OBJECTIVE
To explore the efficacy, safety and toxicity of **E+P** in women with advanced ovarian cancer.

METHODS

**Key Inclusion Criteria**
- Advanced epithelial ovarian cancer
- Platinum resistant with unlimited prior therapy
- Normal organ function (Child-Pugh 50)
- Measurable target lesions (RECIST 1.1) or evaluable tumor marker CA125 (OC125)

**Randomized evaluation at each cycle for CA125 and every 3 cycles by RECIST 1.1**
- Evaluation of safety parameters

**BACKGROUND**

- **EP-100 (E)** is a synthetic cytotoxic peptide conjugated to Luteinizing Hormone Releasing Hormone (LHRH) that targets cells that overexpress LHRH receptors and kills them by membrane disruption.
- Preclinical studies demonstrated synergy between E and paclitaxel (P). This randomized phase 2 trial explored the efficacy, safety and toxicity of **E+P** in women with advanced ovarian cancer.
- **Methods:** Run-in dose escalation specified at least 1 patient would be treated with A without dose level patients were randomized 1:1 to receive weekly P (80 mg/m² IV) + biweekly E (30 mg/m² IV, E+P) vs. weekly P (80 mg/m² IV). Unlimited prior regimens were allowed. Central IHC for tumoral LHRH receptors was required. The 1st endpoint was overall response rate (ORR) per RECIST 1.1. The 2nd endpoint was disease control rate (DCR = CR+PR+SD). For an improvement in ORR and DCR of at least 30% with E+P vs. P, a sample size of 20 patients/arm estimated CIs of 6.47% (P alone) vs. 27.23% (E+P). Patients progressing on P were allowed to receive E (30 mg/m² IV) plus continuation of P (80 mg/m² IV). Time to progression (TTP) was assessed. Results: The “run-in” consisted of 6 patients and established PPO dose of E=30 mg/m² IV biweekly and 80 mg/m² IV weekly. Forty patients were enrolled in the phase 2 study. The ORR 54.8% (E+P 95% CI: 16.57.3%) vs. 33.3% (P; 95% CI: 14.6-57.8%). The DCR was 70.8% (E+P vs. 95% CI: 51.6-89.3%) vs. 41.4% (P; 95% CI: 47.8-86.4%). Of the patients, 90% (E+P) and 47.6% (P) had grade 3 or 4 adverse events, primarily GI and related to underlying disease. The incidence of infusion-related reactions of all grades was greater with E+P (52%, n = 12) than with P (33.6%, n = 5). 10 patients progressed on P and received E+P 50% had >3 months of disease stabilization with TTP of 3-7 months, including 1 PR, 60% of these patients had 3 times >TTP E+P compared to their respective previous TTP after P alone (Mick et al). The additional of E did not complicate the AE profile of P and was well tolerated. Conclusions: EP-100 appears to sensitize paclitaxel-resistant ovarian tumors leading to further shrinkage of target and non-target lesions and prolongation of treatment response. A larger study comprising paclitaxel resistant patients is warranted. Clinical trial information: NCT01458486

**RESULTS**

**Target Lesion responses were observed in 7/10 of the patients receiving EP-100.**

**Target Lesion responses in the randomized groups were similar**

**Addition of EP-100 reduced target lesions in 4/7 heavily treated patients after progression on paclitaxel alone**

**EP-100 combination with paclitaxel is safe and did not exacerbate toxicity of paclitaxel with continued treatment up to 18 cycles**

**EP-100 prolonged TTP by 3 fold compared to paclitaxel alone**

**EP-100 reversed target lesion progression when added to paclitaxel**

**SUMMARY**

- **EP-100 and paclitaxel** are well tolerated and safe
- **EP-100 appears to sensitize paclitaxel-resistant ovarian cancer tumors leading to shrinkage of target and non-target lesions and to prolongation of treatment response**
- **A proposed study based on encouraging results and phase 3 findings**

**CONCLUSIONS**

- **Addition of EP-100 to paclitaxel does not exacerbate toxicity of paclitaxel**
- **EP-100** is a promising option for patients with recurrent LHRH receptor expressing ovarian cancer.