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12 December 2022

IMPORTANT PRESCRIBING INFORMATION

Subject: Rubraca (rucaparib) Important Prescribing Information for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy and who do not have a tumor *BRCA* (t*BRCA*) mutation

Dear Healthcare Professional,

This letter is to inform you that, at the request of the United States (US) Food and Drug Administration (FDA), Clovis Oncology, Inc. (Clovis) will restrict the indication of Rubraca® (rucaparib) for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy received in the second or later line setting **to patients with a t*BRCA* mutation only**. Clovis is in discussion with the FDA regarding an update to the USPI for Rubraca.

Background and Data Summary

The Phase 3 ARIEL3 study evaluated the efficacy and safety of rucaparib versus placebo as maintenance treatment for patients with platinum-sensitive recurrent ovarian cancer (inclusive of fallopian tube and primary peritoneal cancer). The primary endpoint of progression-free survival (PFS) demonstrating the benefit of rucaparib treatment was met in all 3 nested analysis populations (t*BRCA*, HRD, and ITT).

- The t*BRCA* population included all patients with a deleterious *BRCA* mutation in tumor.
- The homologous recombination deficiency (HRD) population included the t*BRCA* group as well as those without a deleterious *BRCA* mutation, but with high genomic loss of heterozygosity (LOH) in tumor.
- The ITT population included all randomized patients.

Results of the final overall survival (OS) analysis in ARIEL3 (visit cutoff date of 04-Apr-2022) are included below:

- In the t*BRCA* population (n=196), the median OS was 45.9 months for patients treated with rucaparib compared to 47.8 months for patients treated with placebo (HR = 0.83 [95% CI 0.58, 1.19]).
- In the HRD population (n=354), the median OS was 40.5 months for patients treated with rucaparib compared to 47.8 months for patients treated with placebo (HR = 1.01 [95% CI 0.77, 1.32]).
- In the ITT population (n=564), the median OS was 36.0 months for patients treated with rucaparib compared to 43.2 months for patients treated with placebo (HR = 1.00 [95% CI 0.81, 1.22]).

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Additional OS analyses were performed in the non-nested, non-t*BRCA* subgroups. These results are included below:

- In the non-t*BRCA* LOH+ subgroup (n=158), the median OS was 36.8 months for patients treated with rucaparib compared to 44.7 months for patients treated with placebo (HR = 1.28 [95% CI 0.84, 1.95]).
- In the non-t*BRCA* LOH- subgroup (n=161), the median OS was 28.6 months for patients treated with rucaparib compared to 32.6 months for patients treated with placebo (HR = 1.15 [95% CI 0.78, 1.70]).
- In the non-t*BRCA* LOH unknown subgroup (n=49), the median OS was 33.9 months for patients treated with rucaparib compared to 26.7 months for patients treated with placebo (HR = 0.67 [95% CI 0.31, 1.48]).
- In the entire non-tBRCA subgroup (n=368), the median OS was 32.2 months for patients treated with rucaparib compared to 38.3 months for patients treated with placebo (HR = 1.08 [95% CI 0.84, 1.40]).

The OS Kaplan Meier (KM) curves for the non-t*BRCA* LOH+ subgroup and entire non-t*BRCA* subgroup are included below:

