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The SCOPE 2 Trial: Study of chemoradiotherapy in oesophageal cancer including PET response and dose escalation

Submission date 12/09/2016	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 26/10/2016	**Overall study status** Ongoing	
Last Edited 05/03/2025	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-improving-chemoradiotherapy-for-people-with-cancer-of-the-food-pipe-scope-2

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-001740-11

Integrated Research Application System (IRAS)
169633

ClinicalTrials.gov (NCT)
NCT02741856

Protocol serial number
20358, IRAS 169633

Study information

Scientific Title
A randomised Phase II/III trial to study radiotherapy dose escalation in patients with oesophageal cancer treated with definitive chemoradiation with an embedded Phase II trial for patients with a poor early response using positron emission tomography (PET)

Acronym
SCOPE2

Study objectives
Phase II/III trial:
The aim of this study is to evaluate whether increasing the dose of radiotherapy improves outcomes in patients with tumour of the oesophagus.

Embedded Phase II trial:
The aim of this study is to compare the effects of the standard drugs used in chemotherapy (cisplatin and capecitabine) with an alternative combination (carboplatin and paclitaxel) in patients that do not show a response to chemotherapy with standard drugs early on in treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)

National Institute for Social Care and Health Research Research Ethics Committee, 22/01/2016, ref: 15/WA/0392

Study design
Factorial open-label randomised parallel phase II/III trial with embedded factorial open-label randomised parallel phase II trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Oesophageal cancer

Interventions
Prior to the commencement of treatment each patient will have a PET scan. Consenting patients will receive a second PET scan two weeks after the start of standard chemotherapy. The changes between the two scans will then be used to allocate treatment into the different arms of the study.

All study subjects will be randomised to receive either the standard radiotherapy dose or the high radiotherapy dose. The participants that do not respond to the first cycle of standard chemotherapy will be eligible to take part in the aspect of the trial looking at an alternative chemotherapy regimen.

On the basis of the second PET scan, patients who are not responding to standard chemotherapy will be allocated by a computer to one of the four groups detailed below:

Experimental: Arm 1 (carboplatin/paclitaxel+standard RT dose)
Cycle 1: Week 1-3: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 2: Week 4-6: carboplatin AUC 5 on D1 and paclitaxel 175mg/m2 on D1
Week 7-11: Weekly carboplatin AUC 2 and paclitaxel 50mg/m2 concomitant with radiotherapy (50Gy/25 fractions)
Interventions:
Drug: Carboplatin
Drug: Paclitaxel
Drug: Cisplatin
Drug: Capecitabine
Radiation: Radiotherapy

Experimental: Arm 2 (cisplatin/capecitabine+standard RT dose)
Cycle 1: Week 1-3: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 2: Week 4-6: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 3: Week 7-9: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 4: Week 10-11: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-12
Cycles 3 and 4 are given concomitantly with radiotherapy (50Gy/25 fractions). Capecitabine stops on last day of RT.
Interventions:

Drug: Cisplatin
Drug: Capecitabine
Radiation: Radiotherapy

Experimental: Arm 3 (carboplatin/paclitaxel+high RT dose)
Cycle 1: Week 1-3: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 2: Week 4-6: carboplatin AUC 5 on D1 and paclitaxel 175mg/m2 on D1
Week 7-11: Weekly carboplatin AUC 2 and paclitaxel 50mg/m2 concomitant with radiotherapy (60Gy/25 fractions)
Interventions:
Drug: Carboplatin
Drug: Paclitaxel
Drug: Cisplatin
Drug: Capecitabine
Radiation: Radiotherapy

Experimental: Arm 4 (Cisplatin+Capecitabine+high RT dose)
Cycle 1: Week 1-3: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 2: Week 4-6: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 3: Week 7-9: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-21
Cycle 4: Week 10-11: cisplatin 60mg/m2 on D1 and capecitabine 625mg/m2 bd D1-12 Cycles 3 and 4 are given concomitantly with radiotherapy (60Gy/25 fractions). Capecitabine stops on last day of RT.
Interventions:
Drug: Cisplatin
Drug: Capecitabine
Radiation: Radiotherapy

Patients who are responding to standard chemotherapy (or where the response is unknown or those who were not eligible for PET scan portion of the study) will be allocated by a computer to either Arm 2 or Arm 4.

