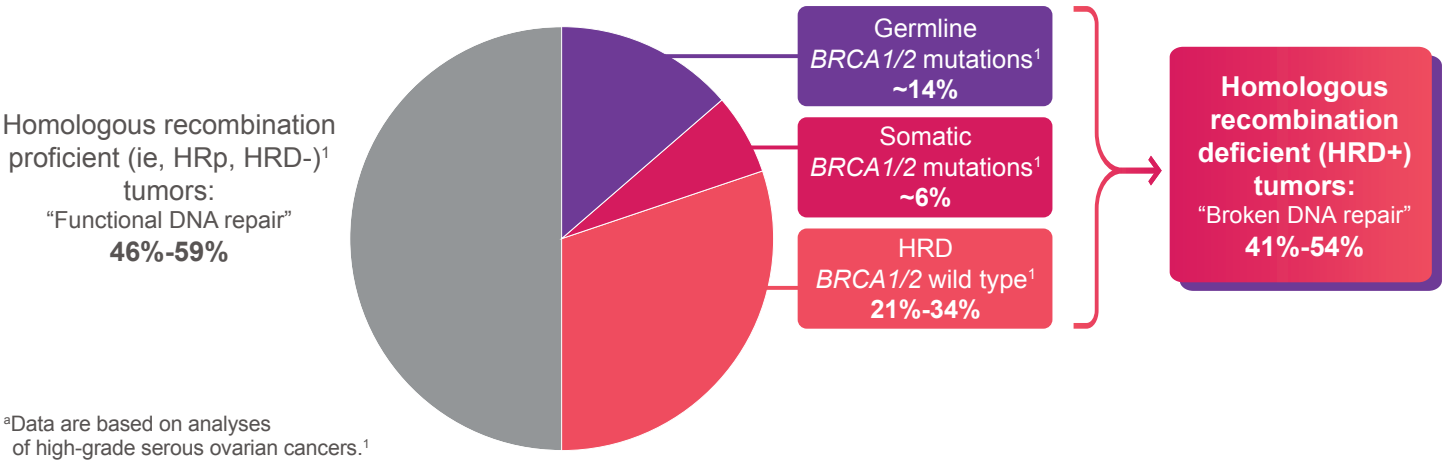
BRCA and HRD are biomarkers of DNA repair function, which correlate with the degree of PARP inhibitor sensitivity[1]

Up to half of advanced ovarian cancer tumors are associated with homologous recombination deficiency (HRD)[1,a]

Biomarker status of high-grade serous ovarian tumors



[a]Data are based on analyses of high-grade serous ovarian cancers.[1]

The HRD biomarker is inclusive of *BRCA* status but also includes multiple other genes[1]

- Mutations in several genes have been shown to be indicative of HRD+ status; these genes include, but are not limited to[1]:

BRCA1 | ***BRCA2*** | ***RAD51*** | ***CDK12*** | ***PALB2*** | ***FANCA***

- In addition to detecting mutations in homologous recombination genes using next-generation sequencing, other methods of evaluating HRD status exist, including the genomic instability score (GIS)[1-4]

GIS is determined by assessing[1,2,4]:

- **Loss of heterozygosity (LOH)[b]**
- **Telomeric allelic imbalance (TAI)**
- **Large-scale state transitions (LST)**

[b]LOH status on its own has also been used as a biomarker for HRD status.[4]

A GIS above the threshold designates a positive HRD status.[4]
Studies in advanced ovarian cancer have reported thresholds of ≥33 and ≥42.[2,4-7]

