**INTRODUCTION**

In high-grade ovarian cancer, including fallopian tube and primary peritoneal cancers, approximately 18% of patients have tumors with a germline BRCA1 or BRCA2 mutation and approximately 7% of patients have tumors with a somatic BRCA1 or BRCA2 mutation. The poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib has demonstrated efficacy in tumors with homologous recombination deficiency (HRD), including a BRCA1 or BRCA2 mutation. In cells with HRD, PARP inhibition results in accumulation of double-strand DNA breaks that cannot be repaired, leading to cell death. Based on data from 2 single-arm clinical trials, rucaparib has received accelerated approval in the United States as monotherapy for the treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with ≥2 chemotherapies. Although PARP inhibitors have demonstrated clinical activity in high-grade ovarian cancer in both treatment and maintenance settings, data comparing PARP inhibitors to standard of care (SOC) treatment for relapsed ovarian cancer are limited. Randomized studies in patients with BRCA1- or BRCA2-mutated, relapsed, high-grade ovarian cancer are needed to assess the benefit-risk profile of PARP inhibitors vs current SOC for this patient population, particularly in the third-line or later treatment setting.

**ARIEL4 TRIAL OVERVIEW**

ARIEL4 (CO-338-043; NCT02859444) is an international, multicenter, randomized phase 3 study evaluating rucaparib 600 mg twice daily vs SOC chemotherapy as treatment for patients with germline or somatic BRCA1- or BRCA2-mutated, relapsed, high-grade ovarian cancer (platinum sensitive or resistant) who have received ≥2 prior chemotherapy regimens (Figure 1).

**PATIENT ELIGIBILITY**

### Key inclusion criteria

- ≥18 years of age
- Histologically or cytologically confirmed high-grade serous or grade 2 or grade 3 endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Received ≥2 prior chemotherapy regimens and currently has relapsed or progressive disease as confirmed by radiologic assessment
- Had treatment-free interval of ≥26 months following the first chemotherapy regimen received
- Evaluable disease, ie, ≥1 target or non-target lesion that can be assessed for RECIST
- Deleterious BRCA1 or BRCA2 mutation by local testing or central laboratory HRD test
- Adequate screening and/or archival (formalin-fixed, paraffin-embedded) tissue available for analysis
- Adequate organ function

### Key exclusion criteria

- Prior PARP inhibitor treatment or treatment with single-agent paclitaxel for platinum-resistant disease
- Prior known hypersensitivity to paclitaxel (patients with PFI <12 months)
- Platinum-refractory disease (ie, disease progression during or within 4 weeks of completion of most recent platinum-based therapy)
- Symptomatic and/or untreated CNS metastases
- Active secondary malignancy for which patient may be (but not necessarily) currently receiving treatment
- Ongoing grade ≥2 adverse event, with exception of peripheral neuropathy, which may be permitted with prior advanced approval

**STUDY ENDPOINTS**

- **Primary Endpoint**
  - Investigator-assessed progression-free survival by Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST)

- **Secondary Endpoints**
  - Overall survival
  - Objective response rate by RECIST and by RECIST/cancer antigen 125 (CA-125) criteria
  - Duration of response
  - Patient-reported outcomes by European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire (QLQ-C30) and the ovarian cancer module (QLQ-0V28)
  - Safety and tolerability of rucaparib vs SOC chemotherapy

**TRIAL SUMMARY**

- Rucaparib has demonstrated efficacy in the treatment setting in patients with ovarian cancer and a deleterious BRCA1 or BRCA2 mutation.
- The ARIEL4 phase 3 study aims to assess the benefit-risk profile of rucaparib vs current SOC chemotherapy as treatment for patients with BRCA1- or BRCA2-mutated, relapsed, high-grade ovarian cancer.
- ARIEL4 is actively recruiting patients, with a goal of enrolling 345 patients from >100 sites worldwide (Figure 2).

**REFERENCES**