A Study to Examine Olaparib Maintenance Retreatment in Patients With Epithelial Ovarian Cancer. (OReO)

ClinicalTrials.gov Identifier:
NCT03106987

Recruitment Status: Recruiting
First Posted: April 11, 2017
Last Update Posted: March 20, 2019

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Sponsor:
AstraZeneca

Collaborator:
European Network of Gynaecological Oncological Trial Groups (ENGOT)

Information provided by (Responsible Party):
AstraZeneca

Study Description

Brief Summary:
The OReO study will be a Phase IIIb, randomised, double-blind, placebo-controlled, multicentre study to assess the efficacy and tolerability of Olaparib retreatment, versus matching placebo, in non-mucinous epithelial ovarian cancer (EOC) patients (including patients with primary peritoneal and/or fallopian tube cancer).

<table>
<thead>
<tr>
<th>Condition or disease</th>
<th>Intervention/treatment</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial Ovarian Cancer</td>
<td>Drug: Active Comparator: Olaparib tablets</td>
<td>Phase 3</td>
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<td></td>
<td>Drug: Placebo</td>
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Detailed Description:
The OReO study will investigate the efficacy and safety of Olaparib maintenance re-treatment in patients with relapsed non-mucinous EOC, who have had disease progression following maintenance therapy with a Polyadenosine 5′diphosphoribose [poly (ADP ribose)] polymerisation inhibitor (PARPi) and a complete or partial radiological response to subsequent treatment with platinum-based chemotherapy or may have no evidence of disease (if optimal cytoreductive surgery was conducted prior to chemotherapy), and no evidence of a rising CA-125. Patients will be enrolled on the basis of their breast cancer susceptibility gene (BRCA1, BRCA2) status into one of two cohorts (BRCA1/2 [+ve] and BRCA1/2 [-ve]). The BRCA1/2 (+ve) and BRCA1/2 (-ve) cohorts will be randomised separately. Within each cohort, patients will be randomised by prospective allocation in a 2:1 ratio (Olaparib: matching placebo).

Study Design

- **Study Type**: Interventional (Clinical Trial)
- **Estimated Enrollment**: 228 participants
- **Allocation**: Randomized
- **Intervention Model**: Parallel Assignment
- **Masking**: Double (Participant, Investigator)
- **Primary Purpose**: Treatment
- **Official Title**: A Phase IIIb, Randomised, Double-blind, Placebo-controlled, Multicentre Study of Olaparib Maintenance Retreatment in Patients With Epithelial Ovarian Cancer Previously Treated With a PARPi and Responding to Repeat Platinum Chemotherapy

- **Actual Study Start Date**: June 8, 2017
- **Estimated Primary Completion Date**: November 8, 2020
- **Estimated Study Completion Date**: May 7, 2021

Resource links provided by the National Library of Medicine

- **Genetics Home Reference** related topics: Ovarian cancer
- **MedlinePlus** related topics: Ovarian Cancer
- **Drug Information** available for: Olaparib
**Arms and Interventions**

<table>
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<tr>
<th>Arm</th>
<th>Intervention/treatment</th>
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| Experimental: Active Comparator: Olaparib | Drug: Active Comparator: Olaparib tablets  
Olaparib  
300mg Olaparib tablets taken orally twice daily (except where this dose and formulation was previously not tolerated) until objective radiological disease progression as per RECIST 1.1 or as long as in the Investigator's opinion they are benefiting from treatment and they do not meet any other discontinuation criteria.  
Other Name: Olaparib tablets |
| Placebo Comparator: Placebo | Drug: Placebo  
Placebo  
300mg placebo tablets taken orally twice daily (except where this dose and formulation was previously not tolerated) until objective radiological disease progression as per RECIST 1.1 or as long as in the Investigator's opinion they are benefiting from treatment and they do not meet any other discontinuation criteria. |

**Outcome Measures**

**Primary Outcome Measures**:

1. Efficacy: Progression-free survival (PFS). [Time Frame: At randomization visit and at every 12 weeks (+/- 7 days) until objective radiological disease progression as determined by the investigator or other discontinuation criteria are met.]

   PFS measured from the date of randomisation to the date of investigator assessed disease progression (according to RECIST version 1.1 criteria) or death from any cause (in the absence of progression).
Secondary Outcome Measures:

1. Efficacy: Overall survival (OS) [Time Frame: From randomisation till Long-term follow-up (12-weekly beyond 30 days after last dose of study treatment)]
   
   OS measured from the date of randomisation to the date of death from any cause.

