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EMA recommends restricting use of cancer medicine Rubraca

On 21 July, EMA's human medicines committee, CHMP, recommended that Rubraca (rucaparib camsylate) should no longer be used as third-line treatment for cancers of the ovary, fallopian tubes or peritoneum with a BRCA mutation in patients whose cancer has come back after at least two platinum-based chemotherapies and who cannot have further platinum-based therapy.

The recommendation followed the review of final data from the ARIEL4 study,[1] which compared Rubraca with chemotherapy in patients whose cancer had come back after at least two previous treatments and who were still eligible for further chemotherapy. The final analysis of overall survival showed that Rubraca was not as effective as chemotherapy at prolonging patients' lives: those treated with Rubraca lived for an average of 19.4 months, compared with 25.4 months for patients receiving chemotherapy.

As a result, doctors should not start third-line treatment with Rubraca in new patients. Doctors should inform patients already receiving Rubraca for this indication of the latest data and recommendations, and consider other treatment options.

This recommendation does not affect the use of Rubraca as maintenance treatment following chemotherapy.

Information for patients

- The medicine Rubraca should no longer be used to treat cancer of the ovary, fallopian tubes or peritoneum with a BRCA mutation (genetic defect) in patients whose cancer has come back after at least two platinum-based chemotherapies and who cannot have further platinum-based therapy (so-called 'third-line treatment').
- This is because a study that was designed to confirm the benefit of Rubraca failed to do so, and showed that treatment may be associated with a higher risk of death.
- Rubraca should not be started as third-line treatment. If you are taking Rubraca as third-line treatment, your doctor will consider other treatment options.
- If you have any concerns about your treatment, speak with your doctor.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=ARIEL4

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Information for healthcare professionals

- Rubraca should no longer be authorised as monotherapy for the treatment of 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.
- The recommendation followed the final analysis of data from a phase 3 study, ARIEL4, comparing Rubraca with chemotherapy in patients with relapsed, BRCA-mutated, high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer.
- A difference in favour of Rubraca was observed for the primary endpoint of progression free survival by investigator (invPFS) (7.4 months for the Rubraca group compared with 5.7 months for the chemotherapy group (hazard ratio (HR)=0.665 (95% CI: 0.516, 0.858); p=0.0017)).
- However, overall survival with Rubraca was lower than that with chemotherapy (19.4 months versus 25.4 months, respectively, with a HR of 1.31 (95% CI: 1.00, 1.73); p=0.0507).
- The CHMP therefore concluded that the benefit of Rubraca, when used in the above-mentioned indication, had not been confirmed and that treatment may be associated with an increased risk of death. Ongoing treatment in this setting should be reconsidered and patients should be informed of the latest data and recommendations.
- This recommendation does not affect the use of Rubraca as 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.

A direct healthcare professional communication (DHPC) has been sent to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC has also been published on a dedicated page on the EMA website.

More about the medicine

Rubraca is a cancer medicine that has been authorised to treat high-grade cancers of the ovary, fallopian tubes (the tubes connecting ovaries to the uterus) and the peritoneum (the membrane lining the abdomen).

It can be used as maintenance treatment in patients whose recurring cancer has cleared (partially or completely) after treatment with platinum-based cancer medicines. Rubraca is no longer recommended for use if the patient's cancer has a BRCA mutation and has returned or worsened after two treatments with platinum-based medicines and the patient can no longer have these medicines (third-line treatment).

Rubraca was granted a 'conditional approval' on 24 May 2018. At the time of its approval, data on the size of the effect of Rubraca treatment were limited. The medicine was therefore granted a marketing authorisation on condition that the company provided additional data from the ARIEL4 study to confirm the safety and effectiveness of the medicine in the third-line treatment indication.

More about the procedure

The review of Rubraca was initiated at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review was carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use.

While the review was ongoing, the CHMP issued temporary recommendations to restrict the use of Rubraca as third-line treatment in new patients as an interim measure to protect public health. The recommendation was forwarded to the European Commission (EC), which issued a temporary legally binding decision applicable in all EU Members States on 4 May 2022.

The CHMP concluded its evaluation of the final study data from ARIEL4 and issued its final recommendation on 21 July 2022. The final CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 21 September 2022.