Cancer Research Consortium of West Michigan
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FAST FACTS

GOG 3012: **A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Niraparib Maintenance Treatment in Patients with HRD-Positive Advanced Ovarian Cancer Following Response on Front-Line Platinum-Based Chemotherapy**

Provided Drug: Niraparib/Placebo

Inclusion Criteria

1. Patients must be female ≥18 years of age, able to understand the study procedures and agree to participate in the study by providing written informed consent
2. Histological and staging criteria:
    a. Patients must have histologically diagnosed high-grade serous or endometrioid, or high-grade predominantly serous or endometrioid ovarian cancer, fallopian tube cancer, or primary peritoneal cancer that is Stage III or IV according to FIGO criteria. 3.
3. Surgical criteria:
    a. Patients with inoperable Stage III and IV disease are eligible;
    b. All Stage IV patients with operable disease are eligible;
    c. Patients with stage III or IV disease treated with neoadjuvant chemotherapy and interval debulking surgery are eligible
    d. Patients with stage III disease who have visible residual disease after primarydebulking surgery are eligible.
4. Chemotherapy criteria:
    a. Patients who have received intraperitoneal chemotherapy are eligible;
    b. Patients treated with primary debulking surgery must have had ≥6 and ≤9 cycles of platinum-based therapy;
    c. Patients must have had ≥2 post-operative cycles of platinum-based therapy following interval debulking surgery
    d. Patients must have physician assessed CR or PR after ≥ 3 cycles of therapy;
    e. e. Any residual tumor after completion of chemotherapy must measure ≤2 cm;
    f. Patients must have either CA-125 in the normal range or CA-125 decrease by more than 90% during their front-line therapy that is stable for at least 7 days (ie, no increase >15% from nadir).
5. Patients must be randomized within 12 weeks of the first day of the last cycle of chemotherapy.
6. Patients must agree to undergo tumor HRD testing.
    a. The HRD test result must be available for randomization as it is a stratification factor. Patients with documented g*BRCA*1 or g*BRCA*2 mutation or s*BRCA1/2* mutation may be randomized without HRD test results
    b. The tumor sample may be submitted for HRD testing prior to the screening period if it appears the patient is likely to meet other eligibility requirements. Patients are not required to have repeat HRD testing if HRD result is "not determined" (eg, due to insufficient tumor specimen)
7. Patients of childbearing potential must have a negative serum pregnancy test (beta human chorionic gonadotropin [hCG]) within 7 days prior to receiving the first dose of study treatment

8. Patients must be postmenopausal, free from menses for >1 year, surgically sterilized, or willing to use adequate contraception to prevent pregnancy (see Appendix A) or must agree to abstain from activities that could result in pregnancy throughout the study,
starting with enrollment through 3 months after the last dose of study treatment
9. Patients must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 Appendix H
10. Patients must have adequate organ function, defined as follows (Note: complete blood count [CBC] test should be obtained without transfusion or receipt of stimulating factors within 2 weeks before obtaining screening blood sample):
    a. Absolute neutrophil count ≥ 1,500/μL
    b. Platelets ≥ 100,000/μL
    c. Hemoglobin ≥ 10 g/dL
    d. Serum creatinine ≤ 1.5 x upper limit of normal (ULN) or calculated creatinine clearance ≥ 60 mL/min using the Cockcroft-Gault equation
    e. Total bilirubin ≤ 1.5 x ULN
    f. Aspartate aminotransferase and alanine aminotransferase ≤ 2.5 x ULN unless liver metastases are present, in which case they must be ≤ 5 x ULN
11. Patients must agree to complete PROs during study and then at 4 weeks, 8 weeks, and 12weeks after treatment discontinuation. Thereafter, PROs will be collected every 12 weeks (± 2 weeks), regardless of subsequent treatment
12. Patients must have formalin-fixed, paraffin-embedded tumor samples available from the primary cancer or agree to undergo fresh biopsy prior to study treatment initiation
13. Patients must be able to take oral medications
14. Patients must agree to blood samples during screening and at the end of treatment (EOT)for cytogenetic analysis

Exclusion Criteria

1. Patient has mucinous or clear cell subtypes of epithelial ovarian cancer, carcinosarcoma or undifferentiated ovarian cancer
2. Patients with Stage III disease who have had complete cytoreduction (i.e., no visible residual disease) after primary debulking surgery;
3. Patient has undergone more than two debulking surgeries;
4. Patient is pregnant, breastfeeding, or expecting to conceive children, while receiving study treatment and for 3 months after the last dose of study treatment
5. Patient has a known hypersensitivity to the components of niraparib or its excipients;
6. Patient is simultaneously enrolled in any clinical trial of niraparib or any other investigational therapy;
7. Patient has received prior treatment with a known PARP inhibitor or has participated in a study where any treatment arm included administration of a known PARP inhibitor;
8. Patient has received bevacizumab with their first-line platinum based therapy;
9. Patient has had investigational therapy administered within 4 weeks, or within a time interval less than at least 5 half-lives of the investigational agent, whichever is longer, prior to the first scheduled day of dosing in this study;
10. Patient has had any known ≥Grade 3 anemia, neutropenia or thrombocytopenia due to prior chemotherapy that persisted >4 weeks
11. Patient has any known history or current diagnosis of MDS or AML;
12. Patient has undergone major surgery (per Investigator judgment) within 3 weeks of starting the study or patient has not recovered from any effects of any major surgery;
13. Patient has had drainage of ascites within 4 weeks prior to enrollment;

14. Patient has undergone palliative radiotherapy encompassing >20% of the bone marrow within 1 week of the first dose of study treatment;
15. Patient has a condition (such as transfusion dependent anemia or thrombocytopenia), therapy, or laboratory abnormality that might confound the study results or interfere with the patient's participation for the full duration of the study treatment, including:
    - Patient received a transfusion (platelets or red blood cells) within 2 weeks of the first dose of study treatment;
    - Patient received colony-stimulating factors (eg, granulocyte colony stimulating factor [G-CSF], granulocyte macrophage colony-stimulating factor [GM-CSF] or recombinant erythropoietin) within 2 weeks prior to the first dose of study treatment.
16. Patient is planning to donate blood during the study or for 90 days after the last dose of study treatment.
17. Other than ovarian cancer, patient has been diagnosed and/or treated for invasive cancer. Patients with cervical carcinoma in situ, non-melanomatous skin cancer and ductal carcinoma in situ (DCIS) definitively treated more than 5 years prior to this study are allowed.
18. Patient has known brain or leptomeningeal metastases that are untreated or uncontrolled (ie, new or worsening symptom or signs, or unstable steroid requirements);
    - Note: A scan to confirm the absence of brain metastases is not required. Patients with spinal cord compression may be considered if they have received definitive treatment for this and demonstrate evidence of clinically stable disease for 28 days.
19. Patient is considered a poor medical risk due to a serious, uncontrolled medical disorder, nonmalignant systemic disease, or active, uncontrolled infection;
    - Examples include, but are not limited to, uncontrolled ventricular arrhythmia, recent (within 90 days) myocardial infarction, uncontrolled major seizure disorder, unstable spinal cord compression, superior vena cava syndrome, or any psychiatric disorder that prohibits obtaining informed consent.
20. Patient is immunocompromised (patients with splenectomy are allowed).
21. Patient has known, active hepatic disease (ie, hepatitis B or C).
22. Patient has a corrected QT interval (QTc) prolongation > 470 milliseconds at screening;
    - If a patient has a prolonged QTc interval and the prolongation is deemed to be due to a pacemaker upon Investigator evaluation (ie, the patient otherwise has no cardiac abnormalities), then the patient may be eligible to participate in the study following discussion with the Medical Monitor

Treatment

- Experimental: Niraparib (once daily continuously during a 28 day cycle)
- Placebo Comparator: Placebo (once daily continuously over a 28 day cycle)

Pre-Study Parameters

- History/Physical exam, vitals, height, weight, PS
- AE Assessments
- Con meds assessment
- CBC/diff/platelets
- CMP, Magnesium, Amylase

- INR, aPTT, serum CA-125
- Pregnancy test
- Urinalysis
- 12 lead ECG
- Chest CT or MRI
- QOL questionnaires
- Blood sample for PK analysis
- Optional tumor submission