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SOPRANO - Stereotactic radiotherapy alone or stereotactic radiotherapy follow by niraparib treatment for ovarian cancer with progressive disease in three or less lesions, or recurrence of 3 or less metastatic lesions that had previously achieved complete response.

Submission date 02/08/2023	**Recruitment status** Recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 30/10/2023	**Overall study status** Ongoing	
Last Edited 09/07/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

Oligometastases or oligoprogression (spreading) of ovarian cancer whilst being treated with a PARP Inhibitor (PARPi) may occur due to a secondary mutation causing resistance to treatment in a small volume of the tumour rather than total tumour resistance. Eradication of the resistant disease with stereotactic radiotherapy (SBRT) would enable the continuation of the PARPi treatment to maintain control of the part of the tumour that has retained drug sensitivity and this has the potential to extend the time to disease progression. The aim of this study is to determine whether the use of SBRT with or without niraparib increases the number of patients without disease progression at 6 months.

Who can participate?

Patients aged 18 years and over with oligometastatic or oligoprogressive ovarian, fallopian tube or primary peritoneal carcinoma.

What does the study involve?

Patients will be randomly allocated to receive either SBRT followed by the PARPi niraparib (cohort 1) or SBRT alone (cohort 2). SBRT will be administered in accordance with the SOPRANO Radiotherapy and Quality Assurance Guidelines for each site of metastases and will consist of between three and eight fractions of radiotherapy spread over 5 to 19 days. Patients in cohort 1 will then receive niraparib once daily until disease progression (200 or 300 mg depending on weight and blood results). All patients will attend follow-up visits for clinical and imaging assessments every 8 weeks during the first year, reducing to every 12 weeks thereafter until disease progression.

What are the possible benefits and risks of participating?
There is no guarantee that patients will benefit directly from taking part in this trial. SBRT is given with the aim of shrinking cancer and/or delaying time to cancer worsening. The aim of this trial is to find out whether SBRT is helpful in the treatment of recurrent or metastatic ovarian cancer and if treatment with SBRT either with or without Niraparib, may help increase the length of time before patients need to start a different treatment such as chemotherapy, as this is not currently known. The information gained from this trial may help in the treatment of patients with recurrent or metastatic ovarian cancer in the future.
Patients randomised to cohort 1 will be required to undergo additional blood tests, blood pressure and heart rate assessments to comply with the safety requirements for niraparib. All other visits will be in line with standard of care visits. The visit schedule and the assessments that will take place at each visit are explained in the SOPRANO patient information sheet.
Patients' GPs will be informed of their participation in the trial.
Patients will have regular blood tests which may cause discomfort, bruising, bleeding or, rarely, infection. We have coordinated research blood collections alongside the mandatory safety blood tests which will help minimise the discomfort and ensure the safety of patients. All blood draws are completed before the patient receives treatment.
As part of the patient's involvement in this study they will undergo CT/MRI/PET CT scans every 8 weeks (scan modality is not mandated, but sites are asked to ensure the same modality is used at each time point). The x-rays used for CT/PET CT scans mean that they will be exposed to ionising radiation. There is a small increased risk from any radiation dose of inducing cancer several years after exposure. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. The current clinical condition of SOPRANO patients means the chance of this happening is extremely small. There is no radiation risk from MRIs.
Niraparib has been or is currently under evaluation as a single agent or in combination with other anticancer therapies in Phase 1 through Phase 3 clinical studies and has included over 1600 participants in studies of ovarian cancer. Niraparib is licensed in Europe including UK for the following indications:
• as monotherapy for the maintenance treatment of adult patients with advanced epithelial (FIGO Stages III and IV) high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy.
• as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.
A joint Independent Data Monitoring and Steering Commitee (IDMSC) will be set up for the SOPRANO trial. The IDMSC will meet regularly to review safety and assess the adverse events of all patients on trial. All patients will be encouraged to inform their clinician if they are experiencing any ill effects, whether they think it is related to the trial treatment or not. Investigators will be kept informed of any emerging safety data that may impact their patients' participation in the trial as the sponsors becomes aware of it.
The dose and fractionation schedule of SBRT treatment will be in accordance with the SOPRANO Radiotherapy and Quality Assurance Guidelines for each site of metastases. The NCRI Radiotherapy Trials Quality Assurance (RTTQA) group will oversee the quality assurance of the SBRT delivered within the trial to ensure the safety and consistency of radiotherapy delivery at participating centres. Prior to inclusion in the trial, individual centres will need to demonstrate they have robust procedures in place to ensure high-quality RTTQA planning and delivery guidelines will be met. During recruitment and prior to any repeat SBRT treatment, prospective review will be performed for all patients.

