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Defying platinum resistance: Boosting overall survival in platinum-resistant ovarian cancer patients

Objectives

The purpose of this study was to determine if the number of treatment regimens given to patients after the diagnosis of platinum-resistant ovarian cancer improves their overall survival.

Methods

Our single-institution ovarian cancer database was queried for patients diagnosed with ovarian cancer between the years 2010 and 2022. Of the 326 patients enrolled, 105 had confirmed platinum resistance, defined as recurrence of disease evident on CT or PET scans within 6 months of any platinum treatment. Platinum-resistant patients were divided into three groups based on the number of treatments administered after the diagnosis of platinum-resistant disease. Group 1 had no treatment lines (n=19), group 2 had 1-2 treatment lines (n=58), and group 3 had 3-10 treatment lines (n=28). The primary outcome was a difference in overall survival via the Kaplan-Meier method. The effect of the number of treatment lines on overall survival was assessed using a log-rank test followed by pairwise comparison. The group receiving no lines of treatment after platinum resistance served as the control. A <P-value of <=0.05 was considered significant.

Results

The average age at diagnosis for the cohort was 63.5 years. Most patients had stage III disease (95.24%), and 88.57% were of the serous subtype. Age distribution, disease stage at the time of diagnosis, and histologic subtype compositions were not statistically different between the three groups (P>0.05). Patients in group 2 had no significant improvement in overall survival (median OS: 11.4 months) compared to group 1 (median OS: 3.8 months). Patients in group 3 had significant improvement in overall survival (median OS: 25.7 months) compared to those in group 1 (HR: 0.36; 95% CI: 0.17-0.78; P<0.001) and those in group 2 (HR: 0.35; 95% CI: 0.22-0.55; P<0.0001).

Conclusions

Increasing the number of treatments after becoming platinum-resistant was associated with improved overall survival in this patient cohort. These findings suggest that while no specific treatment regimen has shown an increase in overall survival, patients who continue to receive additional therapies after platinum resistance have increased overall survival. These results support further research to determine optimal treatment regimens in patients with platinum-resistant ovarian cancer.

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A phase II study of weekly paclitaxel, lenvatinib and pembrolizumab among patients with recurrent endometrial, ovarian, fallopian tube, or primary peritoneal cancer

Objectives

Weekly paclitaxel/lenvatinib, paclitaxel/pembrolizumab, and lenvatinib/pembrolizumab have shown encouraging activity in recurrent ovarian (OC) and endometrial cancer (EC); however, a combination of all 3 agents has not been studied to date. The objective of this study was to estimate the efficacy of the triplet regimen and describe toxicities associated with lenvatinib, weekly paclitaxel, and pembrolizumab among patients with recurrent EC or platinum-resistant epithelial OC.

Methods

A multisite investigator-initiated study (NCT04781088; IND153033) was conducted among patients with recurrent EC or recurrent platinum-resistant/refractory OC who had received at least 1 prior line of platinum. Starting with a safety lead-in, patients were given weekly paclitaxel 60-80 mg/m2 IV day 1, 8, 15, pembrolizumab 200 mg IV day 1, and oral lenvatinib 16 mg daily on a 21-day cycle. Toxicities were recorded using CTCAE v5, and the response was determined with imaging after cycle 2, then every 3rd cycle, using RECIST 1.1 criteria.

Results

A total of 35 patients were enrolled: 24 (69%) with OC and 11 (31%) with EC. The median age was 64 (37-78); 17% identified as Asian, Black, or mixed race, and 2 as Hispanic; 21 patients had high-grade serous carcinoma, 4 endometrioid, 4 clear cell, 4 carcinosarcoma, 1 mixed, and 1 dedifferentiated carcinoma, 89% high grade, and there was a median of 2 prior lines of therapy (1-3). Nine patients were included in the safety lead-in. Two out of 4 patients on dose level (DL)-1 developed dose-limiting toxicity (proteinuria and hyponatremia) while none on DL-2, thus the recommended phase II dose was confirmed at paclitaxel 60 mg/m2; 28 patients were evaluable for response; 2 had a complete response (6%, both OC), 13 (37%) partial response, 11 (31%) stable disease, 2 (6%) progressive disease, and 7 were not evaluable or not assessed yet. The objective response rate (ORR) was 15/35 (43%), 47% in OC, and 36% in EC, and 15/28 (54%) in evaluable patients. Median progression-free survival (PFS) was 5.8 months (95% CI: 4.4-8.2). The median PFS and duration of response (DoR) in EC were 7.3 and 8.9 months, respectively, compared to 4.6 and 4.2 months in OC. Overall survival was 10.3 months (95% CI: 7.3-14.2); 10 patients remained on treatment. The most common toxicities (all grades) were anemia (81%), leukopenia (84%), lymphopenia (72%), fatigue (72%), hypertension (66%), diarrhea (63%), mucositis (63%), nausea (59%), hypothyroidism (59%), anorexia (59%), proteinuria (56%), rash (56%), and weight loss (44%). The most common grade >=3 toxicities were hypertension (28%), neutropenia (25%), anemia (19%), rash (19%), leukopenia (16%), lymphopenia (16%), fatigue (16%), diarrhea (13%), proteinuria (9%), and mucositis (6%). Eleven of 35 patients (31%) discontinued treatment for toxicity or patient preference (5) and 14 patients for progression.

Conclusions

Activity was seen in both EC and OC with an encouraging response rate (ORR: 43%) and clinical benefit rate (74%), which is favorable compared to the response seen in other studies with weekly paclitaxel combinations or lenvatinib/pembrolizumab. Survival is immature, with 10 patients still on treatment. The regimen is tolerable with manageable side effects; however, a high number of patients discontinued treatment for toxicity per protocol or patient preference. Regardless, weekly paclitaxel/lenvatinib/pembrolizumab may be a good option in both recurrent EC and OC.

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