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Integrated efficacy and safety analysis of the poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib in patients (pts) with high-grade ovarian carcinoma (HGOC)

Background: In the phase 2 studies ARIEL2 (NCT01891344) and Study 10 (NCT01482715), rucaparib has shown promising clinical activity in pts with HGOC (Shapira-Frommer R et al. *Eur J Cancer* 2015;51:S545;abs. 2746; Coleman R et al. *J Clin Oncol* 2016;34;suppl;abs. 5540). Data from these studies were pooled to evaluate the efficacy of rucaparib in pts with *BRCA* mutated (*BRCA*^{mut}) HGOC. Safety was assessed in pts with HGOC (*BRCA*^{mut} and *BRCA* wild-type [*BRCA*^{wt}] combined).

Materials and Methods: Pts (n=106) with *BRCA*^{mut} (88 germline; 13 somatic; 5 origin uncertain), relapsed HGOC who received ≥2 prior chemotherapies and enrolled in ARIEL2 Part 1 or 2 (n=64) or Study 10 Part 2a (n=42) by 1 Oct 2015 were included in the integrated efficacy analysis. The data cutoff dates were 30 Nov 2015 (Study 10) and 29 Feb 2016 (ARIEL2). The integrated safety analysis included 377 pts with HGOC who received ≥1 prior chemotherapy (data cutoff dates, 31 Mar 2016

and 29 Apr 2016 for Study 10 and ARIEL2, respectively). All pts received a starting dose of oral rucaparib (600 mg BID) in continuous 21- or 28-day cycles until disease progression or other reason for discontinuation.

Results: In the primary efficacy analysis population (n=106), median age was 59 (range, 33–84) years. Pts received a median of 3 (range, 2–6) prior chemotherapies. The investigator-assessed confirmed objective response rate (ORR) was 53.8% (95% confidence interval [CI], 43.8–63.5); 8.5% of pts had a complete response, and 45.3% had a partial response. ORR in pts with a germline or somatic *BRCA*^{mut} tumor was 53.4% (95% CI, 42.5–64.1) and 46.2% (95% CI, 19.2–74.9), respectively. ORR was 80.0% (95% CI, 28.4–99.5) in pts with a tumor *BRCA* mutation of uncertain origin. ORR in pts with platinum-sensitive (n=79), platinum-resistant (n=20), or platinum-refractory (n=7) disease was 65.8% (95% CI, 54.3–76.1), 25.0% (95% CI, 8.7–49.1) and 0% (95% CI, 0–41.0), respectively. Median duration of response was 9.2 months (95% CI, 6.6–11.7). In the safety population (n=377), the median duration of treatment was 5.5 (range, 0.1–28.0) months. Common treatment-emergent adverse events included nausea (76.9%; grade ≥3, 5.0%), asthenia/fatigue (76.7%; grade ≥3, 10.9%), vomiting (46.2%; grade ≥3, 4.0%), and anemia (41.4%; grade ≥3, 24.1%). Grade 3–4 laboratory abnormalities included decreased hemoglobin (23.3%), increased ALT (12.5%), decreased lymphocytes (9.8%), decreased platelets (6.9%), decreased neutrophils (6.1%), and increased AST (4.5%). Increases in ALT or AST normalized over time with continued rucaparib treatment.

Conclusions: Rucaparib has clinical activity in HGOC tumors with a germline or somatic *BRCA* mutation and an acceptable safety profile in pts with HGOC. The efficacy of rucaparib will be compared to standard chemotherapy in a phase 3 study (ARIEL4; NCT02855944).