The effects of the different treatment, together with the costs of the different treatment and the effects on quality of life will be analysed to see which is more effective for each of the different groups. This study will also compare the way that this treatment affects the two different cell types found in oesophageal tumours.

Intervention Type
Other

Primary outcome(s)
1. Treatment failure free survival (TFFS) is measured using endoscopic biopsy and CT scan at 24 weeks
2. Overall survival is measured using clinical assessment at all trial visits up to 5 years

Key secondary outcome(s))
1. Progression free survival is measured using CT scan and/or endoscopic biopsy for clinically suspected progression at all trial visits up to 5 years
2. Quality of life is measured using EORTC QLQ-C30 and EORTC QLQ-OES18 questionnaires at baseline, week 7, end of treatment, 6, 12 and 24 months
3. Safety is assessed by looking at toxicities using CTCAE v4.03 at baseline, after each treatment

cycle, and follow up visits. Patients in the dose escalation arm will have additional assessment at 6 and 9 weeks post RT to monitor toxicities.
4. Health economics are measured by looking at health resource utilisation log and the EQ-5D at baseline, end of treatment, 6, 12 and 24 months

Completion date
30/11/2026

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 14/02/2024:
Patients meeting the following criteria may be included in the trial:
1. 16 years of age or older
2. Has been selected and is fit to receive potentially curative definitive chemoradiotherapy by a specialist Upper GI MDT*.
3. Histologically confirmed adenocarcinoma, undifferentiated cancer or squamous cell carcinoma.
4. Tumours of the cervical, thoracic oesophagus, or gastro-oesophageal junction (GOJ) with proximal extent of disease no more proximal than 15cm ab oral and distal extent of primary tumour no more than 2 cm beyond the GOJ.
5. Tumours staged as T1-4 and N+/-, to be determined by TNM 7th (2010) edition of the AJCC /UICC manual. M1 nodes which are encompassable within the radical radiotherapy volume are eligible.
6. Total disease length (including primary tumour and involved lymph nodes) ≤13cm. The primary tumour should also be ≤10cm.
7. WHO performance status 0-1 (appendix 1).
8. Adequate cardiovascular function for safe delivery of chemo-radiation in the opinion of the principal investigator. Where there is clinical concern patients should have an adequate cardiac ejection fraction ≥ 40% as determined by MUGA scan or ECHO (within 4 weeks prior to enrolment).
9. Adequate respiratory function for safe delivery of chemo-radiation in the opinion of the Principal Investigator. Where there is clinical concern FEV1 ≥ 1 litre as determined by spirometry (within 4 weeks prior to enrolment).
10. Patients may receive cisplatin and capecitabine (or 5FU) OR carboplatin and paclitaxel. For those patients selected for a platinum/fluoropyrimidine but deemed unfit for cisplatin (for example but not exclusively, due to advanced age, poor renal function, neurotoxicity or clinically significant hearing impairment), they may instead receive carboplatin (AUC5) upon the discretion of the treating clinician.
11. Patients with known DPD deficiency (partial or complete) may still be eligible for SCOPE2, but sites should follow local policy with regard to appropriate fluoropyrimidine dose reduction or move to carbo-taxol regimen**.
12. Adequate haematological, hepatic and renal function, measured within 2 weeks prior to enrolment.
12.1. Absolute neutrophil count (ANC) ≥ 1.5x109/L
12.2. Platelets ≥ 100x109/L
12.3. Serum bilirubin ≤ 1.5x ULN
12.4. ALT / AST ≤ 2.5x ULN
12.5. ALP ≤ 3x ULN
12.6. Glomerular filtration rate ≥40 mls/min using locally agreed methodology.
12.6.1. If GFR ≥60 mls/min by Cockroft-Gault or equivalent (equation in section 8.1.2), dose modifications are not required.

12.6.2. If GFR is 40 to 60 ml/min and cisplatin is to be given, then formal GFR estimation (EDTA, DTPA clearance or 24-hour clearance or local institutional equivalent***) should be performed and the appropriate dose modifications for cisplatin used. Dose reduction details for GFR 40 to 60 ml/min are in section 8.6.1. Please note, if GFR is 40 to 60ml/min and carboplatin is to be given, formal GFR estimation is not mandatory.
13. Patients with reproductive potential (male or female), who are sexually active during the duration of the trial consent to using a highly effective method of contraception for at least six months after the last dose of chemoradiotherapy. Effective forms of contraception are described in section 11.6.
14. Patients who have provided written informed consent prior to enrolment.

