A randomised, double-blind, parallel group, placebo-controlled multi-centre Phase III study to assess the efficacy and safety of olaparib versus placebo as adjuvant treatment in patients with germline BRCA1/2 mutations and high risk HER2 negative primary breast cancer who have completed definitive local treatment and neoadjuvant or adjuvant chemotherapy.

Published: 12-05-2014
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This study has been transitioned to CTIS with ID 2024-511096-15-00 check the CTIS register for the current data. To assess the safety and tolerability of adjuvant treatment with olaparib

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast disorders
Study type	Interventional

Summary

ID

NL-OMON47654

Source
ToetsingOnline

Brief title
Olympia

Condition

- Breast disorders

Synonym
Breastcancer

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Adjuvant, BRCA, Breastcancer, Olaparib

Outcome measures

Primary outcome

Invasive Disease Free Survival (IDFS)

Secondary outcome

Overall Survival (OS)

Distant Disease Free Survival (DDFS)

New primary invasive breast cancer and/or epithelial ovarian cancer in patients

at risk for these events

FACIT-fatigue symptom scale and EORTC-QLQ-C30 HrQoL scale (questionnaires)

IDFS, DDFS and OS based on patients with gBRCA mutations confirmed by the

central test (only required if population differs from the ITT (intention to

treat) population)

To determine the exposure to olaparib (in plasma) in patients receiving

olaparib as adjuvant therapy

Study description

Background summary

Breast cancer is a life-threatening disease and is the second leading cause of cancer death among women.
Approximately 5% of breast cancers are associated with a mutation in the BRCA1 and/or BRCA2 gene with approximately 3% associated with the BRCA1 gene (generally presenting with TNBC phenotype) and approximately 2% associated with the BRCA2 gene (generally ER/PgR positive phenotype). In the general population, BRCA mutation carriers have an increased relative risk of breast cancer. Although there are phenotypic differences in breast cancers resulting from BRCA1 or BRCA2 mutations, their important commonality is that mutations in either gene result in tumours that are deficient in homologous recombination, making both appropriate for treatment with PARP inhibitors whereby the process of synthetic lethality can be exploited.
Olaparib (AZD2281) is a new agent that inhibits the protein called PARP. PARP allows DNA repair. Cancer is often caused by genetic abnormality and if that happens, the PARP activity can be increased. Olaparib can inhibit or block the activity of PARP, and has the potential to be effective, both as a single agent or in combination with chemotherapy. Olaparib can prevent the survival of cancer cells because the repair meganism of damaged DNA is prevented, so that the cancer cells die.
This Phase III study will investigate the efficacy and safety of olaparib administered as adjuvant therapy in patients with germline BRCA1/2 mutations and high risk HER2 negative primary breast cancer who have completed definitive local treatment and neoadjuvant or adjuvant chemotherapy or of when olaparib together with the hormaonal therapy (ER/PgR-positive patients)received.

Study objective

This study has been transitioned to CTIS with ID 2024-511096-15-00 check the CTIS register for the current data.

To assess the safety and tolerability of adjuvant treatment with olaparib

Study design

Phase 3, randomised, double-blind, parallel group, placebo-controlled multi-centre
Randomisation 1:1 with Olaparib 300 mg twice daily or Placebo twice daily 12 months treatment

Intervention

Treatment with Olaparib 300 mg or Placebo.

Study burden and risks

Patient will get a mammogram (patients older than 50 years) or breast MRI scan (patients younger than 50 years) every 6 months after start study treatment. Assessments will be done on a regular base, like physical examination, vital signs, blood sampling, ECGs and questionnaires. Pregnancy or breastfeeding is not allowed. The risks associated with the use of olaparib are: Anemia, neutropenea, lymphopenia, thrombocytopenie, heartburn, nausea, dizziness, diarrhea, vomiting and fatigue.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Histologically confirmed non-metastatic primary triple negative invasive adenocarcinoma of the breast.
TNBC or
ER and/or PgR positive/HER 2 negative patients
Documented mutation in BRCA1 or BRCA2 that is predicted to be deleterious or suspected deleterious (known or predicted to be detrimental/lead to loss of function).
Completed adequate breast and axilla surgery. Completed at least 6 cycles neoadjuvant or adjuvant chemotherapy containing anthracyclines, taxanes or the combination of both. Prior platinum as potentially curative treatment for prior cancer (e.g. ovarian) or as adjuvant or neoadjuvant treatment for breast cancer is allowed.
ECOG performance status 0-1.

Exclusion criteria

Any previous treatment with a PARP inhibitor, including olaparib and/or known hypersensitivity to any of the excipients of study treatment
Patients with second primary cancer, EXCEPTIONS: adequately treated non-melanoma skin cancer, curatively treated in situ cancer of the cervix, Ductal Carcinoma in situ (DCIS) of the breast, stage 1 grade 1 endometrial carcinoma, or other solid tumours including lymphomas (without bone marrow involvement) curatively treated with no evidence of disease for >= 5 years prior to randomization. More than one course of chemotherapy for previous malignancies
Resting ECG with QTc > 470 msec detected on 2 or more time points within a 24 hour period or family history of long QT syndrome. If ECG demonstrates QTc >470 msec, patient will be eligible only if repeat ECG demonstrates QTc <=470 msec
Whole blood transfusions in the last 120 days prior to entry to the study which may interfere with gBRCA testing

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-02-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nog niet bekend
Generic name:	Olaparib

Ethics review

Approved WMO Date:	12-05-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	26-08-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-01-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	27-01-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	04-05-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	11-05-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	10-07-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	06-10-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	26-02-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	16-03-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	06-07-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	23-08-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	12-11-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	14-03-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	23-04-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	04-07-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	31-03-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	28-09-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	19-01-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	16-04-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	23-04-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-03-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	22-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	17-07-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	19-12-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	19-01-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

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
Other	02032823
EU-CTR	CTIS2024-511096-15-00
EudraCT	EUCTR2013-003839-30-NL
CCMO	NL48725.058.14