Virginia Spadoni, PharmD, BCOP
Senior Director, Global Medical Communications
and Information
gspadoni@clovisoncology.com
415-409-5440

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NCCN Guidelines Panel: Ovarian Cancer

On behalf of Clovis Oncology, Inc., I respectfully request that the NCCN Ovarian Cancer Guidelines Panel review the enclosed data and consider the inclusion of rucaparib in the NCCN Guidelines for Oncology Ovarian Cancer as an option for the use in patients with platinum-sensitive relapsed ovarian cancer in the maintenance therapy setting.

Specific Changes: We recommend the inclusion of rucaparib for the maintenance therapy of patients with epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to the immediate prior platinum-based chemotherapy.

FDA Approval: Rucaparib (Rubraca®) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated as monotherapy for the treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for Rubraca®.[1]

This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[1]

Rationale: ARIEL3 is a phase III, randomized multicenter trial which evaluated the efficacy and safety of rucaparib monotherapy vs. placebo in 564 patients with response to second-line or later platinum-based chemotherapy with high-grade, recurrent, platinum-sensitive ovarian cancer (including epithelial ovarian, fallopian tube or primary peritoneal cancer). Patients were randomized to rucaparib (n=375) or placebo (n=189). The primary endpoint of progression-free survival (PFS) by investigator review achieved statistical significance over the placebo arm. The median progression-free survival in patients with a *BRCA*-mutant carcinoma was 16·6 months in the rucaparib group versus 5·4 months in the placebo group (hazard ratio 0·23 [95% CI 0·16–0·34]; p<0·0001). In patients with a homologous recombination deficient carcinoma (236 *vs* 118), it was 13·6 months versus 5·4 months (hazard ratio 0·32 [95% CI 0·24–0·42]; p<0·0001). In the intention-to-treat population, it was 10·8 months versus 5·4 months (hazard ratio 0·36 [95% CI 0·30–0·45]; p<0·0001).[2]

The most common (≥5%) grade 3 or greater treatment-emergent adverse events (TEAEs) among all patients treated with rucaparib in the ARIEL3 study were anemia/decreased hemoglobin (19%), alanine aminotransferase (ALT)/aspartate aminotransferase (AST) increase (10%), asthenia/fatigue (7%), neutropenia/decreased neutrophil count (7%), and thrombocytopenia/decreased platelet count (5%). The discontinuation rate due to TEAEs (excluding disease progression) was 13% for rucaparib arm and 2% for the placebo arm.[2]

The following articles and presentations are submitted in support of this proposed change. We would like to acknowledge the contributions of the NCCN panel members who are also co-authors or co-contributors to many of these publications.

1. Rubraca®. Prescribing Information, February 2017. http://clovisoncology.com/files/rubraca-prescribing-info.pdf
2. Coleman RL, Oza AM, Lorusso D, *et al*. (2017). Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): a ransomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. Advanced online publication. http://dx.doi.org/10.1016/S0140-6736(17)32440-6 .

Sincerely,

Virginia Spadoni, PharmD, BCOP
Senior Director, Global Medical Communications and Information