2. Efficacy: Time to progression by Gynecologic Cancer Intergroup (GCIG) criteria [Time Frame: At screening (Visit 1) and at every 12 weeks (±7 days), until objective disease progression, based on progressive serial elevation of serum CA-125 according to the GCIG criteria, or until discontinuation for other reasons.]
   
   Time to progression measured from randomisation to the earliest of Investigator-assessed disease progression by RECIST or cancer antigen 125 (CA-125), or death (by any cause in the absence of progression).

3. Efficacy: Time to first subsequent treatment commencement (TFST) [Time Frame: From follow-up i.e. 30 days after last dose of study medication till Long-term follow-up i.e. 12-weekly beyond 30 days after last dose of study treatment.]
   
   This will be assessed by checking:
   
   - Time from randomisation to first subsequent treatment commencement or death if this occurs before commencement of first subsequent treatment.

4. Efficacy: Time to second subsequent treatment commencement (TSST). [Time Frame: From follow-up i.e. 30 days after last dose of study medication till long-term follow-up i.e. 12-weekly beyond 30 days after last dose of study treatment.]
   
   This will be assessed by checking:
   
   - Time from randomisation to second subsequent treatment commencement or death if this occurs before commencement of second subsequent treatment.

5. Efficacy: Time to study treatment discontinuation (TDT). [Time Frame: From follow-up 30 days after last dose of study medication till long-term follow-up i.e. 12-weekly beyond 30 days after last dose of study treatment.]
   
   This will be assessed by checking:
   
   - Time from randomisation to study treatment discontinuation or death if this occurs before discontinuation of study treatment.

6. Efficacy: Health-related quality of life (HRQoL) [Time Frame: At Baseline, and from Day 1 till Long-term follow-up (12-weekly beyond 30 days after last dose of study treatment)]
   
   HRQoL of olaparib maintenance retreatment will be compared against matching placebo as
measured by the Functional Assessment of Cancer Therapy - Ovarian (FACT-O) Trial Outcome Index (TOI). The Change from baseline, time to deterioration and proportion improved will be recorded.

7. Safety and tolerability: Number of patients with Adverse Events (AEs), and Serious Adverse Events (SAEs). [Time Frame: At Baseline and from Day 1 till follow-up i.e. 30 days after last dose of study medication.]

   All AEs/serious adverse events (SAEs) reported during the study will be recorded.

8. Safety and tolerability: Number of patients with Adverse Event of Special Interest (AESI). [Time Frame: At Baseline and from Day 1 till long-term follow-up i.e. 12-weekly beyond 30 days after last dose of study treatment.]

   All AESIs reported during the study will be recorded.

Eligibility Criteria

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study: 18 Years to 130 Years (Adult, Older Adult)

Sexes Eligible for Study: Female

Accepts Healthy Volunteers: No

Criteria

Inclusion criteria

- Provision of informed consent prior to any study specific procedures
- Female patients ≥18 years of age, with histologically diagnosed relapsed non-mucinous epithelial ovarian cancer (EOC) (including primary peritoneal and/or fallopian tube cancer) (Non-mucinous EOC includes patients with serous, endometrioid, and transitional cell tumours, and those with mixed histology where one of these subtypes is predominant (>50%). Inclusion of other subtypes should first be discussed with the Medical Monitor).
- Documented BRCA1/2 status.
- Patients must have received one prior PARPi therapy PARPi therapy includes any agent (including...
Olaparib) used in a maintenance setting For the BRCA1/2 (+ve) cohort, the duration of first PARPi exposure must have been ≥18 months following a first line of chemotherapy or ≥12 months following a second or subsequent line of chemotherapy For the BRCA1/2 (-ve) cohort, the duration of first PARPi exposure must have been ≥12 months following a first line of chemotherapy or ≥6 months following a second or subsequent line of chemotherapy For the last chemotherapy course immediately prior to randomisation on the study Patients must have received a platinum-based chemotherapy regimen (carboplatin, cisplatin or oxaliplatin) and have received at least 4 cycles of treatment. Patients must be, in the opinion of the investigator, in response (partial or complete radiological response) or may have no evidence of disease (if optimal cytoreductive surgery was conducted prior to chemotherapy) and no evidence of a rising CA-125, as defined below, following completion of this chemotherapy course. Pre-treatment CA-125 measurements must meet criterion specified below.

