1 DAILY DOSE

Zejula
niraparib
tablets 100/200/300 mg

How are you treating patients with newly diagnosed advanced ovarian cancer with a high risk of progression?

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.

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, MDS/AML occurred in 6 out of 484 (1.2%) patients treated with ZEJULA, and in 3 out of 244 (1.2%) patients treated with placebo. The duration of therapy with ZEJULA in patients who developed secondary MDS/cancer therapy-related AML varied from 3.7 months to 2.5 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.

Please see additional Important Safety Information throughout, as well as the accompanying Prescribing Information.

GSK

Up to half of advanced ovarian cancers are HRp[1]

Homologous recombination status is defined as either[1]:

- HRp (homologous recombination proficient): "no deficiency in DNA repair"
- HRd (homologous recombination deficient): "deficient DNA repair"
  - HRd can arise from mutations in multiple components of the HR pathway, most commonly *BRCA*[1]

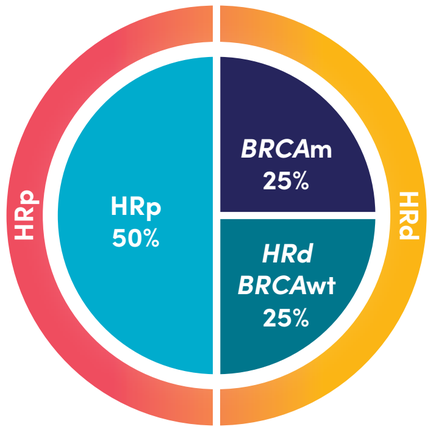

Figure adapted from Konstantinopoulos PA et al. 2015.

ZEJULA has been studied in[2]:

HRd	*BRCA*m	✓
	*BRCA*wt	✓
HRp		✓

Important Safety Information (continued)

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.

BRCA = breast cancer susceptibility gene; *BRCA*m = *BRCA* mutated; *BRCA*wt = *BRCA* wild-type; HR = homologous recombination; HRd = homologous recombination deficient; HRp = homologous recombination proficient.

PRIMA enrolled a broad range of patients, including patients with poor prognoses who were at higher risk of progression[2-7]

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Study design[2,3]:

- PRIMA, a randomized, double-blind, phase 3 trial of safety and efficacy of ZEJULA vs placebo in newly diagnosed advanced ovarian cancer after CR or PR to 1L platinum chemotherapy

Of patients in the overall population, which consisted of patients with HRd, HRp, and HRnd advanced ovarian cancer (N=733):

35%

had **stage IV** disease[2,3]

~67%

had received **neoadjuvant chemotherapy**[2,3]

~84%

had **residual disease** after primary debulking surgery[7,a]

[a] Stage III and IV disease with visible residual tumor (>0 cm) after primary debulking surgery.[7]

72% of patients on placebo estimated to have progressed or died within 2 years of diagnosis[3]

Important Safety Information (continued)

Hematologic adverse reactions (continued) 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.

Please see additional Important Safety Information throughout, as well as the accompanying Prescribing Information.

1L = first-line; CR = complete response; HRd = homologous recombination deficient; HRnd = homologous recombination status not determined; HRp = homologous recombination proficient; PR = partial response.

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The PRIMA population may be reflective of your clinical practice[8]

Patient characteristics at baseline in PRIMA[3]

