Managing Adverse Reactions

Healthcare Provider Overview and Patient Take-Home Guide

CLOVIS ONCOLOGY

Discussing adverse reactions with your patients

This resource was designed to facilitate proactive conversations about dosing and adverse reaction (AR) management with your Rubraca patients. Use this guide to help patients create a dosing schedule that will keep them adherent, to educate patients about which ARs to expect, and to provide customized recommendations for handling ARs when they occur.

There's space for your patients and/or their care partner to record your recommendations and strategies for managing certain side effects.

INDICATIONS

Rubraca is indicated:

- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy
- 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. Select patients for therapy based on an FDA-approved companion diagnostic for Rubraca

SELECT IMPORTANT SAFETY INFORMATION

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) have occurred in patients treated with Rubraca, and are potentially fatal adverse reactions. In 1146 treated patients, MDS/AML occurred in 20 patients (1.7%), including those in long term follow-up. Of these, 8 occurred during treatment or during the 28 day safety follow-up (0.7%). The duration of Rubraca treatment prior to the diagnosis of MDS/AML ranged from 1 month to approximately 53 months. The cases were typical of secondary MDS/cancer therapy-related AML; in all cases, patients had received previous platinum-containing regimens and/or other DNA damaging agents.

Do not start Rubraca until patients have recovered from hematological toxicity caused by previous chemotherapy (≤ Grade 1). Monitor complete blood counts for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities (> 4 weeks), interrupt Rubraca or reduce dose and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks or if MDS/AML is suspected, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue Rubraca.

Based on its mechanism of action and findings from animal studies, Rubraca can cause fetal harm when administered to a pregnant woman. Apprise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of Rubraca.

Most common adverse reactions in ARIEL3 (≥ 20%; Grade 1-4) were nausea (76%), fatigue/asthenia (73%), abdominal pain/distention (46%), rash (43%), dysgeusia (40%), anemia (39%), AST/ALT elevation (38%), constipation (37%), vomiting (37%), diarrhea (32%), thrombocytopenia (29%), nasopharyngitis/upper respiratory tract infection (29%), stomatitis (28%), decreased appetite (23%), and neutropenia (20%).

Please see additional Select Important Safety Information throughout this document.

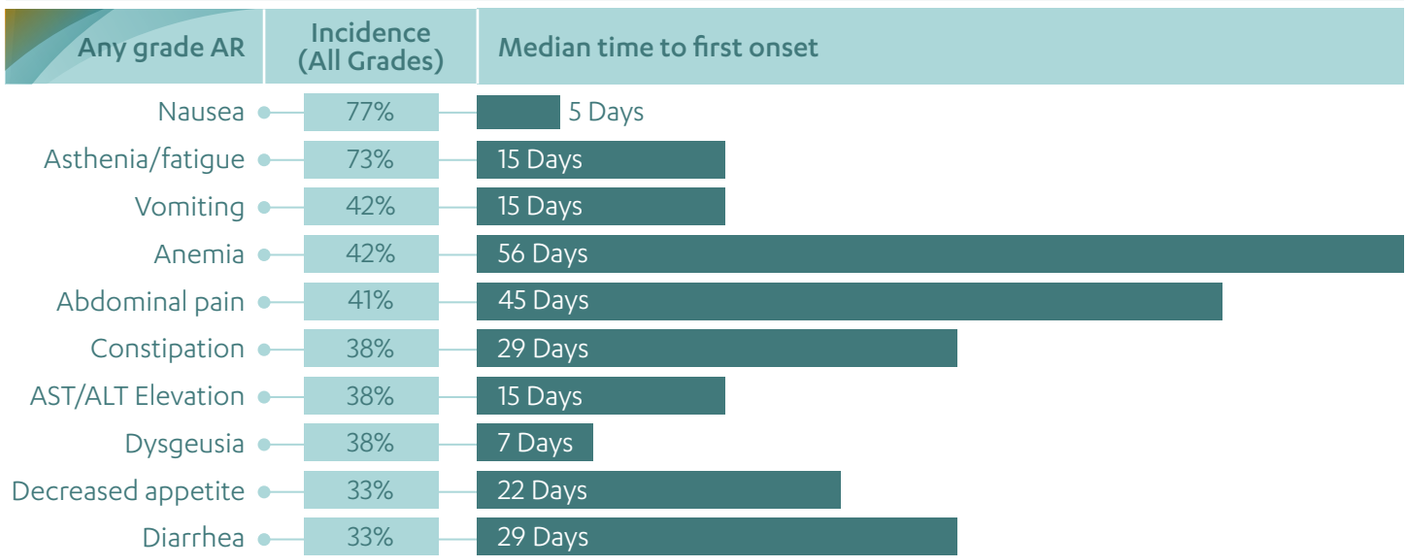
Rubraca® (rucaparib) 300 mg tablets

Manage patient expectations with proactive conversations about ARs

Across clinical trials with Rubraca,

THE MAJORITY OF ARs AND LABORATORY ABNORMALITIES WERE GRADE 1 OR 2, MANAGEABLE & TRANSIENT[1-3]

