EPIK-O: A Phase III, multi-center, randomized (1:1), open-label, active-controlled study to assess the efficacy and safety of alpelisib (BYL719) in combination with olaparib as compared to single agent cytotoxic chemotherapy, in participants with no germline BRCA mutation detected, platinum-resistant or refractory, high-grade serous ovarian cancer.

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The purpose of the study is to determine whether treatment with alpelisib in combination with olaparib can delay the time to cancer progression compared to standard-of-care chemotherapy in participants with your type of ovarian cancer known as...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52195

Source
ToetsingOnline

Brief title
CBYL719K12301

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
high-grade serous ovarian cancer, platinum-resistant or refractory

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: BCRA non-mutant, high-grade serous ovarian cancer, interventional, randomized

Outcome measures

Primary outcome

Radiological tumor assessments by a Blinded Independent Review Committee (BIRC)

per RECIST 1.1 will be performed and used for the primary analysis of PFS:

1. At screening within 28 days prior to Cycle 1 Day 1.

2. Imaging assessments for response evaluation will be performed every 8 weeks

(±7 days) after randomization during the first 18 months and every 12 weeks (±7

days) thereafter

Additionally, tumor assessments will be used for a supplemental analysis where

PFS will be defined by one of the following:

1. Radiological tumor progression as assessed by investigator (RECIST 1.1);

2. Identification of new lesions or unequivocal progression of existing lesions

by additional diagnostic tests (e.g. histology/cytology, ultrasound, endoscopy

or any other imaging technique) AND CA-125 progression according to the Gynecologic Cancer Intergroup (GCIG)

3. Definitive clinical signs and symptoms of disease progression ([i] intractable cancer-related pain, [ii] malignant bowel obstruction/worsening dysfunction, or [iii] unequivocal symptomatic worsening of ascites or pleural effusion) AND CA-125 progression according to GCIG criteria.
Disease progression will not be diagnosed based on CA-125 progression in the absence of at least 1 of the criteria defined above.

Secondary outcome

Pharmacokinetic profile of alpelisib+olaparib.

Safety assessments (physical exam, ECOG status, body weight, vital signs, lab assessments, pregnancy testing, ECG(s), cardiac imaging, AE-severity, relationship with the study drug, seriousness).

Biormarker assessments and patient reported outcomes.

Study description

Background summary

Alpelisib belongs to a group of medicines called phosphatidylinositol 3-kinases (PI3K) inhibitors. Alpelisib blocks the activity of a biological pathway called the PI3K pathway. PI3K pathway activation depends on changes of multiple molecules. In particular, the changes of PIK3CA (a gene coding for the PI3K protein) or a molecule called PTEN (phosphatase and tensing homolog) are responsible for keeping the PI3K pathway active all the time. This continuous PI3K pathway activation is thought to contribute to the onset and growth of tumours. Therefore, alpelisib has been designed to stop these types of cells

from multiplying, which might help to reduce or delay tumour growth.

Olaparib (LynparzaTM) is a PARP (poly [adenosine diphosphate-ribose] polymerase) inhibitor, this means that olaparib stops an enzyme found in the body known as PARP from working. In our cells when DNA is damaged, PARP and the genes involved in the Homologous Recombination Repair (HRR) mechanism (such as the BRCA1 and BRCA2 genes) help to repair the broken strand of DNA. Olaparib aims to block the repair of DNA which can cause cancer cells to die. Previous studies have shown that olaparib significantly reduces the risk of progression in patients with recurrent ovarian cancer.

The combinatino of alpelisip and olaparib will be compared in this study to paclitaxel or PLD. PLD stands for pegylated liposomal doxorubicine. Paclitaxel or PLD are forms of chemotherapy, and are registered in the Netherlands. Both drugs will be administered through an IV directly into a vein. Paclitaxel every week and PLD once every 4 weeks.