Where is the study run from?
Institute of Cancer Research Clinical Trial & Statistics Unit (UK)

When is the study starting and how long is it expected to run for?
July 2023 to June 2027

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
Lorna Smith, SOPRANO-icrctsu@icr.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1006425

ClinicalTrials.gov (NCT)
NCT05990192

Protocol serial number
ICR-CTSU/2022/10082, IRAS 1006425, CPMS 54603

Study information

Scientific Title
Stereotactic radiotherapy alone or followed by niraparib for oligometastases or oligoprogression in ovarian cancer following PARP inhibitor therapy

Acronym
SOPRANO

Study objectives
Primary objectives:
The primary objective of the trial is to determine whether in patients with oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma the use of SBRT with or without niraparib increases progression free survival (PFS) at 6 months.

Secondary objectives:
1. To determine whether in patients with oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma the use of SBRT with or without niraparib increases the time to first subsequent therapy
2. To evaluate if SBRT with or without niraparib improves progression free survival outcomes in this patient population
3. To evaluate if SBRT with or without niraparib increases the proportion of patients who are free from disease progression after 6 months from randomisation
4. To evaluate the lesion local control rates in those receiving SBRT with or without niraparib
5. To evaluate the time to disease progression occurring outside the SBRT-treated field
6. To evaluate the acute and late toxicity in patients receiving SBRT with or without niraparib

7. To evaluate the quality of life (QoL) in patients receiving SBRT with or without niraparib
8. To demonstrate feasibility of recruitment to a trial of SBRT with or without Niraparib in this patient population

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 26/10/2023, London - Brighton & Sussex Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London , E20 1JQ , United Kingdom; +44 (0)207 104 8202, +44 (0)207 104 8016, +44 (0)207 104 8140; brightonandsussex.rec@hra.nhs.uk), ref: 23/LO/0719

Study design
Randomized parallel trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Oligometastatic or oligoprogressive ovarian, fallopian tube or primary peritoneal carcinoma

Interventions
Cohort 1
SBRT followed by niraparib
Stereotactic body radiotherapy (SBRT) treatment will commence within 7 days post-randomisation and will be administered as detailed in the SOPRANO Radiotherapy Planning and Delivery Guidelines document. Doses will vary between three fractions over 5 days to eight fractions over 19 days depending on the location of the lesions being treated.
Niraparib treatment will start 4 weeks post-completion of SBRT treatment and will continue daily until disease progression or other discontinuation criteria are met. Niraparib comes in oral tablet form and the starting dose will be 200 mg per day (once a day) or 300 mg per day (once a day) calculated by the participant's weight and platelet count. Patients will remain on niraparib treatment until disease progression or other discontinuation criteria are met. Clinic visits will be monthly for 6 months reducing to 2 monthly at the investigator's discretion. Disease assessments will be 2 monthly for the first year and 3 monthly thereafter until disease progression meeting the primary endpoint.

Cohort 2
SBRT alone
SBRT treatment will commence within 7 days post-randomisation and will be administered as detailed in the SOPRANO Radiotherapy Planning and Delivery Guidelines document. Doses will vary between three fractions over 5 days to eight fractions over 19 days depending on the location of the lesions being treated. Disease assessments will be 2 monthly for the first year and 3 monthly thereafter until disease progression meeting the primary endpoint.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Progression-free survival is defined as time from randomisation to evidence of progression of cancer at any site or death from any cause. Progression events should be imaging defined in all tumour types according to RECIST v1.1 criteria. Where SBRT-specific consensus response assessment criteria exist for specific sites (e.g. spine), progression of SBRT-treated lesions will be defined according to these guidelines. The primary timepoint of most interest for PFS is at 6 months after randomisation.

