22 April 2022
EMA/CHMP/223740/2022

CHMP List of questions

To be addressed by the marketing authorisation holder for Rubraca

Procedure under Article 20 of Regulation (EC) No 726/2004

Rubraca EMEA/H/A-20/1518/C/4272/0033

Marketing authorisation holder(s): Clovis Oncology Ireland Limited

INN/active substance: rucaparib

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The marketing authorisation holder (MAH) is requested to address the following questions:

Question 1

Please provide all available data form study CO-338-043 (ARIEL4). This should include but not be limited to:

a) Tabular summaries of baseline demographics and disease characteristics at the time of randomisation for three different subgroups of patients: patients randomised to rucaparib, patients randomised to chemotherapy who crossed over to rucaparib after progression and patients from the chemotherapy arm who did not cross over. Data for these 3 subgroups should be included in the same tables for a better comparison.
b) Complete information on patients who crossed over to the rucaparib arm. In this regard, among patients with disease progression, it should be specified which patient crossed over or not and the reasons thereof.
c) Supportive analyses adjusting for cross-over, including the analysis censoring the data at cross-over (method 1 of the guideline "Question and answer on adjustment for cross-over in estimating effects in oncology trials (EMA/845963/2018)") and at least one or two of the proposed methods for handling cross-over.
d) The final analysis for overall survival (OS) and updated Progression Free Survival - 2 (PFS2) results. This report should include OS results by platinum sensitivity randomisation status. In addition, potential cases of secondary myelodysplastic syndrome (MDS)/ acute myeloid leukaemia (AML) are expected to be presented at the time of this final analysis.
e) The reported OS detriment should be explained. To this end the MAH is asked to provide information on (the reasons for) deaths irrespective of treatment, for both the experimental and control arms and according to platinum sensitivity.
f) Safety data of intestinal obstruction adjusted by treatment exposure as well as the narratives for all patients that reported an event of intestinal obstruction during the study.

Question 2

The MAH is asked to discuss the OS findings resulting from the final OS analysis in study ARIEL-4 in the context of all available evidence for the impact on OS of the platinum chemotherapy in the control arm, compared to no treatment.

Question 3

Considering the above, the MAH should provide an updated assessment of the benefit-risk balance of Rubraca in the approved "*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*"" indication and describe the circumstances in which the use of Rubraca in the above indication could be justified.

Question 4

Please provide information on the estimated patient exposure to rucaparib in the different EEA Member States and worldwide 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 should include data from ongoing and completed clinical trials, non-interventional studies and post-marketing sources stratified by number of treatment cycles. An overview of the approved indication(s) worldwide should also be provided.