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Heated intraperitoneal chemotherapy for the treatment of primary ovarian cancer

Submission date 05/12/2024	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 10/04/2025	**Overall study status** Completed	
Last Edited 10/04/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

This trial is for patients with FIGO stage III epithelial ovarian cancer who are eligible for primary cytoreductive surgery. Patients will receive primary cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy.

Hyperthermic intraperitoneal chemotherapy (HIPEC) involves administering a heated chemotherapy solution at a temperatures of 41-42°C into the peritoneal cavity [abdomen and pelvis] after cytoreductive surgery. Heated chemotherapy increases the penetration of chemotherapy administered into tissues in the abdominal and pelvic cavity.

A previous study (OVHIPEC-1) showed that combining hyperthermic intraperitoneal chemotherapy (HIPEC) with interval cytoreductive surgery (that is, surgery performed in patients initially treated with intravenous chemotherapy) significantly improves recurrence-free and overall survival for patients. A survival benefit of nearly one year was shown in patients who underwent HIPEC compared to those who did not have HIPEC. Patients in the OVHIPEC-1 study were ineligible for primary cytoreductive surgery due to extensive intra-abdominal disease and were instead initially treated with intravenous chemotherapy .

Who can participate?

Patients aged 18 years or older, with histologically proven FIGO stage III primary epithelial ovarian, fallopian tube, or extra-ovarian cancer, treated with primary complete cytoreduction, or primary cytoreduction with no more than 2.5 mm residual disease.

What does the study involve?

In the OVHIPEC-2 study, all patients will initially be treated with cytoreductive surgery with or without HIPEC. The study will evaluate whether patients treated with initial cytoreductive surgery and HIPEC have an increased overall survival compared to the overall survival in patients who are initially treated with surgery alone.

Follow-up visits will be scheduled every 3 months in the first two years and every six months during years 3-5.

What are the possible benefits and risks of participating?

Benefits:

Not provided at time of registration

Risks:
Potential for kidney toxicity - offset by use of sodium thiosulphate. Patients who receive HIPEC will have an additional 2-2.5 hours of general anaesthesia. Multiple studies indicate that patient safety is not compromised in those receiving HIPEC . If during the surgical procedure the patient is not well, or the surgical goal is not achieved [no visible disease, or any residual disease must be < 2.5mm in maximum diameter] then they will not be randomised in the study and will not receive HIPEC

Where is the study run from?
The Netherlands Cancer Institute

When is the study starting and how long is it expected to run for?
January 2020 to April 2026

Who is funding the study?
Dutch Cancer Foundation (Netherlands)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
2018-003346-17

Integrated Research Application System (IRAS)
1010654

ClinicalTrials.gov (NCT)
NCT03772028

Protocol serial number
Nil known

Study information

Scientific Title
Heated intraperitoneal chemotherapy (HIPEC) for the treatment of primary ovarian cancer

Acronym
OVHIPEC-2

Study objectives
Primary objective:
To compare the overall survival rates in patients with primary ovarian cancer whose initial treatment was with surgery alone or surgery with heated intraperitoneal chemotherapy.

Secondary objectives:
1. To look at recurrence-free survival rates in patients with primary ovarian cancer whose initial treatment was with surgery alone or surgery with heated intraperitoneal chemotherapy.
2. To look at the time to the first subsequent anticancer treatment after first recurrent disease in patients with ovarian cancer whose initial treatment was with surgery alone or surgery with heated intraperitoneal chemotherapy.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 28/01/2025, South Central - Berkshire Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048143; berkshire.rec@hra.nhs.uk), ref: 24/SC/0412

Study design
Interventional randomized controlled trial

Primary study design

Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Stage III epithelial ovarian cancer

Interventions
There are two trial arms.

1. HIPEC – Intervention Arm
•Primary cytoreductive surgery with HIPEC (Hyperthermic Intraperitoneal Chemotherapy) with cisplatin
Cytoreductive Surgery is performed to remove all visible disease from the abdomen and pelvis. After 90 minutes the abdomen and pelvis are thoroughly irrigated and sodium thiosulphate is administered intravenously to protect the kidney function.

