Signal TrAnsduction Pathway activity analysis for OVarian cancER treatment. STAPOVER study

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

Summary

ID

NL-OMON50803

Source
ToetsingOnline

Brief title
STAPOVER study

Condition

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

Synonym
Cancer of the ovary, ovarian carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis
Source(s) of monetary or material Support: Philips Molecular Pathway

Diagnostics,Philips Research

Intervention

Keyword: Ovarian cancer, Signal transduction pathways, Targeted therapy

Outcome measures

Primary outcome

The primary outcome is therapy response defined as PFS2/PFS1 ratio according to RECIST 1.1 criteria.

Secondary outcome

Secondary outcomes include the proportion of patients with an actionable active pathway and the proportion of patients receiving matched targeted therapy, best overall response (according to RECIST 1.1 criteria), one-year overall survival and overall survival, predictive value of STA-analysis results, side effects, quality of life, cost-effectiveness and change in pathway activity score after disease progression compared to the pathway activity score before the start of targeted therapy.

Study description

Background summary

Ovarian cancer is one of the most lethal cancers in the world due to late stage disease at diagnosis. Standard therapy consists of debulking surgery and chemotherapy. However, despite this aggressive treatment, recurrent disease almost invariably occurs resulting in a five-year survival rate of approximately 30%. Tumour growth is driven by several signal transduction pathways (STPs), and twelve major STPs have been identified as important for carcinogenesis. Currently, several targeted therapy drugs are available and new targeted drugs are being developed. With a newly developed technique, Signal Transduction Activation (STA) analysis, it is possible to assess which pathway is predominant in a specific (ovarian) cancer sample. Therefore, we hypothesize

that specifically targeting the predominant STP might impair tumour growth and improve survival.

Study objective

This study aims to investigate the progression-free survival (PFS) according to RECIST 1.1 criteria on matched targeted therapy by STA-analysis (PFS2) in comparison to the PFS recorded on the therapy administered immediately prior to enrolment (PFS1) in women with recurrent ovarian cancer.

Study design

Multicentre prospective cohort study with multiple stepwise executed treatment arms.

Intervention

STA-analysis will be performed on a biopsy taken from the recurrent tumour. Patients will be included if a predominant pathway is identified for which a matched targeted drug is available and deemed adequate by the multidisciplinary tumour board. We will start with targeted therapy in patients with oestrogen receptor, androgen receptor, phosphoinositide 3-kinase and Hedgehog pathway active tumours, since targeted therapy interceding these pathways are easily available with tolerable side effects.

Study burden and risks

Patients could experience potential benefits when they participate in this study, namely, that the strategy of selecting patients for treatment with targeted therapy based on STA-analysis will result in improved PFS, by tumour regression or stabilization, with maintaining quality of life. The potential risks for patients are the side effects of the targeted drug(s) used and thereby diminished quality of life, and the risk of ineffective treatment. The extra burden that comes with participation in this study consists of a histological biopsy with risk of pain and haemorrhage. This procedure is considered safe as there is ample experience with performing biopsies in patients with recurrent ovarian cancer.

Contacts

Public
Catharina-ziekenhuis

Michelangeloaan 2

Eindhoven 5623EJ
NL
Scientific
Catharina-ziekenhuis

Michelangeloaan 2
Eindhoven 5623EJ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age 18 years or older
- Patients with recurrent ovarian cancer who meet one of the following criteria:
1. Platinum-resistant disease or;
2. Patients refrains from standard therapy or;
3. Asymptomatic patients who are not yet eligible for standard palliative chemotherapy but have an increase of CA125 tumour marker at two consecutive timepoints 28 days apart with a value of two times nadir above 35 U/ml).
- Progressive disease after at least one prior line of systemic treatment for recurrent disease.
- Radiologically evaluable disease according to RECIST 1.1 criteria.
- Ability and willingness to obtain a tumour biopsy after the last course of standard treatment and before start of the study.
- Ability and willingness to provide written and oral consent.
- Able to speak and understand the Dutch language.
- WHO performance status 0-II.
- Adequate renal and liver function to start matched targeted therapy (according to the local clinician).
- Adequate use of contraceptives in case of patients with childbearing

potential.

Exclusion criteria

- Age < 18 years.
- Patient is receiving any other anti-cancer therapy (e.g. cytotoxic or targeted drug or radiation) or is chemotherapy naïve. The required wash out period prior to start of matched targeted therapy is at least three weeks.
- Patient is diagnosed with or treated for a second primary tumour (except non-melanoma skin tumour) one year prior to study inclusion.
- Inability to obtain (sufficient) tumour material.
- Previous use of the selected targeted drug as anti-cancer agent.
- Physical condition WHO III-IV.
- Pregnant or lactating women.
- Contra-indication for the use of the matched targeted therapy.
- Simultaneous participation in another treatment-related clinical trial.
- Patients with any other clinically significant medical condition which, in the opinion of the local clinician, makes it undesirable for the patient to participate in this study or which could jeopardize compliance with study requirements including, but not limited to: ongoing or active infection, severe psychiatric illness, or complicated social situations.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	31-01-2023
Enrollment:	148

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Afinitor
Generic name:	Everolimus
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Bicalutamide
Generic name:	Bicalutamide
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Itraconazole
Generic name:	Itraconazole
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Letrozole
Generic name:	Letrozole
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-05-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-08-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-11-2021
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2020-005091-36-NL
Other	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□NCT□□□□□□□□03458221
CCMO	NL77022.100.21

Study results

Date completed: 20-11-2024

Summary results
Trial ended prematurely