DISCOVER THE BENEFITS OF RUBRACA

BEYOND *BRCA*

FOR YOUR **HRD+ PATIENTS** IN RESPONSE TO PLATINUM-BASED CHEMOTHERAPY

ARIEL3 is the first and largest trial[1-4]
to prospectively assess PFS as a primary endpoint in HRD+ patients with recurrent ovarian cancer.

INDICATION

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.

SELECT IMPORTANT SAFETY INFORMATION

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) occur uncommonly in patients treated with Rubraca, and are potentially fatal adverse reactions. In approximately 1100 treated patients, MDS/AML occurred in 12 patients (1.1%), including those in long term follow-up. Of these, 5 occurred during treatment or during the 28 day safety follow-up (0.5%). The duration of Rubraca treatment prior to the diagnosis of MDS/AML ranged from 1 month to approximately 28 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.

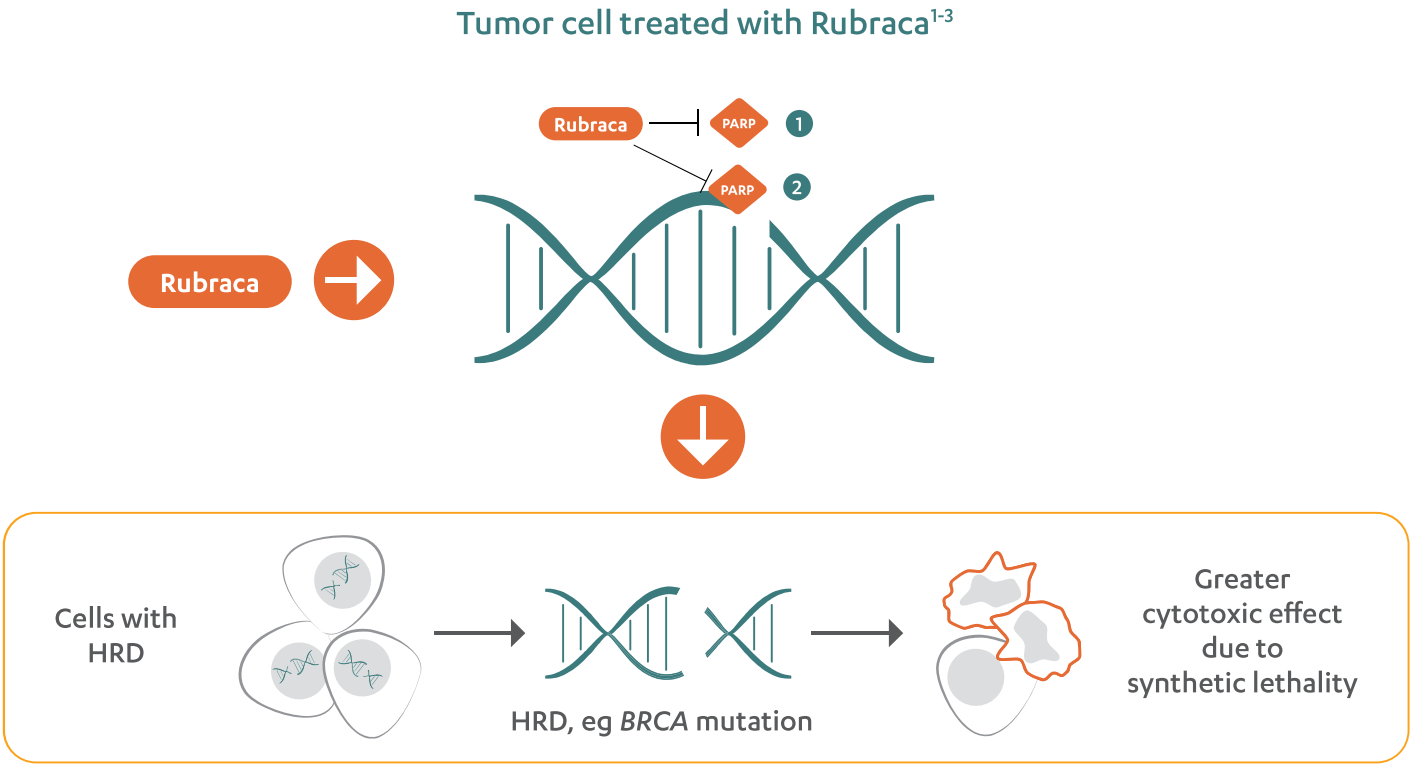
Please see additional Select Important Safety Information throughout this document.

