A Phase 2, Single-Arm, Open-Label Study to Evaluate the Safety and Efficacy of Niraparib Combined with Bevacizumab as Maintenance Treatment in Patients with Advanced Ovarian Cancer, Fallopian Tube Cancer, or Primary Peritoneal Cancer Following Frontline Platinum-Based Chemotherapy with Bevacizumab (OVARIO)

**Background**

- Mutations in homologous recombination-related genes lead to homologous recombination deficiency (HRD). In the absence of genetic defects, hypoxia can induce transcriptional downregulation of homologous recombination-related genes, including RAD51 and BRCA2, creating a functional HRD state.

- Ovarian cancer cells are particularly sensitive to PARP inhibitors and druggable with PARP antagonists.

- The ENGOT-OV10/Avastin (NCT02245945) study showed that platinum-based treatment was significantly improved in PARP inhibitors versus placebo in BRCA-mutant patients.

- Currently, the combination of niraparib and bevacizumab is being explored in patients with recurrent platinum-sensitive ovarian cancer as part of an ongoing phase 1 study (AVANOVA, NCT02245945). Protocols in combination with niraparib is a critically unmet and a predictable and manageable toxicity profile.

- Patients who meet the criteria for the phase 1 portion of AVANOVA had 95% and the overall response rate was 58%, including 12% of CRs and PRs.

**Methods**

- Primary endpoint: progression-free survival (PFS) in patients with advanced ovarian cancer who have received prior platinum-based chemotherapy with bevacizumab and have recovered from primary debulking surgery.

- Secondary endpoints: overall survival (OS), clinical benefit rate, proportion of patients with CA-125 of ≤15 mm Hg, and other biomarkers.

**Endpoints**

- **PFS**
  - Niraparib: n=35; PFS=20.9 months
  - Placebo: n=56; PFS=3.8 months

- **OS**
  - Median OS was 27.0 months in the niraparib group and 16.0 months in the placebo group.

**Safety**

- Grade 3/4 adverse events were reported in 74% of patients treated with niraparib and 61% of patients treated with placebo.

- The most common adverse events were thrombocytopenia, hypertension, nausea, and proteinuria, which were reported in 80%, 36%, 25%, and 17% of patients, respectively.

- The most common treatment-related adverse events were thrombocytopenia, hypertension, and proteinuria.

**Conclusion**

- Niraparib combined with bevacizumab significantly extended PFS in patients with recurrent platinum-resistant ovarian cancer, with a median PFS of 20.9 months compared to 3.8 months with placebo.

- The combination was well-tolerated, with the most common adverse events being thrombocytopenia, hypertension, and proteinuria.

- Niraparib and bevacizumab should be considered as a promising combination for patients with recurrent platinum-resistant ovarian cancer.