Characteristic		ZEJULA		Placebo	
		HRd Population (n=247)	Overall Population (N=487)	HRd Population (n=126)	Overall Population (N=246)
Median age (range), y		58 (32–83)	62 (32–85)	58 (33–82)	62 (33–88)
ECOG score	0	182 (73.7%)	337 (69.2%)	97 (77.0%)	174 (70.7%)
	1	65 (26.3%)	150 (30.8%)	29 (23.0%)	72 (29.3%)
International FIGO stage	III	161 (65.2%)	318 (65.3%)	78 (61.9%)	158 (64.2%)
	IV	86 (34.8%)	169 (34.7%)	48 (38.1%)	88 (35.8%)
Primary tumor location	Ovary	201 (81.4%)	388 (79.7%)	105 (83.3%)	201 (81.7%)
	Other	46 (18.7%)	99 (20.3%)	21 (16.6%)	45 (18.3%)
Histologic type[a]	Serous	234 (94.7%)	465 (95.5%)	116 (92.1%)	230 (93.5%)
	Endometrioid	5 (2.0%)	11 (2.3%)	6 (4.8%)	9 (3.7%)
Received neoadjuvant chemotherapy		156 (63.2%)	322 (66.1%)	80 (63.5%)	167 (67.9%)
Clinical response after platinum chemotherapy	CR	185 (74.9%)	337 (69.2%)	93 (73.8%)	172 (70.0%)
	PR	62 (25.1%)	150 (30.8%)	33 (26.2%)	74 (30.0%)
Cancer antigen 125 level[a]	≤ULN	236 (95.5%)	450 (92.4%)	120 (95.2%)	226 (91.9%)
	>ULN	9 (3.6%)	34 (7.0%)	5 (4.0%)	18 (7.3%)
No. of cycles of platinum chemotherapy[a]	6	165 (66.8%)	333 (68.4%)	84 (66.7%)	170 (69.1%)
	7–9	52 (21.1%)	124 (25.5%)	28 (22.2%)	62 (25.2%)

Adapted from González-Martín et al. 2019. [a]Does not sum to 100% due to missing data.

ZEJULA is the only once-daily oral PARP inhibitor monotherapy for patients with advanced ovarian cancer[2,9,10]

Important Safety Information (continued)

Hematologic adverse reactions (continued) 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.

CR = complete response; ECOG = Eastern Cooperative Oncology Group; FIGO = International Federation of Gynecology and Obstetrics; HRd = homologous recombination deficient; PARP = poly (ADP-ribose) polymerase; PR = partial response; ULN = upper limit of normal.

More than doubled 4-year PFS rates observed with ZEJULA in patients with HRd advanced ovarian cancer vs placebo[11]

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Primary analysis

13.8-month median follow-up[2,3]

Median PFS by BICR in the HRd population (n=373)

21.9 months ZEJULA vs **10.4 months placebo**

HR, 0.43 (95% CI, 0.31–0.59; *P*<0.0001)

Median PFS by BICR in the overall population (N=733)

13.8 months ZEJULA vs **8.2 months placebo**

HR, 0.62 (95% CI, 0.50–0.76; *P*<0.0001)

At the time of the primary analysis, limited overall survival data were available, with 11% deaths in the overall population.[2]

Exploratory ad hoc analysis[b]

3.5-year median follow-up of investigator-assessed PFS in the HRd population (n=373)[11,b]

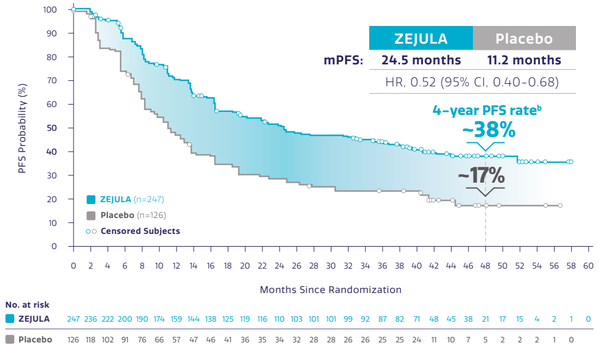


Figure adapted from González-Martín A et al. 2023.

[b]Interpret results with caution.

- Not powered to detect a statistically significant treatment effect
- 4-year PFS rates estimated from Kaplan-Meier curve with median follow-up time of 3.5 years[11]
- The probability of patients in the HRd population to be alive and progression-free at 4 years was 38% in the ZEJULA arm vs 17% in the placebo arm[11]
- With 3.5-year median follow-up, overall survival data were immature at 41.2% for the overall population[11]

ZEJULA was associated with long-term PFS benefits for patients with HRd ovarian cancer[11]

Important Safety Information (continued)

Hypertension and hypertensive crisis 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.

Please see additional Important Safety Information throughout, as well as the accompanying Prescribing Information.

BICR = blinded independent central review; CI = confidence interval; HR = hazard ratio; HRd = homologous recombination deficient; mPFS = median PFS; PFS = progression-free survival.

