Direct Healthcare Professional Communication

17/05/2022

Rucaparib (Rubraca®▼): interim data from Study CO-338-043 (ARIEL4) in the treatment indication show a decrease in overall survival compared to standard of care

Dear Healthcare Professional,

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

Summary

- A detrimental effect in terms of overall survival (OS) has been observed for rucaparib compared to the chemotherapy-containing control arm (19.6 months and 27.1 months, respectively, with a Hazard Ratio (HR) of 1.550 (95% CI: 1.085, 2.214), p=0.0161) following a planned interim analysis (IA) in the post-approval randomised controlled study CO-338-043 (ARIEL4).
- The European Medicines Agency (EMA) is performing a review of all available information to assess the impact of this information on the use of rucaparib as monotherapy for the 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.
- While the review is ongoing, physicians are recommended not to start monotherapy treatment with rucaparib in the above treatment indication.
- The recommendation above does not apply to the indication of 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.
- Safety data reported so far for rucaparib in the ARIEL4 study appear consistent with that reported in other clinical trials of rucaparib.

Background information

Rubraca received a conditional marketing authorisation (CMA) in May 2018 "*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". This indication was based on overall response rate results from a pooled population from two phase 2 single arm studies (Study CO-338-010 and Study CO-338-017).

The approval was subject to confirmation of rucaparib efficacy and safety in study CO-338-043 (ARIEL4), an ongoing phase 3, multicenter, randomised (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.

In the efficacy population in 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=0.639; p=0.0010).

However, an OS detriment was observed at the planned IA with 51% data maturity (final OS analysis planned at 70%) with a median OS of 19.6 months in the rucaparib group compared to 27.1 months in the chemotherapy group resulting in an OS HR of 1.550 (95% CI: 1.085, 2.214), p=0.0161. Patients included in the study were stratified at the time of randomisation according to platinum sensitivity (platinum sensitive vs. partially platinum sensitive vs. platinum resistant). The HRs for OS in that subgroups were 1.12 (95% CI: 0.44-2.88), 1.15 (95% CI: 0.62-2.11) and 1.72 (95% CI: 1.13-2.64), respectively. Final OS data from the ARIEL4 study are not yet available.

The safety data reported for rucaparib in the ARIEL4 study appears to be in line with the known safety profile of the product.

The label of Rubraca was extended in January 2019 to include its use "*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*". This approval was based on a PFS benefit reported in the ongoing randomized, double-blind, placebo-controlled phase 3 study CO-338-014 (ARIEL3). Final OS data from this study will be included in an ongoing review of the authorised use of Rubraca.

All available information is under assessment, including additional OS data from the ARIEL3 study. An update of the OS data from the ARIEL4 study, which will be available soon, will also be part of the assessment. The outcome of this evaluation will be communicated as soon as available.

While the review is ongoing, physicians are recommended not to initiate treatment with rucaparib in the approved third line or more treatment setting, see above.

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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