Rubraca® (rucaparib) 300 mg tablets

Rubraca *inhibits* PARP-1, 2, and 3[1,5]

PARP-1, 2, and 3 are enzymes that play an important role in DNA repair

Rubraca mechanism of action[1,6*]



*Based on *in vitro* studies.

In normal cells, homologous recombination (HR) plays a role in repair of damaged DNA[6]:

- HR is nonfunctional in cells with HR deficiency (HRD), such as a mutation or alteration in *BRCA* or another HR gene[6]
- HRD positivity (HRD+), may potentially improve response to PARP inhibitors[7]
- Rubraca plus HRD may result in synthetic lethality[1,5]

BRCA=breast cancer susceptibility gene; HRD=homologous recombination deficiency; PARP=poly (ADP-ribose) polymerase.

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 (see Dosage and Administration (2.2) in full Prescribing Information) 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.

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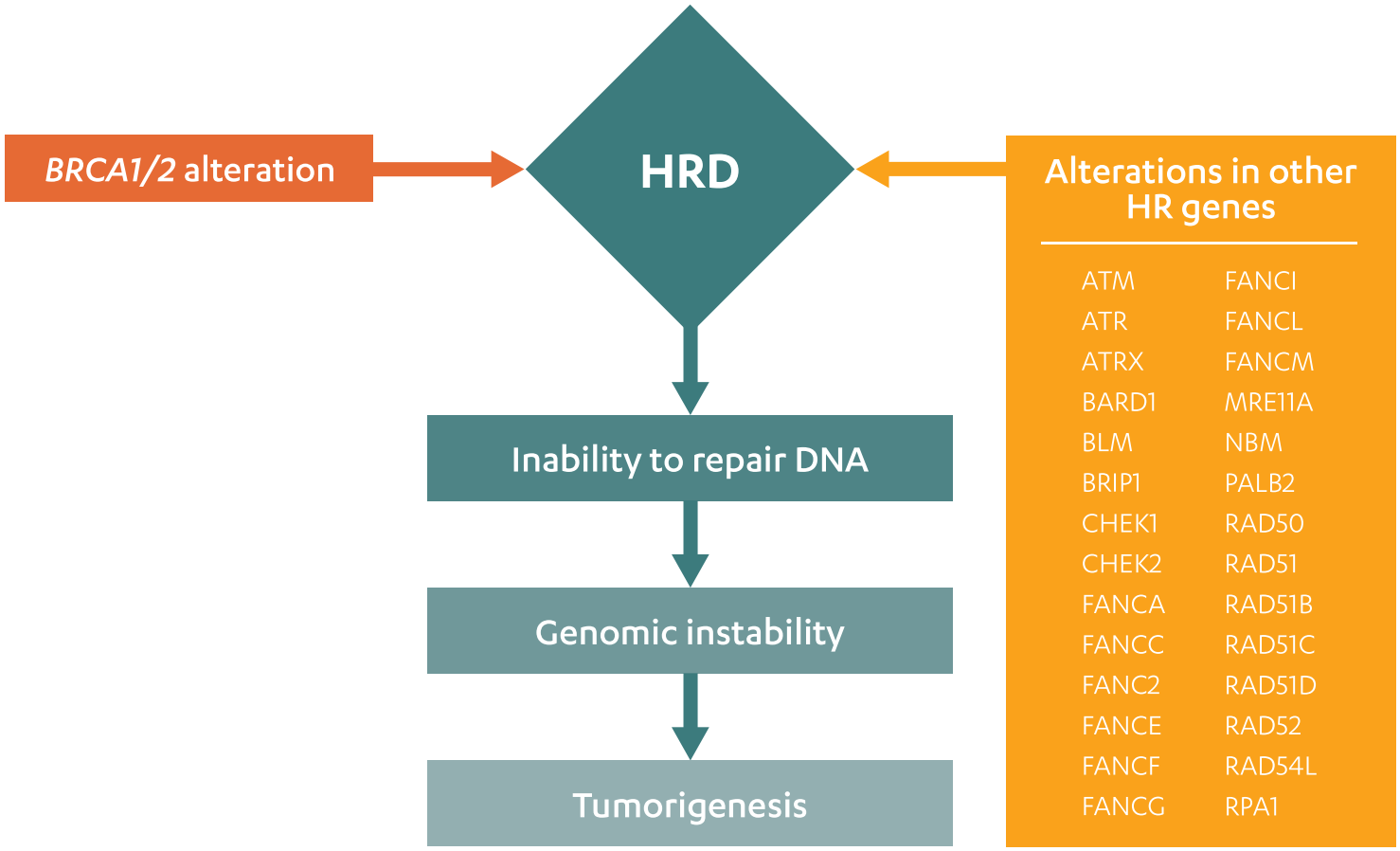
HRD causes genomic instability, a hallmark of cancer[8-10]