Key secondary outcome(s))
1. Time to first subsequent systemic therapy is defined as time from randomisation to commencing the next systemic line of therapy or death from any cause (if this occurs before commencement of first subsequent treatment). Assessed up to 2 years after randomisation.
2. Time to first subsequent anti-cancer therapy is defined as time from randomisation to commencing the next line of therapy (local or systemic) or death from any cause (if this occurs before commencement of first subsequent treatment). Assessed up to 2 years after randomisation.
3. Overall survival (OS) defined as time from randomisation to death from any cause. The primary timepoint of interest for OS is at 2 years after randomisation.
4. Local control at site of SBRT is defined as time from randomisation until radiological evidence of progression at the treated site and be measured on a lesion-based analysis using RECIST v1.1 criteria. Assessed up to 2 years after randomisation.
5. Time to 'Out of SBRT field' progression is defined as time from randomisation until radiological evidence of progression outside of treated area(s) for SBRT treatment using RECIST v1.1. Assessed up to 2 years after randomisation.
6. Clinician reported acute and late toxicity will be graded using NCI CTCAE v5.0. Adverse events will be collected from the start of treatment to disease progression and 30 days post the last dose of niraparib for patients in cohort 1. Acute events are defined as those occurring up to 3 months follow up; late events are reported from 6 months post-randomisation.
7. Quality of life assessed using Functional Assessment of Cancer Therapy - Ovarian (FACT-O) at baseline prior to the start of SBRT treatment, 4 weeks post SBRT treatment, 16, 24 and 48 weeks post-randomisation and at disease progression
8. Quality of life assessed using EQ-5D-5L at baseline prior to the start of SBRT treatment, 4 weeks post SBRT treatment, 16, 24 and 48 weeks post-randomisation and at disease progression
9. Feasibility of recruitment rate for the trial, defined as the recruitment rate for the trial. Time frame: recruitment is expected to be over 2.5 years
10. Proportion of patients receiving SBRT in the absence of new developing widespread disease, defined as greater than or equal to four metastatic sites, regional or distant, or a combination thereof. Assessed up to 2 years after randomisation.

Other pre-specified outcome measures:
1. Time to widespread metastatic disease measured from the time of randomisation until radiological evidence of widespread metastatic disease, defined as greater than or equal to 4 metastatic sites, regional or distant, or a combination thereof. Assessed up to 2 years after randomisation.
2. Time to second subsequent therapy is defined as time from initiation of first subsequent

therapy to commencing second line of therapy (local or systemic) or death (if this occurs before commencement of second subsequent treatment). Assessed up to 2 years after randomisation.
3. Mechanisms of PARP inhibitor resistance, immune-mediated effects, radiosensitivity and toxicities, measured between baseline and 4 weeks post-SBRT, 16, 24 and 48 weeks post randomisation, and disease progression.