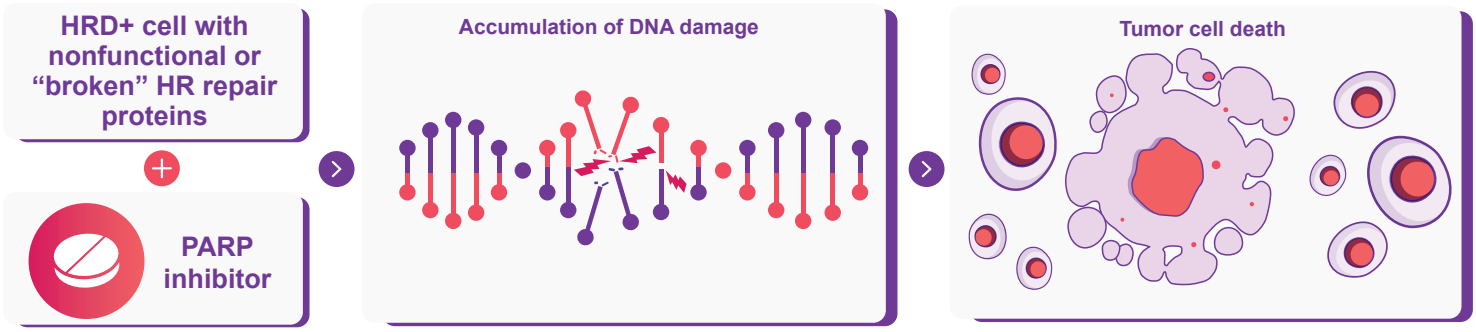
The American Society of Clinical Oncology (ASCO) Guidelines strongly recommend that all patients with epithelial ovarian cancer (EOC) should be offered germline and somatic testing for *BRCA1* and *BRCA2*. Germline testing for other ovarian cancer susceptibility genes is recommended. Somatic tumor testing should include measure(s) of **homologous recombination**. Testing should occur at the time of diagnosis or as soon as feasibly possible. (Evidence quality: High)[8]

BRCA, breast cancer susceptibility gene; ***CDK12***, cyclin-dependent kinase 12; ***FANCA***, Fanconi anemia complementation group A; ***PALB2***, partner and localizer of *BRCA2*; **PARP**, poly (ADP-ribose) polymerase; ***RAD51***, RAD51 recombinase.

How do PARP inhibitors work in patients with advanced ovarian cancer who are HRD positive?

PARP inhibition aims to synergize with HRD to induce tumor cell death[9,10]

The clinical significance of in vitro studies is unknown.
Mechanism of action statements are not meant to imply clinical efficacy.



Like *BRCA*, HRD status may help identify patients most likely to benefit from PARP inhibitor maintenance[1,6,11-14]

BRCA, HRD, and platinum response are all predictive biomarkers of PARP inhibitor maintenance treatment benefit in ovarian cancer[1,6,11-14]

The genetic instability of HRD-positive tumor cells increases the likelihood of[1]:

- Response to platinum-based chemotherapy
- Response to PARP inhibitors

Platinum responsiveness is a key predictor of PARPi treatment response, and can therefore help inform 1L maintenance treatment decisions for advanced ovarian cancer[15-18]

BRCA mutation and HRD status are associated with clinical outcomes with PARP inhibitor maintenance therapy for advanced ovarian cancer[19]

- PARP inhibitors were associated with improvements in progression-free survival (PFS) compared to placebo in HRD-positive *BRCA*m and *BRCA*wt sub-populations[a]

[a]**Interpret results with caution due to the high heterogeneity across trials and the methodological limitations of the underlying studies within the meta-analysis.** A 2024 systematic review and meta-analysis of seven phase 3 randomized clinical trials, including 4013 patients, compared maintenance PARPi to placebo in patients with newly diagnosed stage III (72.58%) and IV advanced ovarian cancer who had a partial or complete response to 1L platinum-based chemotherapy.[19] PFS data in HRD-positive *BRCA*m included ATHENA, FLAMES, PAOLA-1, PRIMA, PRIME, VELIA, and SOLO-1; HR 0.38 (95% CI, 0.32-0.44, *P*<0.01). PFS data in HRD-positive *BRCA*wt included ATHENA, PAOLA-1, and PRIMA; HR 0.49 (95% CI, 0.37-0.64, *P*<0.01). FLAMES and PRIME exclusively included Chinese patients.[19,20] Findings suggest that patients of East Asian descent appeared more likely to have HRD-positive tumors, which may contribute to increased responses to PARPi.[19]

1L, first-line; ***BRCA***, breast cancer susceptibility gene; ***BRCAm***, *BRCA* mutated; ***BRCAwt***, *BRCA* wild type; **HR**, homologous recombination; **HRD**, homologous recombination deficiency; **HRD+**, homologous recombination deficient tumors; **PARP**, poly (ADP-ribose) polymerase; **PARPi**, poly (ADP-ribose) polymerase inhibitor.