HR is the main DNA rescue pathway and repairs double-strand DNA breaks[8,9]

- The HR pathway includes many cellular factors, such as *BRCA1/2*
- A mutation or alteration in *BRCA* or another gene coding for an HR factor results in HR deficiency (HRD) and compromised DNA repair, accumulation of alterations, and subsequent tumorigenesis

Commonly altered biomarkers resulting in HRD[8-11]



Test for HRD for a more informed treatment plan[12]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommends consideration for testing for HRD in patients with recurrent ovarian cancer.[13]

BRCA=breast cancer susceptibility gene; HR=homologous recombination; HRD=homologous recombination deficiency; PARP=poly (ADP-ribose) polymerase.

SELECT IMPORTANT SAFETY INFORMATION (continued)

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.

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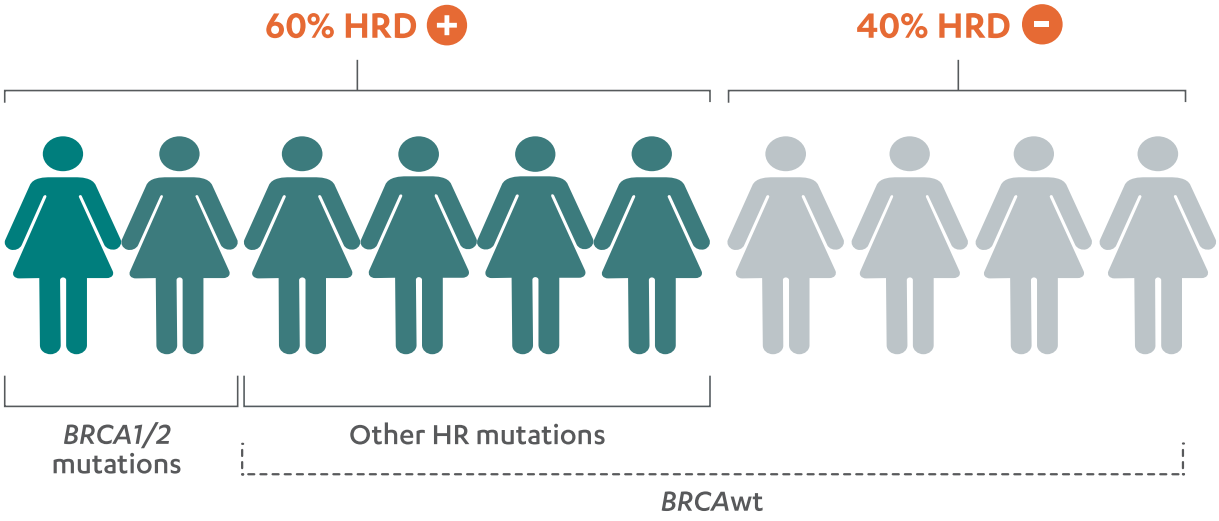
In your practice

Up to 60% of your patients with ovarian cancer may be HRD+[7,14]

Homologous recombination (HR) is an important DNA rescue pathway[8,9]

- A mutation in *BRCA* or another HR gene may result in HR deficiency (HRD) and defects in DNA repair, a hallmark of cancer
- Many of your patients with ovarian cancer may be HRD+, potentially improving their response to Rubraca

All high-grade serous ovarian cancer[7,14]*



- No added testing burden, when using a next-generation sequencing (NGS) assay that can simultaneously report *BRCA1/2* and HRD status (eg, FoundationOne CDx)[12]

*Based on 60% of estimated incidence for 2019 from the National Cancer Institute SEER Statistics.