2. Conventional Surgery – Standard of Care
•Primary cytoreductive surgery without HIPEC
Cytoreductive Surgery is performed to remove all visible disease from the abdomen and pelvis.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Cisplatin

Primary outcome(s)
1. Overall survival is measured using patient records at baseline and at each follow-up visit
2. Survival time points for patients who are alive is measured using patient records at the date of last contact
3. Overall survival for patients with no follow-up is measured using patient records at the date of randomization

Key secondary outcome(s))
1. Recurrence-free survival is measured using GCIG criteria in combination with clinical and/or radiological assessments at baseline and at each follow-up visit
2. Time to first subsequent anticancer treatment after first recurrent disease (TFST) is measured using patient records at the time of recurrence and at each follow-up visit
3. Toxicity and morbidity are measured using patient records and clinical assessments at baseline, during chemotherapy, and 30 days after the end of chemotherapy

Completion date
01/04/2026

Eligibility

Key inclusion criteria
1. Signed and written informed consent
2. Age ≥18 years
3. Histological proven FIGO stage III primary epithelial ovarian, fallopian tube, or extra-ovarian cancer, treated with primary complete cytoreduction, or primary cytoreduction with no more than 2.5 mm residual disease
a. in case of extra-abdominal enlarged lymph nodes, representative cytology/histology or FDG-PET scan must be negative;
b. resectable, local bowel involvement, iatrogenic abdominal wall metastases or umbilical lesions are allowed;
c. in case no histological proof is available before surgery, patients can be randomized during surgery based on histological proof on intraoperative frozen section material
4. Fit for major surgery, WHO performance status 0-2
Adequate bone marrow function (haemoglobin level >5.5 mmol/L; leukocytes >3 x 10^9/L; platelets >100 x 10^9 /L)
6. Adequate hepatic function (ALT, AST and bilirubin <2.5 times upper limit of normal)
a. in case of Gilbert's disease: unconjugated bilirubin <5 times upper limit of normal
7. Adequate renal function (creatinine clearance ≥ 60 ml/min or ml/min/1.73 m² using either MDRD, Cockcroft-Gault formula, or CKD-EPI)
8. Baseline health-outcome questionnaire should be completed before randomization
9. Able to understand the patient information and questionnaires.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. History of previous malignancy treated with chemotherapy
2. History of previous malignancy within five years prior to inclusion, with the exception of carcinoma in situ, radically excised basal cell or squamous cell cancer of the skin or synchronous endometrial carcinoma FIGO IA G1/2
3. If complete primary cytoreduction is not feasible, for the following reasons:
a. diffuse deep infiltration of the root of small bowel mesentery, or;
b. diffuse carcinomatosis of the small bowel that requires resection that leads to short bowel syndrome (remaining bowel <1.5 meter), or;
c. diffuse involvement/deep infiltration of stomach/duodenum, or;
d. diffuse involvement/deep infiltration of head or middle part of pancreas, or;
e. involvement of truncus coeliacus , hepatic arteries or left gastric artery, or;
f. non-resectable enlarged (larger than 10 mm short axis) lymph nodes
4. In case of a known psychiatric disorder, substance abuse disorder, or high suspicion of a

mental disorder that could interfere with cooperation or compliance with the requirements of the trial
5. When opting for fertility sparing surgery, or when breastfeeding
6. In case of a known history of Human Immunodeficiency Virus (HIV, or HIV 1/2 antibodies)
7. In case of known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA [qualitative])
8. Patients who received prior treatment for the current malignancy.

Date of first enrolment
01/01/2020

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
England

Denmark

France

Ireland

Italy

Netherlands

Sweden

Study participating centre
The Royal Marsden NHS Foundation Trust
Downs Road
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SM2 5PT

Sponsor information

Organisation
The Netherlands Cancer Institute

ROR
https://ror.org/03xqtf034

Funder(s)

Funder type
Charity

Funder Name
Dutch Cancer Foundation

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication