NOW APPROVED

RUBRACA: A NEXT STEP FOR PATIENTS WITH *BRCA*mut+ mCRPC

FOLLOWING AR-TARGETED THERAPY AND CHEMOTHERAPY[1]

A first-in-class, oral therapy for a genetically defined population of patients with *BRCA*mut+ mCRPC[1]

AR therapy=androgen receptor-directed therapy; *BRCA*mut+ mCRPC=breast cancer susceptibility gene-positive metastatic castration-resistant prostate cancer.

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. 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.

Please see additional Select Important Safety Information

Rubraca® 300 mg

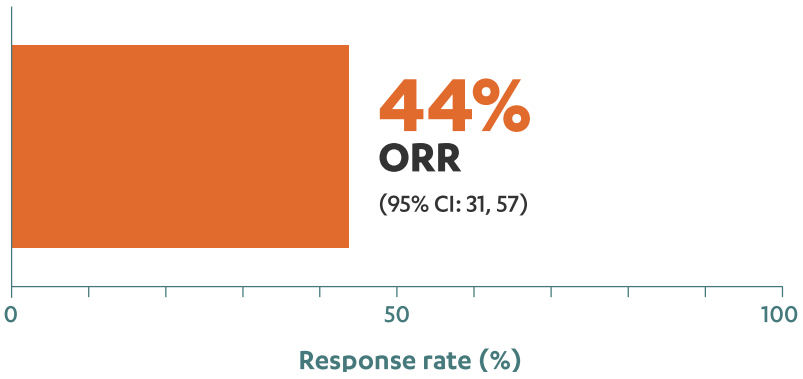
DEMONSTRATED EFFICACY WITH RUBRACA—44% OF PATIENTS HAD A RESPONSE[1]*

A prospective clinical trial of patients with *BRCA*mut+ mCRPC[1,2]

- TRITON2 (a multicenter, single-arm, phase 2 clinical trial) enrolled 209 patients with HRD+ mCRPC who had been previously treated with AR-directed therapy and taxane-based chemotherapy[1]
- Patients received Rubraca 600 mg orally, twice daily until disease progression or unacceptable toxicity, and also received concomitant GnRH analog or had prior bilateral orchiectomy[1]
- 115 patients with *BRCA*mut+ mCRPC were evaluated for safety and efficacy, of which 62 patients had measurable disease at baseline by IRR. Major efficacy outcomes were confirmed ORR by IRR using modified RECIST v1.1/PCWG3 criteria and DOR. PSA response was also evaluated[1,2]

Confirmed objective response rate (ORR): primary endpoint[1]

IRR-assessed response (N=62)



Demonstrated durability with Rubraca—some responses remained ongoing at 2 years[1]

Duration of response (DOR): secondary endpoint[1]

IRR-assessed DOR[1]

Median IRR-assessed DOR was **not evaluable** at data cut-off (95% CI: 6.4, NE)

Responses ranged from 1.7 months to ongoing at 24 months

- 15 of the 27 (56%) patients with a confirmed objective response had a DOR of ≥6 months[1]

*ORR and DOR were assessed by blinded IRR and the investigator according to modified RECIST version 1.1/PCWG3 criteria. ORR was defined per modified RECIST v1.1 criteria and with no confirmed bone progression per PCWG3.
GnRH=gonadotropin-releasing hormone agonist; HRD=homologous recombination deficiency; IRR=independent radiologic review; PSA=prostate-specific antigen; PCWG3=Prostate Cancer Working Group 3; RECIST=Response Evaluation Criteria in Solid Tumors.

SELECT IMPORTANT SAFETY INFORMATION (continued)

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.

Please see additional Select Important Safety Information

Rubraca® 300 mg

AN ORAL MONOTHERAPY YOU CAN PRESCRIBE WITH CONFIDENCE AT THE START[1]

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

Tablets not shown actual size.

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

- Select patients for treatment with Rubraca based on the presence of a deleterious *BRCA* mutation (germline and/or somatic)[1]
- Patients should also receive a GnRH analog concurrently or should have had a bilateral orchiectomy[1]
- Continue until disease progression or unacceptable toxicity[1]

Rubraca is available in 3 strengths to help provide dosing flexibility when needed[1]

Recommended dose adjustments[1]

- **First dose reduction:** 500 mg twice daily (two 250-mg tablets)
- **Second dose reduction:** 400 mg twice daily (two 200-mg tablets)
- **Third dose reduction:** 300 mg twice daily (one 300-mg tablet)

>90% of patients were able to stay on Rubraca without discontinuing therapy due to adverse reactions[1]

The discontinuation rate for Rubraca was **8%**, with none of the adverse reactions leading to discontinuation of Rubraca occurring in more than one patient.[1]*

Dose modifications (N=115)[1]

Dose modification	Rate (%)	Adverse reactions requiring dose modification in >5% of patients
Dose interruption	57	Anemia (21.7%), thrombocytopenia (13.9%), asthenia/fatigue (9.6%), nausea (7.0%), vomiting (6.1%), neutropenia (6.1%)
Dose reduction	41	Anemia (14%), asthenia/fatigue (10%), thrombocytopenia (7%), nausea (6%)

*ECG QT prolonged, acute respiratory distress syndrome, anemia, balance disorder, cardiac failure, decreased appetite/fatigue/weight decreased, leukopenia/neutropenia, ALT/AST increased, and pneumonia.
ALT=alanine aminotransferase; AST=aspartate aminotransferase; ECG=electrocardiogram; QT=an electrocardiogram representation of ventricular depolarization and repolarization.

SELECT IMPORTANT SAFETY INFORMATION (continued)

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

Rubraca® 300 mg

TAKE ACTION: TEST YOUR PATIENTS WITH mCRPC FOR *BRCA* MUTATIONS TODAY AND TREAT ELIGIBLE PATIENTS WITH RUBRACA[1]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend genetic testing for *BRCA1/2* mutations in appropriate prostate cancer patients[3]

To learn more, including how to order, visit RubracaHCP.com

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%).

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.

Please see additional Select Important Safety Information throughout this brochure and full Prescribing Information here.

References: 1. Rubraca [prescribing information]. Boulder, CO: Clovis Oncology. **2.** Data on file. Clovis Oncology; Boulder, CO. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.1.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed March 19, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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