Considerations for biomarker testing in patients with advanced ovarian cancer[10,11]

1 DAILY DOSE
Zejula
niraparib
tablets 100/200/300 mg

HRD testing may identify a **larger number of eligible women** with advanced ovarian cancer, compared to *BRCA* testing alone, who may experience a **benefit from PARP inhibitors like ZEJULA**[1-3,11]

HRD can be detected using **specific biomarkers** that assess genomic instability or using NGS panels that include individual homologous recombination genes (eg, *CDK12*, *RAD51*)[1-4]

HRD test results may provide **predictive information** regarding improvement in PFS with PARP inhibitor maintenance vs placebo[11,19]

ZEJULA is the only once-daily oral PARP inhibitor monotherapy available for eligible 1L platinum responders with HRD-positive advanced ovarian cancer.[6,13,14]

HRD status was a stratification factor in PRIMA, a double-blind, placebo-controlled phase 3 trial of patients with newly diagnosed advanced OC who were randomized 2:1 to ZEJULA or placebo.[6,7] **In PRIMA, HRD status was determined using Myriad MyChoice® CDx assay,** which sets the threshold for a positive GIS at 42.[2,6]

Visit Myriad.com for more information

INDICATION

ZEJULA is indicated for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD) – positive status defined by either a deleterious or suspected deleterious *BRCA* mutation, and/or genomic instability. Select patients for therapy based on an FDA-authorized companion diagnostic for ZEJULA.

IMPORTANT SAFETY INFORMATION

Myelodysplastic syndrome/acute myeloid leukemia (MDS/AML), including cases with a fatal outcome, have been reported in patients who received ZEJULA. In PRIMA, of patients within the HRD-positive population, MDS/AML occurred in 8 out of 245 (3.3%) patients treated with ZEJULA, and in 3 out of 125 (2.4%) patients treated with placebo with a follow-up of 6.1 years. The duration of therapy with ZEJULA in patients who developed secondary MDS/cancer therapy-related AML varied from 5.5 months to 5 years. All patients who developed secondary MDS/cancer therapy-related AML had received previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy. For suspected MDS/AML or prolonged hematological toxicities, refer the patient to a hematologist for further evaluation. Discontinue ZEJULA if MDS/AML is confirmed.

Hematologic adverse reactions (thrombocytopenia, anemia, neutropenia, and/or pancytopenia) have been reported in patients receiving ZEJULA. The overall incidence of Grade ≥3 thrombocytopenia, anemia, and neutropenia were reported, respectively, in 39%, 31%, and 21% of patients receiving ZEJULA in PRIMA. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 4%, 2%, and 2% of patients in PRIMA. In patients who were administered a starting dose of ZEJULA based on baseline weight or platelet count in PRIMA, Grade ≥3 thrombocytopenia, anemia, and neutropenia were reported, respectively, in 22%, 23%, and 15% of patients receiving ZEJULA. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 3%, 3%, and 2% of patients. Do not start ZEJULA until patients have recovered from hematological toxicity caused by prior chemotherapy (≤Grade 1). Monitor complete blood counts weekly for the first month, monthly for the next 11 months, and periodically thereafter. If hematological toxicities do not resolve within 28 days following interruption, discontinue ZEJULA, and refer the patient to a hematologist for further investigations.

Please see additional Important Safety Information on the next page, as well as the full Prescribing Information for ZEJULA at ZEJULAHCP.com.

1L, first-line; ***BRCA***, breast cancer susceptibility gene; **CDK12**, cyclin-dependent kinase 12; **CDx**, companion diagnostic; **GIS**, genomic instability score; **NGS**, next-generation sequencing; **OC**, ovarian cancer; **PARP**, poly (ADP-ribose) polymerase; **PFS**, progression-free survival; ***RAD51***, RAD51 recombinase.

IMPORTANT SAFETY INFORMATION (CONT'D)

Hypertension and cardiovascular effects have been reported in patients receiving ZEJULA. Grade 3-4 hypertension occurred in 6% of patients receiving ZEJULA vs 1% of patients receiving placebo in PRIMA, with no reported discontinuations. Monitor blood pressure and heart rate at least weekly for the first two months, then monthly for the first year, and periodically thereafter during treatment with ZEJULA. Closely monitor patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension. Manage hypertension with antihypertensive medications and adjustment of the ZEJULA dose if necessary.

Posterior reversible encephalopathy syndrome (PRES) occurred in 0.1% of 2,165 patients treated with ZEJULA in clinical trials and has also been described in postmarketing reports. Monitor all patients for signs and symptoms of PRES, which include seizure, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. Diagnosis requires confirmation by brain imaging. If suspected, promptly discontinue ZEJULA and administer appropriate treatment. The safety of reinitiating ZEJULA is unknown.