Study objective

The purpose of the study is to determine whether treatment with alpelisib in combination with olaparib can delay the time to cancer progression compared to standard-of-care chemotherapy in participants with your type of ovarian cancer known as platinum resistant/refractory high-grade serous/ endometrioid ovarian cancer with no BRCA mutation.

Study design

A phase III study with multiple treatment arms, randomized in a 1:1 ratio between the combination therapy of olaparib+alpelisib and a chemotherapy of choice (paclitaxel or PLD).

Intervention

Participants are devided into 2 groups:
Group 1: Participants will receive tablets of alpelisib once a day and olaparib twice a day
Group 2: Participants will receive chemotherapy, with either paclitaxel (infusion each week) or PLD (infusion once every 4 weeks). The choice of drug belongs to the investigator.

Study burden and risks

The risks and side-effects associated with the treatments (olaparib+alpelisib or chemotherapy), aside from those the risks assocaited with the assessments in the study (bloddraw(s) imaging etc).

Burden:
Cycles of 4 weeks:
Cycle 1: 3-4 visits, depending on the group
Cycle 2: 3-4 visits, dpending on the group
Cycle 3 and on: 1-3 vistis depending on the group.

Duration of visits: usually 1-2 hours unless there is a course of blooddraws for pharmacokinetic assessment, depening on the given treatment such a visit can take between 2 and 5 hours.

During study visits other assessments are also performed, frequency and number of these assessments are dependent on the treatment and can include: physical exam, blooddraw(s), ECG(s), imaging studies, pregnancy testing and if necessary a tumor biopsy.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Participant has histologically confirmed diagnosis of high-grade serous or high-grade endometrioid ovarian cancer, fallopian tube cancer, or primary peritoneal cancer.

Measurable disease, i.e., at least one measurable lesion per RECIST 1.1 criteria (a lesion at a previously irradiated site may only be counted as a target lesion if there is clear sign of progression since the irradiation).

If no measurable disease is present, the disease should be assessable by Gynecologic Cancer Intergroup criteria (GCIC) for CA-125.

Participant has no germline BRCA1/2 mutation as determined by an FDA-approved assay.

Participant has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

Participant has received prior bevacizumab or is not eligible to receive bevacizumab due to medical reasons as per investigator*s discretion

Participant has platinum-resistant (progression within one to six months after completing platinum-based therapy) or platinum refractory disease (progression during treatment or within 4 weeks after the last dose), where platinum-based therapy is not an option, according to the GCIG 5th Ovarian Cancer Consensus Conference definitions (Wilson et al 2016). The platinum-based chemotherapy regimen does not necessarily need to be the last regimen the participant received prior to study entry.

Participant must have received at least one but no more than three prior systemic treatment regimens and for whom single-agent chemotherapy is appropriate as the next line of treatment.

Participant has adequate bone marrow and organ function.

Exclusion criteria

Participant has received prior treatment with any PI3K, mTOR or AKT inhibitor.
Participant is concurrently using other anti-cancer therapy.

Participant is in a state of small or large bowel obstruction or has other impairment of gastrointestinal (GI) function or GI disease.

Participant has had surgery within 14 days prior to starting study drug or has not recovered from major side effects.

Participant has not recovered from all toxicities related to prior anticancer therapies to baseline or NCI CTCAE Version 4.03 Grade <=1. Exception to this criterion: participants with any grade of alopecia are allowed to enter the study.

Participants with liver impairment and Child Pugh score B or C

Participant has received radiotherapy <= 4 weeks or limited field radiation for palliation <= 2 weeks prior to randomization, and who has not recovered to baseline, grade 1 or better from related side effects of such therapy (with the exception of alopecia).

Participant has a known hypersensitivity to any of the study drugs or excipients.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-09-2022
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Caelyx
Generic name:	pegylated liposomal doxorubicin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lynparza
Generic name:	olaparib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Piqray
Generic name:	alpelisib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxol / Onxol
Generic name:	paclitaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	24-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-03-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	30-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-004682-40-NL
ClinicalTrials.gov	NCT04729387

Register	ID
CCMO	NL77468.056.21