Figure 1: Overall Survival in the non-t*BRCA* LOH+ Subgroup

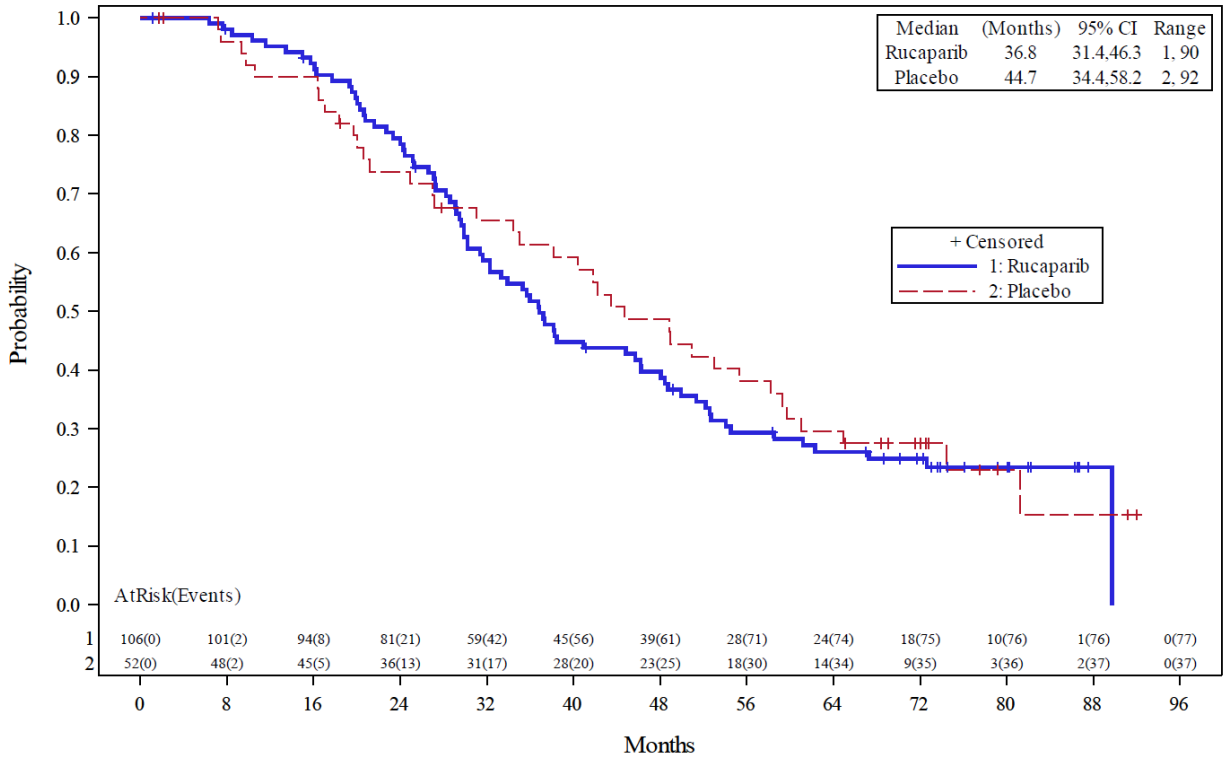

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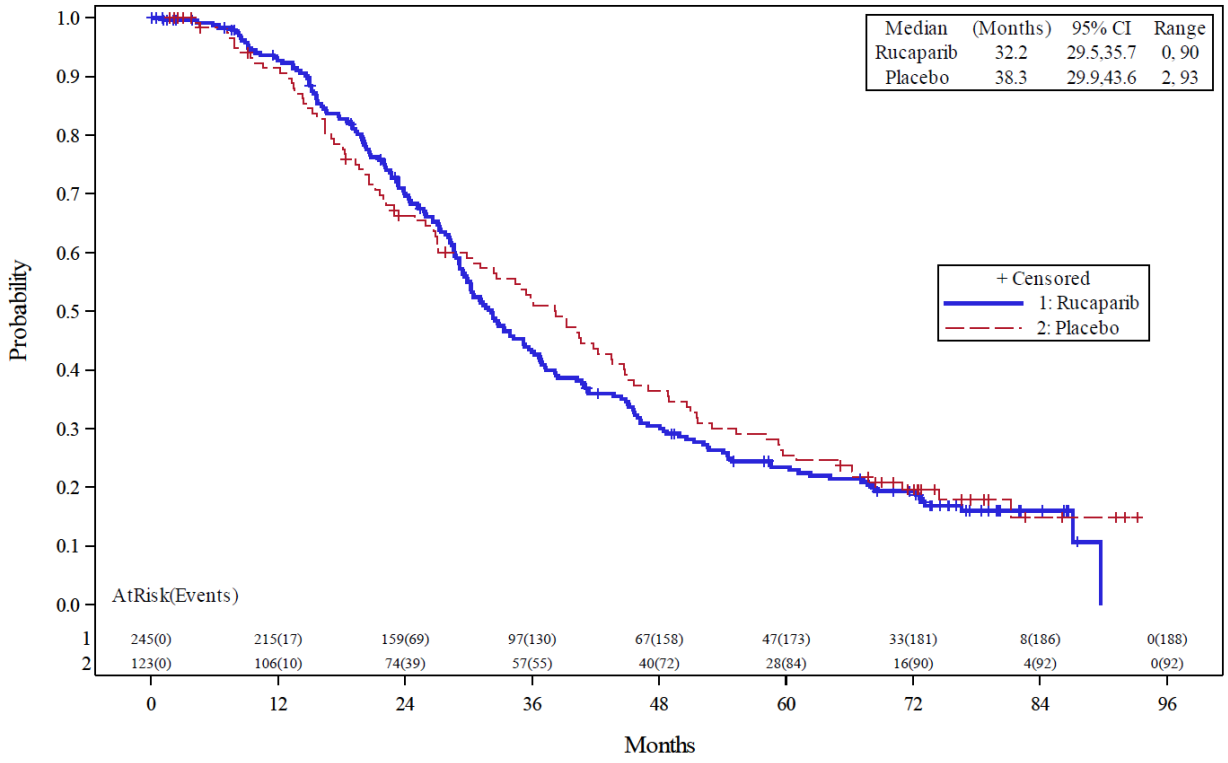
Figure 2: Overall Survival in the Entire non-t*BRCA* Subgroup



Based on the final OS data in the ARIEL3 study, Clovis in consultation with the FDA is taking action to restrict this indication to patients with a t*BRCA* mutation only. Clovis is in active discussion with the FDA about revisions to the Rubraca Prescribing Information related to the restriction of this indication (in ovarian cancer) only.

Prescriber Action

- Physicians should not initiate new treatment with Rubraca (rucaparib) for maintenance treatment of platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in the second or later line setting in patients who do not have a t*BRCA* mutation.
- Physicians with patients who do not have a t*BRCA* mutation and are currently receiving Rubraca (rucaparib) as treatment for platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in the second or later line setting should discuss this information with those patients for an individual benefit-risk assessment so that they can make an informed decision regarding their ongoing care.

Safety of Rucaparib

Safety data, other than OS, reported for Rubraca (rucaparib) in the ARIEL3 study were consistent with that reported in other clinical trials.

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This letter is not intended as a complete description of the benefits and risks related to the use of Rubraca. Please visit the **www.rubracahcp.com** website or see enclosure for full prescribing information.

Reporting Adverse Events

Health care providers and patients are encouraged to report adverse events in patients taking Rubraca (rucaparib) to Clovis Oncology at 1-415-409-7220 (US toll) or 1-844-CLVS-ONC (1-844-258-7662; US toll-free). You are also encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call 1-800-FDA-1088.

Contact for Further Information or Questions

You may contact our medical information department at 1-415-409-7220 (US toll) or 1-844-CLVS-ONC (1-844-258-7662; US toll-free) or send an e-mail to medinfo@clovisoncology.com if you have questions about the information contained in this letter and/or the safe and effective use of Rubraca (rucaparib).

Sincerely,

DocuSigned by Lindsey Rolfe

Lindsey Rolfe | I approve this document
12-Dec-2022 | 4:36:02 PM MST

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Lindsey Rolfe, MBChB
Chief Medical Officer and Executive Vice President