IMPORTANT PRESCRIBING INFORMATION

Subject: Final Data from Study CO-338-043 (ARIEL4) Show a Decrease in Overall Survival for Rubraca® (Rucaparib) Compared to Standard of Care

May 2022

Dear Healthcare Professional,

Important Information for Rubraca (rucaparib) as Treatment for BRCA-mutant Ovarian Cancer

Rubraca is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies.

This letter is to inform you that a detrimental effect in terms of overall survival (OS) has been observed for rucaparib compared to the chemotherapy-containing control arm in the randomized Study CO-338-043 (ARIEL4; NCT02855944), a Phase 3 trial requested by the Food and Drug Administration (FDA) to confirm the clinical benefit of Rubraca (rucaparib) administered as treatment for BRCA-mutated ovarian cancer. FDA and Clovis Oncology, Inc. are in active discussions about revisions to the Rubraca Prescribing Information.

Physicians should not initiate new treatment with rucaparib for adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies.

Note: this recommendation does not apply to the indication of monotherapy 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.

Background and Data Summary

The basis for approval of Rubraca (rucaparib) for the treatment of patients with BRCA-mutated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies was based on objective response rate (ORR) and duration or response (DOR) observed in two single-arm studies: CO-338-010 (Study 10; NCT01482715) and CO-338-017 (ARIEL2; NCT01891344).

ARIEL4 is a Phase 3 multicenter, randomized study evaluating rucaparib versus chemotherapy in patients with relapsed ovarian cancer and a BRCA mutation (inclusive of germline and/or somatic) who received two or more prior lines of chemotherapy. The trial enrolled a heterogenous patient population, with 51% of patients having platinum-resistant disease (progression-free interval [PFI] ≥1 to <6 months) and 49% having platinum-sensitive disease (PFI ≥ 6 months).

Patients initially randomized to chemotherapy had the option of receiving rucaparib as their next treatment within the ARIEL4 clinical trial if/when their disease progressed. At the final OS analysis, 69% of patients (n=80/116) in the control arm had received subsequent treatment with

rucaparib; in total, 90% (313/349) of patients randomized in the ARIEL4 trial had received rucaparib.

Primary Endpoint of Progression-free Survival (PFS)

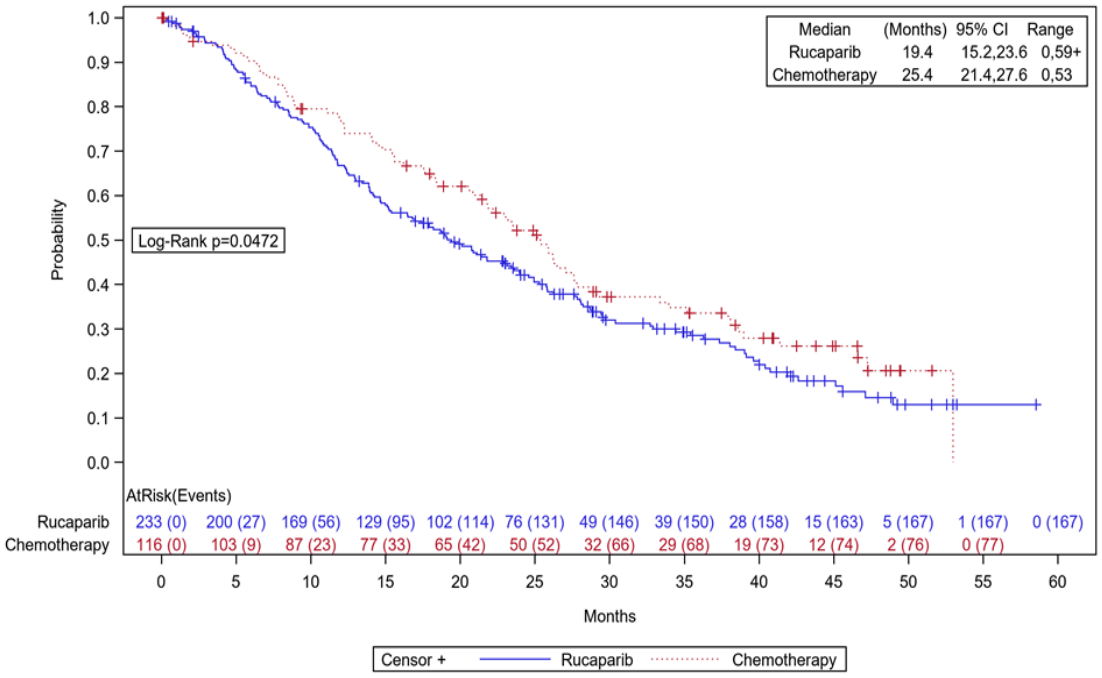
In the intent-to-treat (ITT) population in the ARIEL4 study, a difference in favor of rucaparib was observed for the primary endpoint of progression-free survival by investigator (invPFS), with a reported median invPFS of 7.4 months for the rucaparib group compared to 5.7 months for the chemotherapy group (HR=0.665; p=0.0017).