Completion date
30/06/2027

Eligibility

Key inclusion criteria
1. Patients ≥18 years of age (Updated 07/11/2023: previously ≥16 years of age)
2. Histologically confirmed epithelial ovarian, fallopian tube or primary peritoneal cancer
3. Radiological disease progression whilst on, or following, any prior PARP inhibitor therapy. The PARP inhibitor is required to have been the patient's last systemic therapy
4. Minimum duration of 6 months PARP inhibitor therapy as first-line therapy or treatment for recurrent disease
5. ≤3 lesions of progressive disease
6. Each lesion to undergo SBRT <4 cm axial diameter, and feasible for SBRT as discussed in the virtual SOPRANO virtual MDT (vMDT) meeting.
7. Measurable disease by RECIST criteria v1.1, which can be accurately assessed at baseline by CT or MRI. Patients with CA125 progression in the absence of measurable disease will NOT be eligible
8. No contra-indication to restarting a PARP inhibitor
9. Patients for whom surgery for recurrent disease is not planned.
10. Adequate baseline organ function to allow SBRT to all relevant targets as deemed by the investigator. Note: For Patients randomised to the SBRT followed by the Niraparib Cohort confirm the following prior to Niraparib initiation; Absolute neutrophil count: ≥1,500/μL, Platelets: ≥100,000/μL, Hemoglobin: ≥9 g/dL
11. ECOG performance status of 0 or 1
12. Predicted life expectancy ≥ 6 months
13. Women of child-bearing potential who are confirmed NOT to be pregnant. This should be evidenced by a negative urine or serum pregnancy test within 72 hours prior to the start of trial treatment. Patients will be considered to be not of child-bearing potential if they are:
13.1. Post-menopausal - defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments, OR women under 50 years old who have been amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments and have serum follicle-stimulating hormone (FSH), luteinizing hormone (LH) and plasma oestradiol levels in the post-menopausal range for the institution
13.2. Able to provide documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation
13.3. Radiation or chemotherapy-induced oophorectomy or menopause with >1 year since last menses
14. Willingness to commit to scheduled visits, treatment plans, laboratory tests and trial procedures
15. Histological tissue specimen (tissue block or 8-10 unstained slides) must be available prior to commencing SBRT (specimen can be the sample at diagnosis or taken at relapse or progression). Otherwise, a biopsy must be carried out to obtain sufficient tissue for translational analyses
16. Able to swallow, absorb and retain oral medication
17. Able to provide written, informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Co-morbidities which would preclude the safe use of SBRT
2. Progressing or newly diagnosed brain metastases identified at the time of trial entry, not amenable to radical surgery or stereotactic radiosurgery. Previously treated brain metastases (i.e. palliative radiotherapy or systemic therapy) which have remained clinically and radiologically stable for ≥6 months are permissible
3. Prior radiotherapy near the oligometastatic/oligoprogressive lesion precluding ablative SBRT. Suitability of lesions for ablative SBRT as part of the trial defined in section 6.1 of this document and will be determined by the SOPRANO virtual MDT
4. Treatment with any other investigational medicinal product within the 4 weeks prior to trial entry
5. Pregnant or lactating women
6. Women of childbearing age and potential who are not willing to use a highly effective contraceptive measure as detailed in protocol Section 5.5
7. Any unresolved toxicities from prior therapy should be no greater than CTCAE Grade 1 with the exception of Grade 2 alopecia or chemo-induced neuropathy at trial entry
8. Clinical/radiological evidence of bowel obstruction (e.g. hospitalisation) or symptoms of sub-acute bowel obstruction within 6 weeks prior to trial entry
9. Any other malignancy which has been active or treated within the past 3 years, with the exception of non-melanoma skin cancer. If prior treatment for another malignancy has taken place, then confirmation of ovarian/fallopian tube/peritoneal cancer progression is required e.g. biopsy, and discussion with the Chief Investigator and SBRT Lead
10. Judgment by the Investigator that the patient is unsuitable to participate in the trial and/or the patient is unlikely to comply with trial procedures, restrictions and requirements

Date of first enrolment
01/08/2024

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
The Royal Marsden Hospital (sutton)
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Study participating centre
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Sponsor information

Organisation
Institute of Cancer Research Clinical Trial & Statistics Unit

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from SOPRANO-icrctsu@icr.ac.uk via completion of a data access request form after such time that the primary analysis publication and any other key analyses have been completed. Optional advanced consent/authorisation for the possible future sharing of information collected about patients will be obtained at study entry.

Requests are via a standard proforma describing the nature of the proposed research and the extent of data requirements. Data recipients are required to sign a data release form which describes the conditions for release and requirements for data transfer, storage, archiving, publication and Intellectual Property. Data sharing will be in accordance with the ICR Policy on Sharing Personal Data which is in line with the requirements of the United Kingdom General Data Protection Regulations (UK GDPR). Data is not normally shared until the primary trial results have been published so as not to compromise the principal research question. Restrictions relating to patient confidentiality and consent will be limited by aggregating and anonymising identifiable patient data. Additionally, all indirect identifiers that may lead to deductive disclosures will be removed in line with Cancer Research UK Data Sharing Guidelines. All participants will be required to provide written consent to participate in the clinical trial at which point consent for data sharing will also be sought. Requests for data will be reviewed by the Trial Management Group (TMG) in terms of scientific merit and ethical considerations including patient consent. Data sharing will be undertaken if proposed projects have a sound scientific or patient benefit rationale as agreed by the TMG and approved by the independent IDMSC.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes