IMPORTANT PRESCRIBING INFORMATION

Subject: Rubraca® (Rucaparib) for treatment of BRCA-mutated ovarian cancer after 2 or more chemotherapies is voluntarily withdrawn in the U.S.

June 2022

Dear Health Care Provider,

This letter is to inform you about an important change to the Rubraca® (rucaparib) United States Prescribing Information (USPI) for the treatment of BRCA-mutated ovarian cancer after 2 or more chemotherapies and is an update to the Rubraca DHCP letter dated May 2022.

Indications

Clovis Oncology has voluntarily withdrawn Rubraca for the treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or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. Revisions to the Rubraca USPI resulting from this withdrawal became effective June 10, 2022.

This decision was made in consultation with the U.S. Food and Drug Administration (FDA) after a detrimental effect in terms of overall survival (OS) was 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 FDA to confirm the clinical benefit of Rubraca (rucaparib) administered as treatment for BRCA-mutated ovarian cancer.

This change does NOT impact 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.

Prescriber Action

Physicians who are treating patients with rucaparib for BRCA-mutated ovarian cancer after two or more chemotherapies should share this information with those patients so that they can make an informed decision regarding their ongoing care.

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.

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 of 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. 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.

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=0.67; 95% CI: 0.52, 0.86; p=0.0017). However, 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.

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 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.

Company Contact Point

You may contact our US Medical Information team 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 28-Jun-2022 | 11:38:10 AM MDT
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Lindsey Rolfe, MBChB

Chief Medical Officer & Executive Vice President