Managing Adverse Reactions

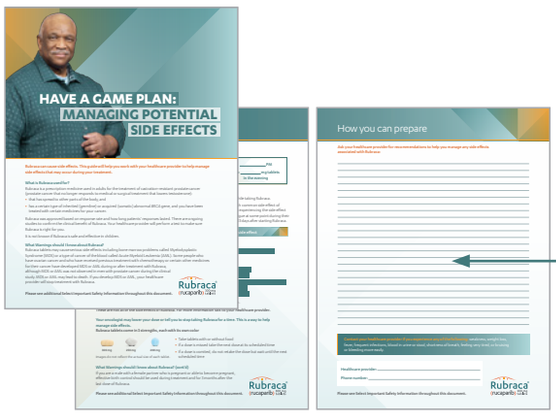
Safety profile evaluated in the TRITON2 clinical study

Healthcare Provider Overview and Patient Take-Home Guide

CLOVIS ONCOLOGY

Discussing adverse reactions with your patients

Open patient communication can help improve care and treatment outcomes[1]



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 regimen that will help them take the dose every day, to educate patients about which ARs to potentially 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.

INDICATION

Rubraca is indicated for the treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Rubraca. This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

SELECT IMPORTANT SAFETY INFORMATION

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) has 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. In TRITON2, MDS/AML was not observed in patients with mCRPC (n=209) regardless of homologous recombination deficiency (HRD) mutation.

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 findings in genetic toxicity and animal reproduction studies, advise male patients with female partners of reproductive potential or who are pregnant to use effective methods of contraception during treatment and for 3 months following last dose of Rubraca. Advise male patients not to donate sperm during therapy and for 3 months following the last dose of Rubraca.

Please see additional Select Important Safety Information throughout this document.

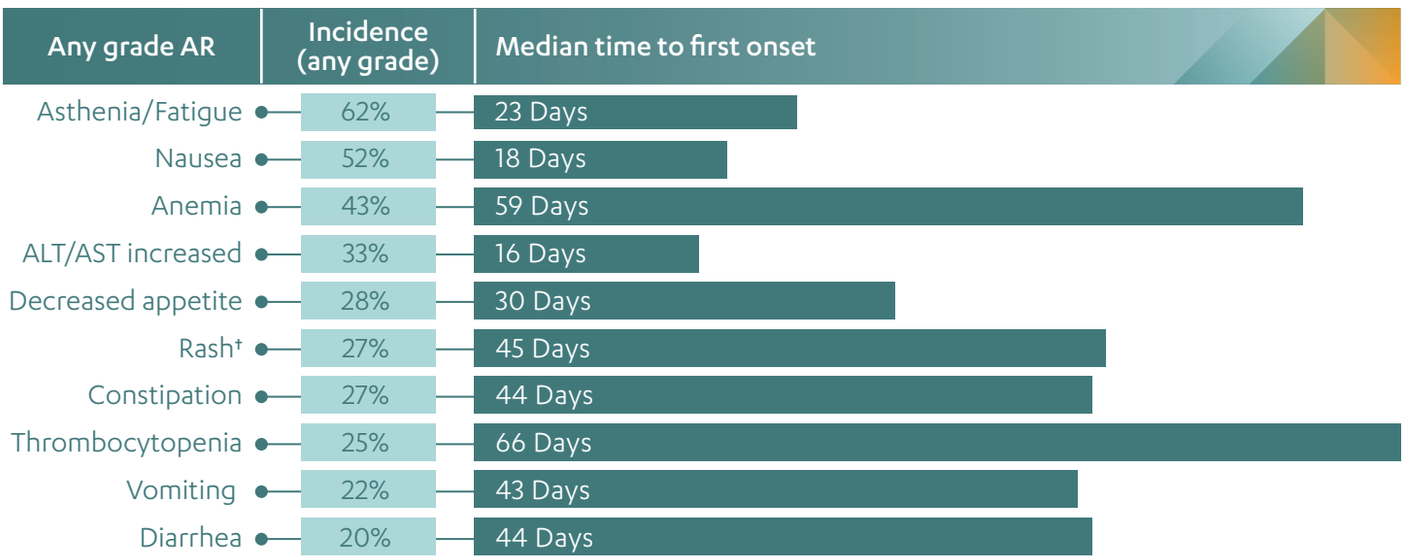
Rubraca® (rucaparib) 300 mg tablets

Manage patient expectations with proactive conversations about ARs

As seen in the TRITON2 clinical trial* with Rubraca,

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

ARs occurring in greater than or equal to 20% of patients treated with Rubraca (N=115)[2,4]



Neutropenia can also occur (7.8%).[4] Monitor complete blood count at baseline and monthly thereafter.

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 a lack of data.[2]

Increases in creatinine may be a class effect of PARP inhibitors due to inhibition of renal transporters rather than compromised renal function.[3]

Elevations in ALT or AST typically occurred within the first 4 weeks of Rubraca treatment and normalized over time with continued treatment. These elevations were not associated with abnormal increases in bilirubin or other signs of drug-induced liver toxicity.[3]

No drug-induced liver toxicity was reported with Rubraca[3]

*TRITON2: A multicenter, single-arm clinical trial in patients with *BRCA*-mutated mCRPC who had been treated with androgen receptor–directed therapy and taxane-based chemotherapy to determine the efficacy and safety of Rubraca.[2]

†Includes blister, blood blister, dermatitis, dermatitis contact, eczema, genital rash, palmar-plantar erythrodysesthesia syndrome, photosensitivity reaction, psoriasis, rash, rash maculo-papular, rash pruritic, skin exfoliation, skin lesion, and urticaria.[2]

Asthenia/fatigue typically occurred within the first month of treatment, and gastrointestinal ARs occurred within the first 2 months[4]

SELECT IMPORTANT SAFETY INFORMATION (continued)

Most common adverse reactions in TRITON2 (≥ 20%; Grade 1-4) were fatigue/asthenia (62%), nausea (52%), anemia (43%), AST/ALT elevation (33%), decreased appetite (28%), rash (27%), constipation (27%), thrombocytopenia (25%), vomiting (22%), and diarrhea (20%).

Please see additional Select Important Safety Information throughout this document.

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Manage ARs with appropriate care and flexible dosing

92% of patients were able to stay on Rubraca[3]

In the safety analysis of the TRITON2 clinical trial, 8% of patients discontinued due to ARs (N=9/115)[3]

- 63.5% of patients received a dose reduction or experienced a dose interruption[3]

Rubraca allows flexible dosing to manage side effects while maintaining therapy[2]

The recommended starting dose for Rubraca is 600 mg twice daily, with or without food[2]

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

Rubraca dose can be adjusted up to 3 times[2]

Images do not reflect the actual size of each tablet.

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)

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

[Clovis Oncology representative email]

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.

References: 1. Partridge AH, Avorn J, Wang PS, Winer EP. Adherence to therapy with oral antineoplastic agents. *J Natl Cancer Inst*. 2002;94(9):652-661. **2.** Rubraca [prescribing Information]. Boulder, CO: Clovis Oncology; 2020. **3.** Abida W, Patnaik A, Campbell D, et al; TRITON2 investigators. Rucaparib in men with metastatic castration-resistant prostate cancer harboring a *BRCA1* or *BRCA2* gene alteration. *J Clin Oncol*. 2020;38(32):3763-3772. **4.** Data on file. Clovis Oncology; Boulder, CO.

Please see additional Select Important Safety Information throughout this document.
Please click here for full Prescribing Information for Rubraca.

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