SOPRANO: Stereotactic radiotherapy alone or followed by niraparib for oligometastases or oligoprogression in ovarian cancer following PARP inhibitor therapy.

SPONSOR	The Institute of Cancer Research
CHIEF INVESTIGATOR	Professor Susana Banerjee
SBRT LEAD INVESTIGATOR	Dr Alexandra Taylor
TARGET DISEASE	Oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma defined as ≤3 metastatic sites of disease or 3 sites of disease progression. For the purposes of this trial, • Oligoprogression refers to the situation whereby 3 or fewer lesions of disease show evidence of progression. If there were previously other sites of disease, these remain in response or with stable disease. • Oligometastatic disease refers to the situation whereby complete response to treatment has previously been obtained and the disease relapse occurs that is limited in number and distribution (≤3 metastatic/recurrent lesions).
BACKGROUND AND RATIONALE	Oligometastases or oligoprogression of ovarian cancer while on a PARP inhibitor (PARPi) may occur due to a secondary sub-clonal mutation causing acquired resistance in a small volume of tumour rather than having global tumour resistance. Eradication of the resistant disease with stereotactic radiotherapy (SBRT) would enable continuation of the PARPi to maintain control of disease that has retained drug sensitivity and this has the potential to impact disease outcomes. This trial explores whether there is activity of SBRT and SBRT followed by niraparib in the case of oligometastatic or oligoprogression disease post prior PARPi in recurrent ovarian cancer.
TRIAL DESIGN	SOPRANO is a multi-centre, randomised phase II trial designed to assess the impact of SBRT and of continuing treatment with a PARPi for patients with oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma. SOPRANO will also establish the feasibility and acceptability of delivering SBRT in this setting. Patients will be randomised to one of two parallel non-comparative treatment cohorts: • Cohort 1: SBRT followed by niraparib • Cohort 2: SBRT alone In both cohorts, therapy continues until disease progression deemed by the investigator to warrant a change in treatment, unacceptable toxicity, withdrawal of consent or if the investigator decides it is not in the best interest of the patient to continue. Adverse events, including toxicity from trial treatment will be collected and graded according to The National Cancer Institute (NCI) Common Terminology Criteria (CTC) Version 5.0 (http://ctep.cancer.gov/reporting/ctc.html). Patients will be asked to consent for future linkage with routinely collected health data via national registries to trace their eventual vital status and assess

	subsequent unexpected comorbidities. Assessment of disease by RECIST will be required 8 weekly following completion of SBRT for the first year and 12 weekly thereafter until disease progression meeting the primary endpoint.
PRIMARY TRIAL OBJECTIVE	To evaluate progression free survival in patients with oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma being treated with Stereotactic Body Radiotherapy (SBRT) with or without niraparib.
KEY SECONDARY OBJECTIVES	• To determine time to first subsequent therapy in patients with oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma being treated with SBRT with or without niraparib • To evaluate overall survival in patients with oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma being treated with SBRT with or without niraparib • To evaluate the lesion local control rates in those receiving SBRT with or without niraparib. • To evaluate the time to disease progression occurring outside the SBRT-treated field. • To evaluate the acute and late toxicity in patients receiving SBRT with or without niraparib. • To evaluate the quality of life (QoL) in patients receiving SBRT with or without niraparib. • To demonstrate feasibility of recruitment to a trial of SBRT with or without niraparib in patients with oligometastatic or oligoprogressive ovarian, fallopian tube and primary peritoneal carcinoma.
PRIMARY ENDPOINT	• Progression free survival
KEY SECONDARY ENDPOINTS	• Time to first subsequent systemic anti-cancer therapy (TFST). • Time to first subsequent anti-cancer therapy (local or systemic). • Overall survival • Local control at site of SBRT • Time to 'Out of SBRT field' progression. • Clinician reported acute and late toxicity (CTCAE v5.0). • Patient reported QoL (FACT-O and EQ-5D questionnaire). • Feasibility of recruitment • Proportion of patients receiving SBRT in the absence of new developing widespread disease.
RECRUITMENT TARGET	~42 patients randomised over 2.5 years: • 21 SBRT followed by niraparib • 21 SBRT alone
NUMBER OF CENTRES	Approximately 4-6 recruiting centres in the UK