BRCA=*BRCA*-mutation; *BRCA*wt= *BRCA* wildtype or non-mutated; HRD=homologous recombination deficiency; HRD+=homologous recombination deficiency positive; HRD-=homologous recombination deficiency negative.

SELECT IMPORTANT SAFETY INFORMATION (continued)

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%).

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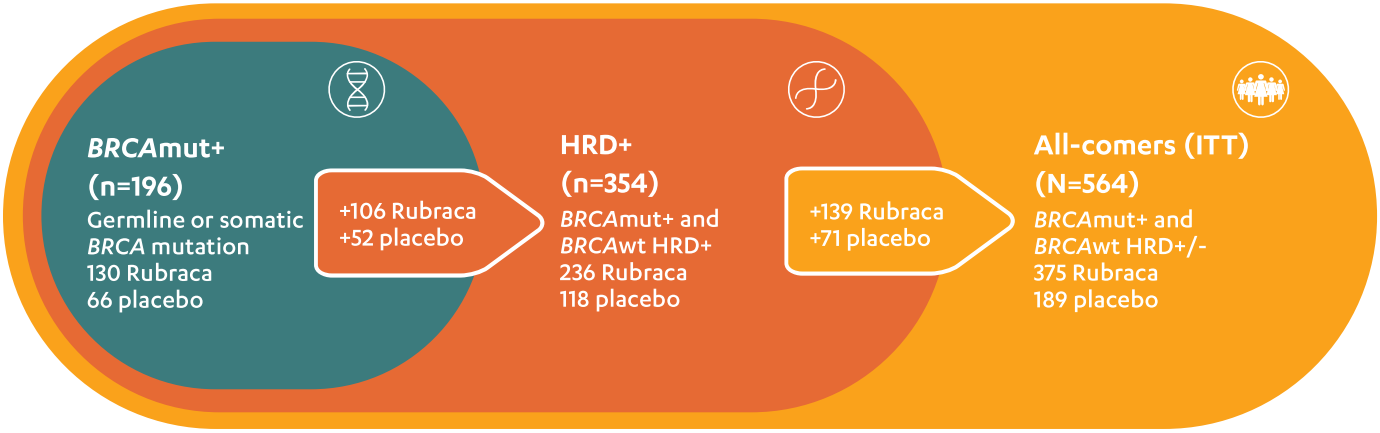
The first and largest trial to prospectively assess PFS as a primary endpoint in HRD+ patients[3,15,16]

Nearly **2 out of 3 patients** enrolled were HRD+ (n=354/564)[1,2]

Randomized, placebo-controlled, double-blind, multicenter trial



Primary endpoint[3]

- PFS by investigator assessment analyzed in 3 prospectively defined molecular subgroups in a step-down manner: 1.) *BRCA*mut+ patients, 2.) HRD+ patients, and 3.) all randomized patients

Secondary endpoint[3,11]

- PFS by independent radiology review

Predefined exploratory endpoint[3]

- Reduction in tumor burden post–platinum-based chemotherapy

ARIEL3 Study design: 2:1 randomized, placebo-controlled, double-blind, multicenter phase 3 maintenance trial of Rubraca tablets (600 mg) BID in patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer (N=564). Treatment was continued until disease progression or unacceptable toxicity. All patients had received ≥2 prior platinum-containing regimens and were in a complete or partial response to their most recent platinum-based chemotherapy.[1,3]

BID=twice a day; *BRCA*mut+=*BRCA*-mutation positive, which includes mutations in the *BRCA1* and/or *BRCA2* gene; CR=complete response.

Please see Rubraca PI for additional cohort efficacy results.

SELECT IMPORTANT SAFETY INFORMATION (continued)

Most common laboratory abnormalities in ARIEL3 (≥ 25%; Grade 1-4) were increase in creatinine (98%), decrease in hemoglobin (88%), increase in cholesterol (84%), increase in alanine aminotransferase (ALT) (73%), increase in aspartate aminotransferase (AST) (61%), decrease in platelets (44%), decrease in leukocytes (44%), decrease in neutrophils (38%), increase in alkaline phosphatase (37%), and decrease in lymphocytes (29%).