Secondary Endpoint of OS

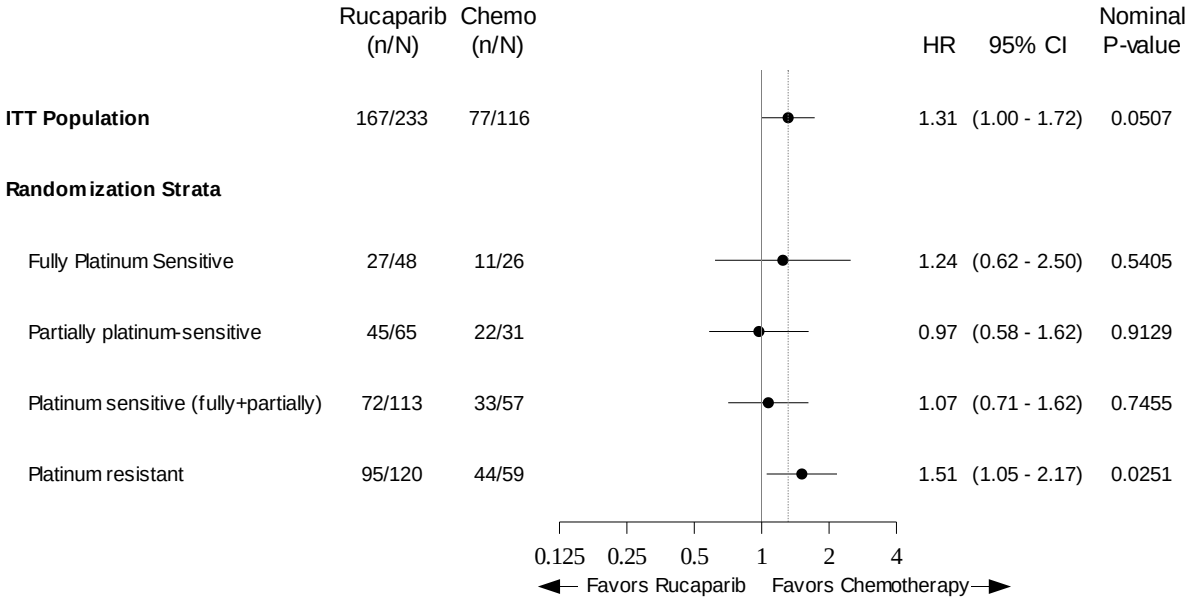
An OS detriment, for patients randomized to rucaparib, was observed at the final analysis of OS (70% of death events reported). In the ITT population, median OS was 19.4 months in the rucaparib group compared to 25.4 months in the chemotherapy group, resulting in a HR of 1.31 (95% CI: 1.00, 1.73), p= 0.0507. Patients included in the study were stratified at the time of randomization according to platinum sensitivity (platinum-sensitive vs. partially platinum-sensitive vs. platinum-resistant). The HRs for OS in those subgroups were 1.24 (95% CI: 0.62, 2.50), 0.97 (95% CI: 0.58, 1.62), and 1.51 (95% CI: 1.05, 2.17), respectively. In all platinum-sensitive patients combined, the HR was 1.07 (95% CI: 0.71, 1.62), favoring chemotherapy.

Below are the OS Kaplan-Meier (KM) curves for the ITT Population and the Forest Plot for the platinum subgroups.

OS in Intent-to-Treat (ITT) Population



OS in ITT Population and Platinum Subgroups



Safety of Rucaparib

Safety data, other than OS, reported for Rubraca (rucaparib) in the ARIEL4 study were consistent with that reported in other clinical trials.

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.

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
11-May-2022 | 1:20:10 PM MDT
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Lindsey Rolfe, MBChB

Chief Medical Officer & Executive Vice President

Clovis Oncology, Inc.