Continued confidence with ZEJULA: long-term PFS benefit observed consistent with primary analysis[2,3,11]

Exploratory ad hoc analysis[a]

3.5-year median follow-up of investigator-assessed PFS in the overall population (N=733)[11,a]

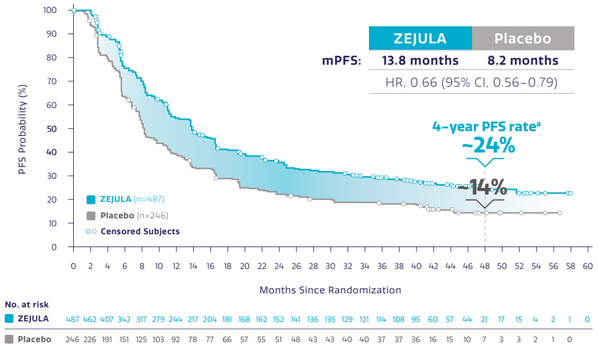


Figure adapted from González-Martín A et al. 2023.

[a]Interpret results with caution.

- Not powered to detect a statistically significant treatment effect
- 4-year PFS rates estimated from Kaplan-Meier curve with median follow-up time of 3.5 years[11]
- The probability of patients in the overall population to be alive and progression-free at 4 years was 24% in the ZEJULA arm vs 14% in the placebo arm[11]
- With 3.5-year median follow-up, overall survival data were immature at 41.2% for the overall population[11]

Reduction in risk of progression or death remained consistent with the primary analysis[2,3,11]

Important Safety Information (continued)

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.

CI = confidence interval; HR = hazard ratio; mPFS = median PFS; PFS = progression-free survival.

In an exploratory analysis, long-term PFS was observed in the HRp population[11]

Prespecified exploratory analysis was included in the primary analysis[3,b]

13.8-month median follow-up

Median PFS by BICR in the HRp population (n=249)

8.1 months ZEJULA vs **5.4** months placebo

HR, 0.68 (95% CI, 0.49–0.94)

[b]This prespecified subgroup analysis is exploratory in nature and was not powered to detect a statistically significant treatment effect; therefore, results should be interpreted with caution.

At the time of the primary analysis, limited overall survival data were available, with 11% deaths in the overall population.[2]

Exploratory ad hoc analysis[c]

3.5-year median follow-up of investigator-assessed PFS in the HRp population (n=249)[11,c]

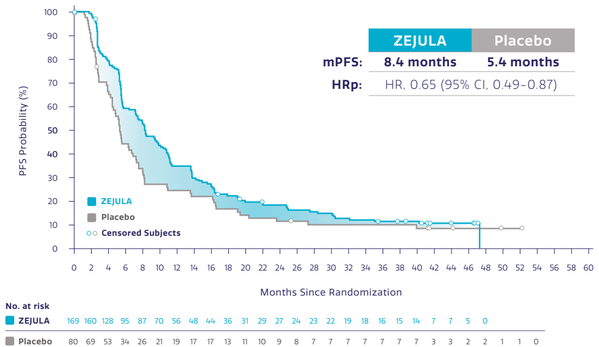


Figure adapted from González-Martín A et al. 2023.

[c]Interpret results with caution.

- Not powered to detect a statistically significant treatment effect
- With 3.5-year median follow-up, overall survival data were immature at 41.2% for the overall population[11]

With ZEJULA, long-term PFS was observed in the HRp population[11]

Important Safety Information (continued)

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.

Please see additional Important Safety Information throughout, as well as the accompanying Prescribing Information.

BICR = blinded independent central review; CI = confidence interval; HR = hazard ratio; HRp = homologous recombination proficient; mPFS = median PFS; PFS = progression-free survival.

In PRIMA, no new safety signals were reported in 3.5-year follow-up exploratory analysis[11]

TEAE overview from 3.5-year follow-up of the overall population[11]

Adverse Event	ZEJULA (n=484)	Placebo (n=244)
Any TEAE	99.0%	93.9%
Grade ≥3	72.9%	23.0%
TEAE leading to treatment discontinuation	14.3%	2.9%
TEAE leading to dose reduction	71.7%	9.4%
TEAE leading to dose interruption	80.4%	20.9%
TEAE leading to death	1.0%	0.8%

Adverse events were consistent with the primary analysis and the known safety profile of ZEJULA[2,3,11]
The discontinuation rate was sustained with 3.5-year follow-up[2,3,11,a]