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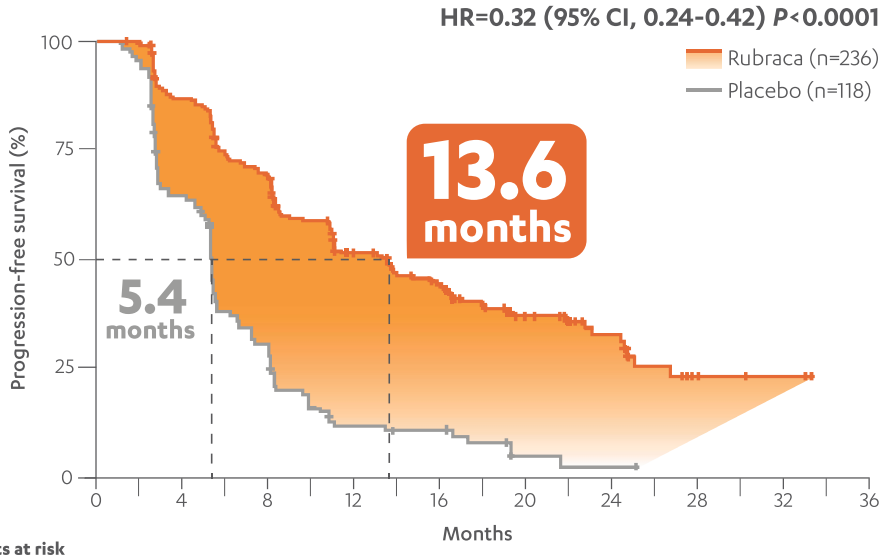
When compared to placebo

Rubraca significantly increased mPFS >2x in HRD+ patients[1]

Primary endpoint: investigator-assessed PFS (n=354)*



Estimated 24-month PFS is 16x greater with Rubraca compared to placebo[17]

Patients at risk (events)

Rubraca	236 (0)	190 (29)	149 (67)	96 (104)	70 (116)	36 (126)	21 (129)	6 (134)	3 (134)
Placebo	118 (0)	71 (40)	32 (76)	11 (95)	9 (96)	2 (100)	1 (101)	0 (101)	–

No multiplicity adjustment method for IRR PFS was specified in the study protocol.

- **68% reduction** in the risk of disease progression or death[1]
- **Estimated 24-month PFS is 33%** with Rubraca vs 2% with placebo[17]

Secondary endpoint: IRR-assessed PFS (n=354)[1,3,4,17]*

More than 4x longer mPFS with Rubraca vs placebo[17]

22.9 months

- **66% reduction** in the risk of disease progression or death[1,3]
- **Estimated 24-month** PFS is 49% with Rubraca vs 11% with placebo[17]
- **5.5 months** with placebo (n=118) HR=0.34 (95% CI, 0.24-0.47); *P*<0.0001[3,4]

*Evaluated according to RECIST v1.1.
At the time of PFS analysis, overall survival data were not mature (22% of events had occurred).
CI=confidence interval; HR=hazard ratio; IRR=independent radiology review; mPFS=median progression-free survival; RECIST v1.1=Response Evaluation Criteria in Solid Tumors. Version 1.1.

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.

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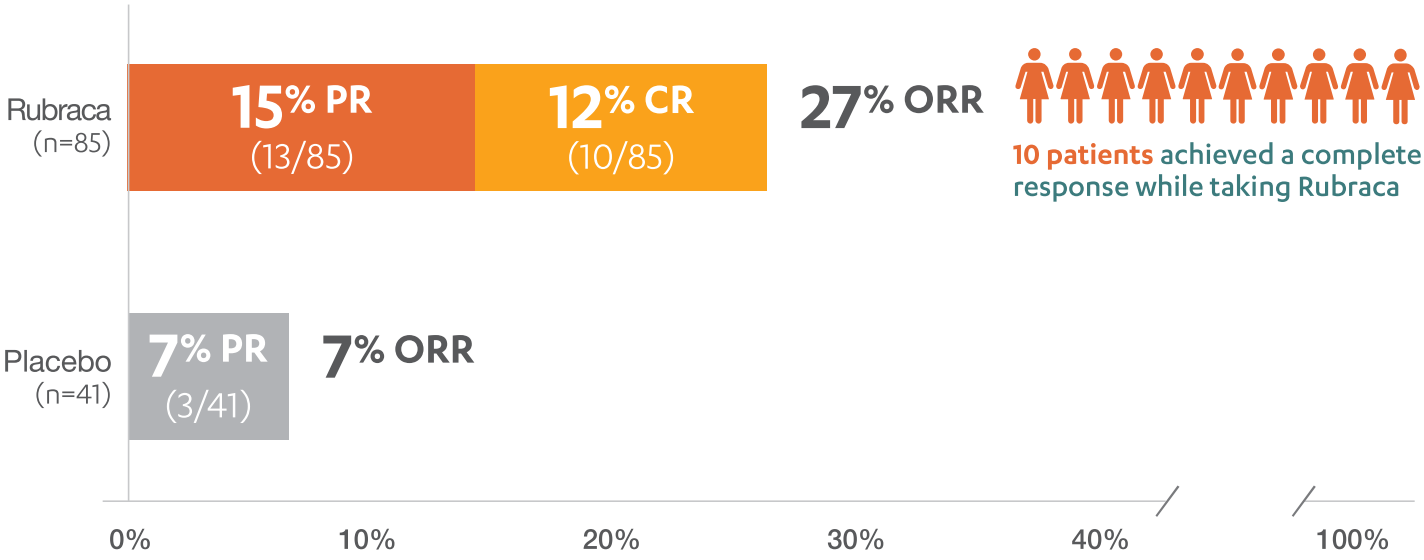
Patients with measurable residual disease showed further reduction in tumor burden with Rubraca[4,11]

