November 2022

IMPORTANT PRESCRIBING INFORMATION

Subject: Zejula (niraparib) Important Prescribing Information for the maintenance treatment of adult patients with non-g*BRCA*mut recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy in second or later line setting.

Dear Health Care Provider:

This letter is an update to the DHCP Letter dated May 2022. This letter is to inform you that, at the request of the FDA, GSK will restrict the indication of ZEJULA® (niraparib) 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 received in the second or later line setting **to the g*BRCA*mut patient population only;** GSK is in discussions with the FDA to update the USPI for Zejula.

The final overall survival (OS) analysis of ENGOT-OV16/NOVA (NOVA) study, a Phase III trial which evaluated the efficacy and safety of niraparib as maintenance treatment for patients with platinum-sensitive recurrent ovarian cancer, is presented below based on GSK retrieval of missing survival status in 2022.

The primary endpoint of the NOVA study was progression-free survival (PFS), evaluated in two independently powered cohorts (g*BRCA*mut and non-g*BRCA*mut), and demonstrated the benefit of niraparib in both cohorts and across the HRD subgroups in the non-g*BRCA*mut cohort.

The final NOVA study OS analysis results (data cutoff date of 31-Mar-2021) are included below:

- In the g*BRCA*mut cohort (n=203), the median OS was 40.9 months for patients treated with niraparib compared to 38.1 months for patients on placebo (HR = 0.85 [95% CI 0.61, 1.20]).
- In the non-g*BRCA*mut cohort (n=350), the median OS was 31.0 months for patients treated with niraparib compared to 34.8 months for patients on placebo (HR = 1.06 [95% CI 0.81, 1.37]).
- In the non-g*BRCA*mut/HRDpos subgroup (n=162), the median OS was 35.6 months for patients treated with niraparib compared to 41.4 months for patients on placebo (HR = 1.29 [95% CI 0.85, 1.95]).

The OS Kaplan Meier (KM) curves for the non-g*BRCA*mut cohort (Figure 1) and the non-g*BRCA*mut/ HRDpos subgroup (Figure 2) are included below.

Additionally, within the non-g*BRCA*mut cohort, an exploratory analysis of OS was performed for patients with HRD negative status (HRDneg) and patients whose HRD status was not determined (HRDnd). These results are summarized below:

- In the non-g*BRCA*mut/HRDneg subgroup (n=134) had a median OS of 27.9 months for patients treated with niraparib or placebo (HR = 0.93 [95% CI 0.61, 1.41]).
- In the non-g*BRCA*mut/HRDnd subgroup (n=54) had a median OS of 29.8 months for patients treated with niraparib compared to 20.2 months for patients on placebo (HR = 0.62 [95% CI 0.29, 1.36]).

