563 A PHASE I CLINICAL TRIAL OF RADIATION THERAPY, DURVALUMAB AND TREMELIMUMAB IN RECURRENT GYNECOLOGIC CANCER

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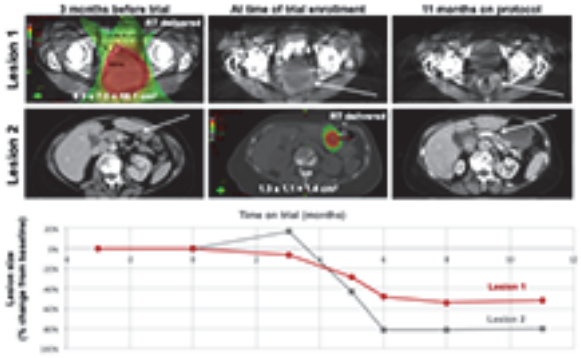
Background Dual immune checkpoint blockade (ICB) may synergize with palliative radiotherapy (RT) to improve response rates in patients with recurrent or metastatic gynecologic cancer. We conducted an open label prospective phase I trial to assess the safety and tolerability of ICB with RT to a single metastatic abdominopelvic site.

Methods Eligible patients included those with recurrent and/or metastatic gynecologic cancer of endometrial, ovarian, cervical, vaginal or vulvar origin without prior immunotherapy treatment. A safety lead-in cohort of patients (cohort A) was treated with durvalumab 1500 mg IV and palliative RT of 25 Gy in 5 fractions delivered to a single measurable lesion >1cm and <10cm in the abdomen or pelvis that was not previously irradiated. RT was initiated within 24 hours of immunotherapy. Durvalumab continued every 4 weeks up to one year or until disease progression. Following a toxicity assessment of cohort A, a second cohort (cohort B) received dual ICB with tremelimumab 75 mg IV given concurrently with the first 4 cycles of durvalumab. The primary endpoint was the rate of dose-limiting toxicities (DLT) in patients still on protocol 8 weeks after RT. Secondary endpoints included the overall response rate (ORR) in non-irradiated lesions.

Results 16 patients were enrolled, with 12 able to be assessed at the end of the 8-week DLT window, split evenly between the cohorts. There were 9 patients with ovarian, 2 with uterine, and 1 with cervical cancer. There were 0 DLTs in cohort A and 1 in cohort B (grade 3 pneumonitis possibly related to treatment). One patient with platinum resistant ovarian cancer in cohort B with two metastatic sites (a 8.3 x 7.0 cm pelvic lesion irradiated with 25 Gy/5 fractions 3 months prior to the study without initial shrinkage and a 1.3 x 1.1 cm peritoneal nodule irradiated on protocol) had a dramatic reduction in disease burden and no new lesions at 11 months of follow up (figure 1). No objective responses were observed in non-irradiated lesions in the remaining patients. The ORR for irradiated lesions was 50% for cohort A and 33% for cohort B.

Conclusions The combination of durvalumab, tremelimumab and RT to a single lesion had limited DLTs but no response in non-irradiated lesions in unselected patients with recurrent gynecologic malignancies. One patient with a previously irradiated lesion and another lesion irradiated on protocol experienced durable benefit in the setting of platinum resistant ovarian cancer.

Trial Registration Clinical trial information: NCT03277482



Abstract 563 Figure 1 Prolonged disease control in best responding patient. Patient 6B was initially diagnosed with FIGO Stage IIIC serous ovarian cancer in 2017 and underwent cytoreductive surgery plus neoadjuvant and adjuvant carboplatin/paclitaxel. She had no evidence of disease until 2020 when she recurred in the pelvis (lesion 1) and in a peritoneal implant on the lesser curvature of the stomach (lesion 2). She progressed in the pelvis on carboplatin and doxorubicin, then progressed again on paclitaxel. She received palliative RT of 25 Gy in 5 fractions to the large pelvic mass 3 months before trial enrollment. Lesion 1 remained stable, then she was enrolled on trial and received 25 Gy in 5 fractions to lesion 2 concurrently with durvalumab and tremelimumab. Both lesions shrank significantly and no new disease emerged.

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