Embryo-fetal toxicity and lactation: Based on its mechanism of action, ZEJULA can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months after receiving their final dose of ZEJULA. Because of the potential for serious adverse reactions from ZEJULA in breastfed infants, advise lactating women not to breastfeed during treatment with ZEJULA and for 1 month after receiving the last dose.

First-line Maintenance Treatment of HRD-Positive Advanced Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of all patients who received ZEJULA in PRIMA were thrombocytopenia (66%), anemia (65%), nausea (62%), fatigue (52%), musculoskeletal pain (46%), neutropenia (43%), constipation (40%), leukopenia (29%), headache (27%), insomnia (25%), vomiting (23%), dyspnea (21%), decreased appetite (20%), dizziness (20%), cough (20%), hypertension (20%), AST/ALT elevation (14%), acute kidney injury (13%), and anxiety (12%).

Common lab abnormalities (Grades 1-4) in ≥25% of all patients who received ZEJULA in PRIMA included: decreased hemoglobin (85%), decreased leukocytes (72%), decreased platelets (71%), decreased neutrophils (64%), increased glucose (62%), decreased lymphocytes (55%), increased alkaline phosphatase (48%), increased creatinine (40%), decreased magnesium (39%), increased AST (35%), increased ALT (32%), and increased calcium (31%).

Please see the full Prescribing Information for ZEJULA at ZEJULAHCP.com.

ALT, alanine aminotransferase; **AST**, aspartate aminotransferase.

References:

1. Konstantinopoulos PA et al. *Cancer Discov*. 2015;5:1137-1154. doi:10.1158/2159-8290 **2.** Myriad genetics. myChoice® CDx. Accessed April 9, 2026. https://myriad-web.s3.amazonaws.com/myChoiceCDx/MyChoice+CDx_POSITIVE+Sample+Report.pdf **3.** FoundationOne®CDx (F1CDx). Accessed April 9, 2026. https://info.foundationmedicine.com/hubfs/FMI%20Labels/FoundationOne_CDx_Label_Technical_Info.pdf **4.** Witz A et al. *Biomark Res*. 2025;13(1):31. doi:10.1186/s40364-025-00740-y **5.** Coleman R et al. *N Engl J Med*. 2019;381(25):2403-2415. doi:10.1056/NEJMoa1909707 **6.** ZEJULA (niraparib). Prescribing information. GSK; 2026. **7.** González-Martín A et al. *N Engl J Med*. 2019;381(25):2391-2402. doi:10.1056/NEJMoa1910962 **8.** Gaillard S et al. *J Clin Oncol*. 2025;43(7):868-891. doi:10.1200/JCO-24-02589 **9.** Sonnenblick A et al. *Nat Rev Clin Oncol*. 2015;12:27-41. doi:10.1038/nrclinonc.2014.163 **10.** Lord CJ, Ashworth A. *Nature*. 2012;481:287-294. doi:10.1038/nature10760 **11.** Longo DL. *N Engl J Med*. 2019;381:2471-2474. doi:10.1056/NEJMe1914488 **12.** Banerjee SN, Lord CJ. *Nat Rev Clin Oncol*. 2020;17:136-137. doi:10.1038/s41571-020-0335-9 **13.** Lynparza (olaparib). Prescribing information. AstraZeneca Pharmaceuticals LP; 2025. **14.** Rubraca (rucaparib). Prescribing information. pharmaand GmbH; 2025. **15.** Caruso G et al. *Int J Gynecol Cancer*. 2023;33(4):431-443. doi:10.1136/ijgc-2022-004149 **16.** Mirza MR et al. *Ann Oncol*. 2020;31(9):1148-1159. doi:10.1016/j.annonc.2020.06.004 **17.** You B et al. *Cancer Treat Rev*. 2021;100:102294. doi:10.1016/j.ctrv.2021.102294 **18.** You B et al. *Clin Cancer Res*. 2020;26(17):4625-4632. doi:10.1158/1078-0432.CCR-20-0054 **19.** Al-Alam O et al. *Clin Oncol*. 2025;10:2123. Accessed May 29, 2026. https://www.clinicsinoncology.com/open-access/maintenance-therapy-with-poly-adp-ribose-polymerase-inhibitors-parpi-in-patients-9795.pdf **20.** Wu X et al. *Nat Med*. 2024;30:1612-1621. doi:10.1038/s41591-024-03003-9

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