- If the first value is within upper limit of normal (ULN) the patient is eligible to be randomised and a second sample is not required
- If the first value is greater than ULN a second assessment must be performed at least 7 days after the first. If the second assessment is ≥ 15% more than the first the patient is not eligible.

Patients must not have received bevacizumab during this course of treatment. Bevacizumab use as part of an earlier line of chemotherapy is permitted. Patients must not have received any investigational agent during this course of treatment. Patients must be randomised within 8 weeks of their last dose of chemotherapy (last dose is the day of the last infusion).

- Patients must have normal organ and bone marrow function measured within 28 days of randomization.
- Eastern Cooperative Oncology Group performance status 0-1
- Patients must have a life expectancy ≥16 weeks.
- Postmenopausal or evidence of non-childbearing status for women of childbearing potential: negative urine or serum pregnancy test within 28 days of study treatment and confirmed prior to treatment on day 1
- At least one lesion (measurable and/or non-measurable) that can be accurately assessed at baseline with computed tomography (CT) or magnetic resonance imaging (MRI) and is suitable for repeated assessment. Or No measurable disease following a complete response to most recent chemotherapy (+/- surgery)
- A formalin fixed, paraffin embedded (FFPE) tumour sample from the cancer of sufficient quantity and quality (as specified in the Covance Central Laboratory Services Manual) must be available for future central testing of tumour genetic status.
- For inclusion in the optional biomarker research, patients must sign an informed consent for biomarker research.

Exclusion criteria:

- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site).
- Participation in another clinical study with an investigational product during the chemotherapy course immediately prior to randomisation.
- Other malignancy within the last 5 years except the ones detailed in the exclusion criteria section of
study protocol.

- Resting electrocardiogram (ECG) with corrected QT interval (QTc) >470 msec on 2 or more time points within a 24 hour period or family history of long QT syndrome. Patients receiving any systemic chemotherapy or radiotherapy (except for palliative radiotherapy) within 3 weeks prior to study treatment.

- Concomitant use of known strong cytochrome P450 (CYP) subfamily 3A (CYP3A) inhibitors or moderate CYP3A inhibitors.

- Concomitant use of known strong or moderate CYP3A inducers.

- Persistent toxicities (Common Terminology Criteria for Adverse Event [CTCAE] grade 2 or higher) caused by previous cancer therapy, excluding alopecia and stable Grade 2 peripheral neuropathy.

- Patients with current or previous myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) or with features suggestive of MDS/AML.

- Patients with symptomatic uncontrolled brain metastases.

- Immunocompromised patients, e.g., patients who are known to be serologically positive for human immunodeficiency virus (HIV).

- Patients with a known hypersensitivity to Olaparib or any of the excipients of the product.

- Patients with a known active hepatitis (i.e., Hepatitis B or C).

- Patient who have received a whole blood transfusion within 30 days prior to screening tests (packed red blood cells and platelet transfusions are acceptable).
European Network of Gynaecological Oncological Trial Groups (ENGOT)

Investigators

Principal Investigator: Eric Pujade-Lauraine, MD, PhD  Hôpital Hôtel-Dieu

More Information

Responsible Party: AstraZeneca
ClinicalTrials.gov Identifier: NCT03106987  History of Changes
Other Study ID Numbers: D0816C00014
First Posted: April 11, 2017  Key Record Dates
Last Update Posted: March 20, 2019
Last Verified: March 2019

Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD: Yes

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No
Product Manufactured in and Exported from the U.S.: No

Keywords provided by AstraZeneca:
polymerisation inhibitor (PARPi) Olaparib
PARPi re-treatment ovarian cancer
BRCA1/2 (+ve) progression free survival (PFS)
BRCA1/2 (-ve)

Additional relevant MeSH terms:
Ovarian Neoplasms Endocrine System Diseases
Carcinoma, Ovarian Epithelial Gonadal Disorders
Endocrine Gland Neoplasms Carcinoma
Neoplasms by Site Neoplasms, Glandular and Epithelial
Neoplasms Neoplasms by Histologic Type
Ovarian Diseases Olaparib
Adnexal Diseases Poly(ADP-ribose) Polymerase Inhibitors
Genital Diseases, Female Enzyme Inhibitors
Genital Neoplasms, Female Molecular Mechanisms of Pharmacological Action
Urogenital Neoplasms Antineoplastic Agents