Rubraca achieved nearly **4x greater ORR** among HRD+ patients with residual disease*

Confirmed response rate: measurable residual disease[4,11†]



Predefined exploratory analysis: responses observed in HRD+ patients with residual measurable disease upon entry into the ARIEL3 trial following their response to platinum-based chemotherapy (n=126).[4]

- **12%** with residual disease receiving Rubraca achieved a CR[4]
- **0%** with residual disease receiving placebo achieved a CR[4]

*This analysis is exploratory in nature and does not control for Type 1 error rate.
†Based on Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1). Complete response as defined by RECIST 1.1 was considered disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.
CR=complete response; ORR=objective response rate; PR=partial response.

SELECT IMPORTANT SAFETY INFORMATION (continued)

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.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Clovis Oncology, Inc. at 1-844-258-7662.

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PRESCRIBE RUBRACA BEYOND *BRCA*

TO HELP DELIVER PROVEN EFFICACY TO YOUR HRD+ PATIENTS

Up to 60% of your patients
with ovarian cancer may be HRD+[7,14]

ARIEL3 is the first and largest trial
to prospectively assess PFS as a primary endpoint in HRD+ patients[3,15,16]

Rubraca provided more than 4x longer mPFS
for HRD+ patients vs placebo (22.9 vs 5.5 months)[1,3,4,17]

Rubraca achieved nearly 4x greater ORR
among HRD+ patients with residual disease vs placebo[4,11]

References: 1. Rubraca [prescribing information]. Boulder, CO; Clovis Oncology. **2.** Mirza MR, et al. *N Engl J Med*. 2016;375 (22);2154-2164. **3.** Coleman RL, et al. *Lancet*. 2017;390(10106):1949-1961. **4.** Data on file, ARIEL3. Clovis Oncology; Boulder, CO. **5.** Rimar KJ, et al. *Cancer*. 2017;123(11):1912-1924. **6.** Iglehart JD, et al. *N Engl J Med*. 2009;361(2):189-191. **7.** Mukhopadhyay A, et al. *Clin Cancer Res*. 2010;16(8):2344-2351. **8.** Chartron E, et al. *Crit Rev Oncol Hematol*. 2019;133:58-73. **9.** Konstantinopolous PA, et al. *Cancer Discov*. 2015;5(11):1137-1154. **10.** TCGA. *Nature*. 2011; 474(7353):609-615. **11.** Coleman RL, et al. Online supplementary appendix. *Lancet*. 2017. **12.** FDA/ https://www.fda.gov/medical-devices/recently-approved-devices/foundationone-cdx-p170019. **13.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer V.2.2019. National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed March 8, 2019. To view the most recent and complete version of the guidelines, 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. **14.** Mukhopadhyay A, et al. *Cancer Res*. 2012; 72(22):5675–5682. **15.** Lynparza [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP. **16.** Zejula [prescribing information]. Waltham, MA: TESARO, Inc. **17.** Data on file. Clovis Oncology; Boulder, CO.

INDICATION

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CLOVIS ONCOLOGY

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