Direct Healthcare Professional Communication

8 August 2022

Rucaparib (Rubraca®▼): restriction of indication

Dear Healthcare Professional,

Clovis Oncology Ireland Ltd, in agreement with the European Medicines Agency (EMA) which covers Northern Ireland (NI) and the Medicines and Healthcare products Regulatory Agency (MHRA) which covers Great Britain (GB), would like to inform you of the following:

Summary

- Rubraca should no longer be used as monotherapy treatment of adult patients with platinum sensitive, relapsed or progressive, BRCA mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum based chemotherapy, and who are unable to tolerate further platinum based chemotherapy.
- A detrimental effect of rucaparib on overall survival (OS) compared with the chemotherapy control, has been observed within the final analysis of data from the phase 3 study CO-338-043 (ARIEL4) for treatment of patients with advanced, recurrent ovarian cancer (HR = 1.31 [95% CI: 1.00, 1.73]).
- Ongoing treatment in this setting should be reconsidered and patients be informed of the latest data and recommendations.
- Rubraca remains authorised as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Background information

Based on overall response rate (ORR) results from a pooled population from two phase 2 single-arm studies (CO-338-010 and CO-338-017), rucaparib received a conditional marketing authorisation (CMA) in May 2018 for the following indication: "*Monotherapy treatment of adult patients with platinum sensitive, relapsed or progressive, BRCA mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum based chemotherapy, and who are unable to tolerate further platinum based chemotherapy*".

This conditional authorisation was subject to confirmation of rucaparib efficacy and safety in study CO-338-043 (ARIEL4); a phase 3, multicentre, open-label, randomized (2:1) study of rucaparib 600 mg BID (N=233) versus chemotherapy (N=116) in patients with relapsed, BRCA-mutant, high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who received two or more prior lines of chemotherapy. The patients included in the study were stratified at the time of randomization according to platinum sensitivity (fully platinum sensitive *vs* partially platinum sensitive *vs* platinum resistant). In addition, patients initially randomized to chemotherapy had the option to cross-over to rucaparib treatment following disease progression; at the final OS analysis, 69% of patients (n=80/116) in the control arm had received subsequent treatment with rucaparib.

In the ITT population of the ARIEL4 study, a difference in favour 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 [95% CI, 0.516-0.858]; p=0.0017). However, at the final analysis of the secondary endpoint of OS, a detrimental effect was observed for patients randomized to rucaparib. Median OS was 19.4 months in the rucaparib group compared with 25.4 months in the chemotherapy group, resulting in a HR of 1.31 [95% CI: 1.00, 1.73] (p=0.0507). The HRs for OS in the subgroups of fully platinum sensitive, partially platinum sensitive and platinum resistant were 1.24 [95% CI: 0.62, 2.50] (p=0.5405), 0.97 [95% CI: 0.58, 1.62] (p=0.9129), and 1.51 [95% CI: 1.05, 2.17] (p=0.0251) respectively.

It is acknowledged that in the context of the approved treatment indication, the subgroup of platinum sensitive patients (particularly those partially sensitive) represents the most relevant population. Although no statistically significant differences were observed in OS (HR = 1.07 [95% CI: 0.71, 1.62]; p=0.5405) in this subgroup of (combined) platinum sensitive patients, results were not considered reassuring.

In view of the above data, the benefit/risk of rucaparib can no longer be considered favourable in the third line treatment indication.

Rucaparib remains authorised as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme.

Rubraca▼ is subject to additional monitoring. This will allow quick identification of new safety information. Please report ANY suspected adverse drug reactions (ADRs) to drugs and vaccines identified by the black triangle▼ to the MHRA through the Yellow Card Scheme.

It is easiest and quickest to report ADRs online via the Yellow Card website - https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name

Suspected adverse drug reactions should also be reported to Clovis Oncology by calling 0800 0093361 (toll-free) or emailing MedInfo.GB@clovisoncology.com.

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Yours sincerely,

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