Figure 1: Overall Survival in the non-g*BRCA*mut cohort

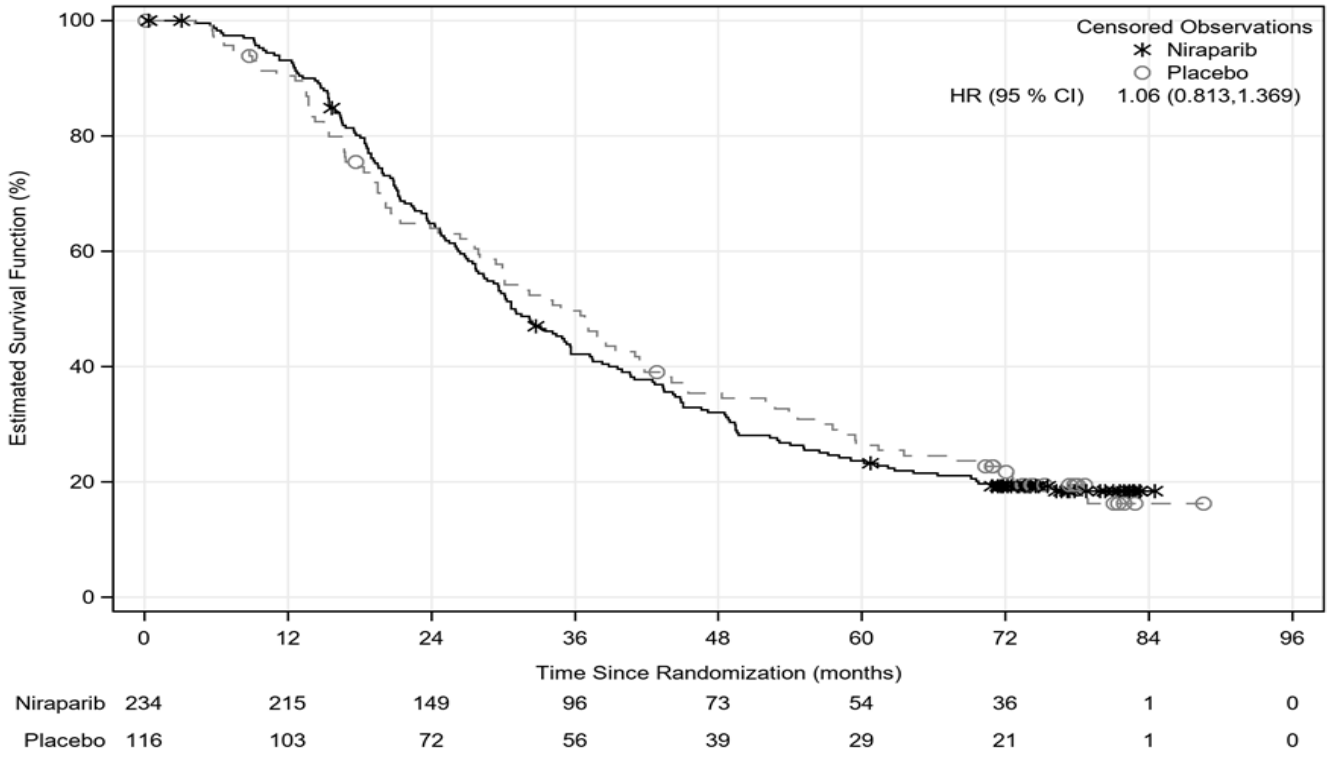
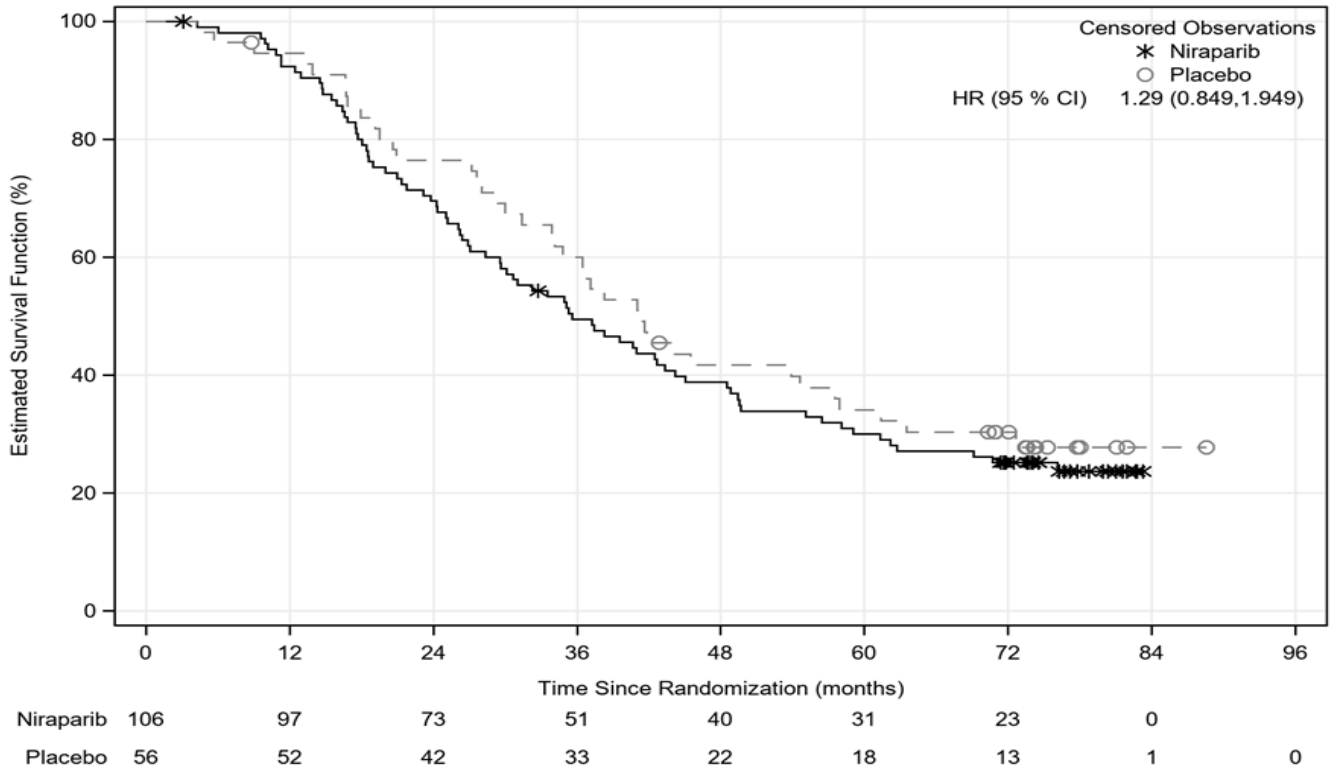


Figure 2: Overall Survival in the non-g*BRCA*mut/HRDpos subgroup



Based on the NOVA study OS analysis, GSK in consultation with the FDA is taking action to restrict this indication to g*BRCA*mut patients only. GSK is in active discussion with the FDA about revisions to the ZEJULA Prescribing Information related to the restriction of this indication only.

Prescriber Action

- Physicians should not initiate new treatment with ZEJULA for maintenance treatment of patients with non-g*BRCA*mut platinum sensitive recurrent high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer in the second or later line setting.
- Physicians who are currently treating patients with ZEJULA for patients with non-g*BRCA*mut platinum sensitive recurrent ovarian cancer in the second or later line maintenance setting are asked to discuss this information with those patients for an individual benefit-risk assessment so that they can make an informed decision regarding their ongoing care.

This recommendation **does not apply to the first line ZEJULA indication** for the 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.

Reporting Adverse Events

Health care providers and patients are encouraged to report adverse events in patients taking ZEJULA to GSK at 1-888-825-5249. You are encouraged to report side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact for Further Information or Questions

You may contact our medical information department at 1-877-GSK-MI4U (6448) if you have any questions about the information contained in this letter or the safe and effective use of ZEJULA. This letter is not intended as a complete description of the benefits and risks related to the use of ZEJULA. Please refer to the enclosed full prescribing information.

Sincerely,

Sabine Luik, MD
Chief Medical Officer (CMO) and SVP Global Medical Regulatory & Quality
GSK

Enclosure(s): ZEJULA Full Prescribing Information