ARs occurring in greater than or equal to 20% of patients treated with Rubraca (N=937)[4]*



Other hematological ARs can occur (thrombocytopenia, 16%; low or decreased platelets, 12%; neutropenia, 10%).[3] Monitor complete blood count at baseline and monthly thereafter.

Creatinine elevations can occur (19.9%).[4] No starting dose adjustment is recommended for patients with mild and moderate renal impairment (creatinine clearance [CLcr] between 30 mL/min and 89 mL/min, as estimated by the Cockcroft-Gault method). There is no recommended starting dose for patients with CLcr <30 mL/min or patients on dialysis due to lack of data.[1]

*Integrated analysis of ARIEL3, ARIEL2, and Study 10. All patients with epithelial ovarian, fallopian tube, or primary peritoneal cancer who received ≥1 dose of rucaparib 600 mg in Study 10, ARIEL2, or ARIEL3[4]:

- Study 10: 4-part, phase 1/2 study to determine the recommended dose, efficacy, and pharmacokinetics of oral rucaparib monotherapy
- ARIEL2: 2-part, open-label, phase 2 study to identify patients with ovarian cancer who are most likely to benefit from rucaparib monotherapy
- ARIEL3: randomized, placebo-controlled, double-blind, phase 3 study to evaluate rucaparib as maintenance treatment in patients with recurrent ovarian cancer

Gastrointestinal ARs and asthenia/fatigue typically occurred within the first month of treatment[4]

SELECT IMPORTANT SAFETY INFORMATION (continued)

Most common adverse reactions in Study 10 and ARIEL2 (≥ 20%; Grade 1-4) were nausea (77%), asthenia/fatigue (77%), vomiting (46%), anemia (44%), constipation (40%), dysgeusia (39%), decreased appetite (39%), diarrhea (34%), abdominal pain (32%), dyspnea (21%), and thrombocytopenia (21%).

Please see additional Select Important Safety Information throughout this document.

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Manage ARs with appropriate care and flexible dosing

Few patients discontinued Rubraca due to treatment-related ARs[1]

In the integrated safety analysis across clinical trials, 11% of patients discontinued due to ARs (n=102/937)[4]

- 68% of patients received a dose reduction or experienced a dose interruption[4]

Rubraca allows flexible dosing to manage side effects while maintaining therapy[1]

The recommended starting dose for Rubraca is 600 mg twice daily, with or without food[1]

2 300 mg tablets (600 mg per dose) **x 2** times a day, with or without food (1200 mg daily)

Tablets not shown at actual size.

Rubraca dose can be adjusted up to 3 times[1]

1st dose reduction

500 mg twice daily
(two 250 mg tablets)

2nd dose reduction

400 mg twice daily
(two 200 mg tablets)

3rd dose reduction

300 mg twice daily
(one 300 mg tablet)

Tablets not shown at actual size.

For questions regarding anything from ARs to access, visit RubracaHCP.com or contact your Clovis Oncology representative

SELECT IMPORTANT SAFETY INFORMATION (continued)

Co-administration of rucaparib can increase the systemic exposure of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, which may increase the risk of toxicities of these drugs. Adjust dosage of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, if clinically indicated. If co-administration with warfarin (a CYP2C9 substrate) cannot be avoided, consider increasing frequency of international normalized ratio (INR) monitoring.

Because of the potential for serious adverse reactions in breast-fed children from Rubraca, advise lactating women not to breastfeed during treatment with Rubraca and for 2 weeks after the last dose.

References: 1. Rubraca [prescribing information]. Boulder, CO: Clovis Oncology; 2020. **2.** Coleman RL, Oza AM, Lorusso D, et al. Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): a phase 3, international, randomised, double-blind trial. Online supplementary appendix. *Lancet*. 2017. Accessed July 27, 2021. **3.** Data on file. Clovis Oncology; Boulder, CO. **4.** Kristeleit RS, Oza AM, Oaknin A, et al. Integrated safety analysis of the poly(ADP-ribose) polymerase inhibitor rucaparib in patients with ovarian cancer in the treatment and maintenance settings. Poster presented at: ESMO Congress; September 27–October 1, 2019; Barcelona, Spain.

Please click here for full Prescribing Information.

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