With 3.5-year median follow-up, the most common adverse events (grades 1-4) in ≥20% of all patients who received ZEJULA in PRIMA were thrombocytopenia (67%), anemia (65%), nausea (58%), neutropenia (43%), constipation (42%), fatigue (37%), headache (28%), insomnia (26%), abdominal pain (25%), vomiting (24%), arthralgia (21%), hypertension (21%), and diarrhea (20%).[11]

[a]At the time of the primary analysis of PRIMA, 12% of patients discontinued treatment with ZEJULA due to adverse events.[2,3]

Adverse events resulting in discontinuation of ZEJULA in >1% of patients included thrombocytopenia (3.7%), anemia (1.9%), and nausea and neutropenia (1.2% each).[2]

Important Safety Information (continued)

First-line Maintenance Advanced Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of all patients who received ZEJULA in PRIMA were thrombocytopenia (66%), anemia (64%), nausea (57%), fatigue (51%), neutropenia (42%), constipation (40%), musculoskeletal pain (39%), leukopenia (28%), headache (26%), insomnia (25%), vomiting (22%), dyspnea (22%), decreased appetite (19%), dizziness (19%), cough (18%), hypertension (18%), AST/ALT elevation (14%), and acute kidney injury (12%).

TEAE = treatment-emergent adverse event.

ZEJULA is the only once-daily oral PARP inhibitor monotherapy for patients with advanced ovarian cancer[2,9,10]

Convenient, one-tablet, once-daily dosing for infusion-free treatment[2,b]

[b]Routine monitoring of blood counts, blood pressure, and heart rate is required as part of treatment with ZEJULA.[2]

Flexible once-daily dosing at a time of their choice, at any time of day or night[2,c]

[c]ZEJULA can be taken any time of day, with or without food. Patients should take ZEJULA at approximately the same time each day. Bedtime administration may be a potential method for managing nausea.[2]

Important Safety Information (continued)

First-line Maintenance Advanced Ovarian Cancer (continued)

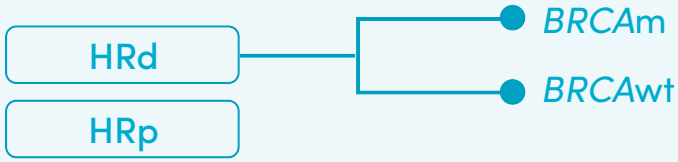
Common lab abnormalities (Grades 1-4) in ≥25% of all patients who received ZEJULA in PRIMA included: decreased hemoglobin (87%), decreased platelets (74%), decreased leukocytes (71%), increased glucose (66%), decreased neutrophils (66%), decreased lymphocytes (51%), increased alkaline phosphatase (46%), increased creatinine (40%), decreased magnesium (36%), increased AST (35%), and increased ALT (29%).

Please see additional Important Safety Information throughout, as well as the accompanying Prescribing Information.

ALT = alanine aminotransferase; AST = aspartate aminotransferase.

ZEJULA tablets are indicated for the 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

ZEJULA has been evaluated in patients with HRd and HRp advanced ovarian cancer[3]



No new safety signals reported in a long-term safety analysis at 3.5 years[11]

ZEJULA is the only PARP inhibitor therapy approved in patients with HRp advanced ovarian cancer[2,9,10]

Learn more at ZEJULAHCP.com

Important Safety Information (continued)

First-line Maintenance Advanced Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of all patients who received ZEJULA in PRIMA were thrombocytopenia (66%), anemia (64%), nausea (57%), fatigue (51%), neutropenia (42%), constipation (40%), musculoskeletal pain (39%), leukopenia (28%), headache (26%), insomnia (25%), vomiting (22%), dyspnea (22%), decreased appetite (19%), dizziness (19%), cough (18%), hypertension (18%), AST/ALT elevation (14%), and acute kidney injury (12%).

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ALT = alanine aminotransferase; AST = aspartate aminotransferase; *BRCA* = breast cancer susceptibility gene; *BRCA*m = *BRCA* mutated; *BRCA*wt = *BRCA* wild-type; HRd = homologous recombination deficient; HRp = homologous recombination proficient; PARP = poly (ADP-ribose) polymerase.

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