Selecting Ovarian Cancer patients for PARP Inhibitor (SOPI) study

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON56928

Source
ToetsingOnline

Brief title
SOPI study

Condition

- Reproductive neoplasms female malignant and unspecified
- Ovarian and fallopian tube disorders

Synonym
ovarian cancer, Ovarian carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: KWF

Intervention

Keyword: HRD tests, Ovarian Cancer, PARP Inhibitor, RAD51

Outcome measures

Primary outcome

Progression Free Survival (PFS), defined as time from start PARP-i until progression of disease or death from any cause, whichever comes first.

Secondary outcome

1 year and 3-year PFS, overall survival, grade 3-4 hematological toxicity or grade >= 2 non-hematological toxicity leading to dose reduction or clinically significant interruption (>2weeks) or stop PARP-i , time to subsequent therapy, QoL and costs. We will collect blood and plasma samples during this research (opt-in) to study whether we are able to identify ct-DNA and to examine whether we are able to detect HRD using ct-DNA analysis. Some of the inclusion centers use other genomic tests to diagnose BRCA1/2 in the tumor-first project (KWF 12732). We will compare the data of these tests with the HRD tests of the SOPI study in an exploratory analysis. The Hartwig Medical Foundation will perform a WGS of all ovarian cancer patients who are included in the SOPI study. We will use and compare the WGS test with the results of our 3 tests.

Study description

Background summary

Epithelial ovarian cancer (EOC), including ovarian, tubal or peritoneal cancer, is one of the most deadly cancers in women in the western world, with a 5-year overall survival (OS) of 40%. The majority of patients present with advanced disease, classified as FIGO stage III-IV. Standard of care consists of

debulking surgery and platinum based chemotherapy, and if applicable, a maintenance therapy with a poly ADP-ribose polymerase (PARP)-inhibitor (PARP-i). PARP-i have been shown to be highly effective for patients with a germline or somatic BRCA1 or BRCA2 pathogenic variant, leading to improvements in OS and progression free survival (PFS). However, for the majority of patients, the benefit of PARP-i is less clear. Patients are selected for PARP-i treatment based on disease characteristics and response to platinum based chemotherapy. However, a reliable predictive test for clinical use is still lacking. This leads to a part of the patients being exposed to highly costly treatment with side effects without clinical benefit. Based on tumor biology, only patients with a homologous recombination deficient (HRD) tumor will benefit from PARP-i. Starting from January 1st 2024, only patients with a positive HRD test are eligible for PARP-i. However, it is not clear which test is the best in predicting HRD and which biomarker test predicts the best response to PARP-i. Preliminary data analyzing HRD in breast cancer showed around 30% discordance between three HRD tests. Direct comparison of HRD tests in clinical trials will therefore be required to evaluate the optimal predictive test for clinical decision making.
In the SOPI study we will evaluate three existing tests for identifying HRD tumors in EOC patients and identify the test that best predicts sensitivity for PARP-i. The societal impact of this project is considerable, since a reliable HRD test that can identify patients that are likely to benefit from PARP-i will reduce health care cost, protect patients from side effects and save time of patients and health care providers.

Study objective

The main objective of the SOPI study is to select the HRD test that best predicts longest PFS on PARP-i in non-BRCA1/2 EOC patients, in order to adequately select patients that will benefit from a PARP-i.
Secondary objectives are: to evaluate the 1-year and 3-year PFS for the non-BRCA1/2 mutant HRD group and the HRP group, defined according to each HRD test, the overall survival, the best test strategy correlated with the longest PFS in patients with advanced non-BRCA1/2 EOC treated with maintenance therapy PARP-i, quality of Life (QoL) of patients (with HRD tumors) using PARP-i, and cost-effectiveness for the three HRD tests.
Exploratory objectives are: to compare our tests to the Oncomine Comprehensive Assay plus HRD tests performed in Leiden, the HRD IHKV tumor-first test performed in Nijmegen and The WGS test performed by the Hartwig Medical Foundation and to compare QoL of patients (with HRD tumors) using PARP-i with a group of patients from the PlaComOv study that did not use PARP-i.

Study design

This is an observational multicenter study in advanced stage EOC patients who will receive standard of care treatment with cytoreductive surgery (CRS) and

platinum-based chemotherapy. PARP-i treatment will also be given in a selected group of patients as standard of care if applicable according to standard European and national guidelines. In general, this includes patients with a FIGO stage III-IV high grade serous/ endometrioid EOC with response to platinum based chemotherapy and a BRCA1/2 pathogenic variant and/or a positive HRD test. In the non-BRCA1/2 patients and we will compare the outcome of three HRD tests and determine which test correlates best with PFS. QoL will be studied throughout the study at predefined time points.

Study burden and risks

During regular procedures, tissue and blood samples will be collected, minimizing any additional burden on the patient. Patients will receive standardized QoL questionnaires pre-surgery, 4-6 weeks post-surgery, end of primary treatment/ before start of PARP-i, after 6-months, and then yearly post-surgery, until a maximum of 10 year after surgery. The time required to complete the QoL questionnaire is approximately 15 minutes each time. No extra hospital visits are planned for study procedures in the SOPI study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

For biopsy:
- Women with suspected EOC, aged 18 years or older who give informed consent for routine diagnostics including the sample for the HRD tests. In a subpopulation we will compare HRD tests on tissue obtained at interval CRS as well.
- Written informed consent

For Follow-up PARP-i:
- Patients with FIGO Stage III and IV EOC cancer who received standard of care with debulking surgery and platinum based chemotherapy and are eligible for PARP-i according to at least one positive HRD test.
- Patients with germline or somatic BRCA1/2 pathogenic variants in the tumor will be asked to participate as (positive) controls
- Patients without BRCA1/2 pathogenic variant or HRD: only registration of PFS, QOL and OS.

Control group:
- Included in the PlaComOv study (MEC-2017-500/NL62035.078.17) and given informed consent for the use of data for future research.

Exclusion criteria

- Impossibility to obtain HRD test
- Other diagnosis than epithelial ovarian cancer
- Mucinous, low grade serous or clear cell type ovarian cancer
- Ineligibility for PARP-i treatment: such as (but not exclusive)
o Not reached at least partial response to neoadjuvant chemotherapy
o FIGO stage I-II disease
o All HRD tests negative and no BRCA 1/2 carrier
- Patients who are not able to understand/sign the Informed Consent.
- Known germline BRAC1/2 mutation

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-08-2024
Enrollment:	778
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	23-07-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL86420.078.24