of study treatment was 3.2 months (range: 0.9–19.6), with a median follow-up of 8.8 months (range: 2.0–29.2). ORR measured 29% (5/17; 95% CI: 13–53; 4 confirmed PRs, 1 unconfirmed CR) (Graph). One patient has an ongoing PR at 24 weeks (−100% reduction of target lesions with residual non-targets), another patient with an unconfirmed CR at 18 weeks developed a solitary new lesion which was radiated and now has no evidence of disease at 90+ weeks, and the rescue patient had prolonged SD on BOT monotherapy for 66 weeks followed by a PR once BAL was added. The safety profile in all 17 patients continues to be favorable, with no cases of hypophysitis, myocarditis, or pneumonitis of any grade. Grade 1/2, 3, or 4 treatment-related adverse events (TRAEs) occurred in 94%, 24%, and 6% of patients, respectively, with no grade 5 TRAEs reported. The only grade 3 or 4 TRAE occurring in more than one patient was diarrhea or colitis (18%). Further evaluation of biomarkers is ongoing, including paired biopsies (before/during treatment).

Conclusions

BOT plus BAL demonstrates meaningful activity in heavily pretreated patients with recurrent platinum-resistant/refractory ovarian cancer who are historically unresponsive to immunotherapy. Randomized studies are planned.

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What are we worth?: The complexity of payment structures to measure and value work in gynecologic oncology (042)

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Objectives

There is little transparency on which physician payment models are used in gynecologic oncology to measure and value work. Our objective was to obtain perspectives from leaders at academic medical or cancer centers to identify what strategies work well and what challenges exist with various payment systems.

Methods

We identified gynecologic oncologists who serve as the chair or service chief of their academic medical or cancer center. To be