Notes
* Patients not fit to receive full protocol treatment may begin treatment on 75% dose. See section 8.1.2 for further details.
** Please inform CTR if you will be giving any participants dose reduced fluoropyrimidine due to DPD deficiency.
***If using method other than EDTA, DTPA or 24 hour clearance, discuss first with CTR.

Previous participant inclusion criteria:
1. Aged 17 years and over
2. Have been selected to receive potentially curative definitive chemoradiotherapy by a specialist Upper GI MDT
3. Histologically confirmed adenocarcinoma, undifferentiated cancer or squamous cell carcinoma
4. Tumours of the cervical, thoracic oesophagus, or gastrooesophageal junction (GOJ) with proximal extent of disease no more proximal than 15cm aboral and distal extent of primary tumour no more than 2 cm beyond the GOJ
5. Tumours staged with spiral CT scan, PETCT with/without endoscopic ultrasound (EUS), to be T14, N/+ (provided total tumour length including nodes is ≤10). To be eligible for PET randomisation, the PETCT must be within 4 weeks of start date of treatment
6. Total contiguous disease length ≤10cm defined by CT, EUS and/or PET. This includes ≤8cm primary tumour plus nodes within 2cm
7. WHO performance status 0 or 1
8. Adequate haematological, renal, respiratory, cardiac and hepatic function, and are fit to receive all protocol treatment
9. Patients with reproductive potential (male or female), who are sexually active during the duration of the trial, should be prepared to use a highly effective method of contraception preferably with low user dependency for at least six months after the last dose of chemoradiotherapy
10. Patients who have provided written informed consent prior to randomisation

Additional inclusion criteria for patient eligibility for PET randomisation:
11. Baseline SUVmax ≥ 5
12. PET scan 14 days after start of chemo (2/+3 days from this date is acceptable)
13. Not responding to early cis/cape chemotherapy (<35% reduction in SUVmax)
14. For diabetics, fasting Blood glucose ≤12 mmol/L

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Sex
All

Total final enrolment
439

Key exclusion criteria
Current participant exclusion criteria as of 14/02/2024:
If any of the following criteria apply, patients cannot be included in the trial:
1. Patients who have had previous treatment for invasive oesophageal carcinoma or gastro-oesophageal junction carcinoma (not including PDT or laser therapy for high-grade dysplasia /carcinoma in-situ).
2. Patients with metastatic disease. (unless M1 encompassable in the radical RT field)
3. Patients with other active malignancy or past malignancy which is deemed to have significant impact on their prognosis over the next three years.
4. Patients with >2cm mucosal extension of tumour into the stomach or where the superior extent is proximal to 15 cm ab oral.
5. Patients with unstable angina or uncontrolled hypertension or cardiac failure or other clinically significant cardiac disease.
6. Patients who need continued treatment with a contraindicated concomitant medication or therapy.
7. Patients with serious infections which in the opinion of the investigator make delivery of chemotherapy inappropriate.
8. Known hypersensitivity to IMPs.
9. Women who are pregnant or breastfeeding.
10. Patients with an oesophageal stent (patients requiring a PEG/RIG/feeding jejunostomy for nutritional purposes ARE eligible).
11. Any other situation, which in the opinion of the local PI, makes the patient an unsuitable candidate for this trial.

Previous participant exclusion criteria:
1. Patients who have had previous treatment for invasive oesophageal carcinoma or gastrooesophageal junction carcinoma
2. Patients with metastatic disease
3. Patients with other active malignancy or past malignancy in remission for less than 3 years except patients that have been curatively treated from the following conditions; basal cell carcinoma, Carcinomainsitu breast and carcinomainsitu cervix
4. Patients with >2cm mucosal extension of tumour into the stomach or where the superior extent is proximal to 15 cm ab oral
5. Patients with unstable angina or uncontrolled hypertension or cardiac failure or other clinically significant cardiac disease
6. Patients who need continued treatment with a contraindicated concomitant medication or therapy
7. Patients with known dihydropyrimidine dehydrogenase (DPD) deficiency
8. Patients with hearing impairment or sensorymotor neuropathy of WHO grade ≥2

9. Known hypersensitivity to IMPs
10. Women who are pregnant or breastfeeding
11. Oesophageal stent (Patients requiring a PEG/RIG/feeding jejunostomy for nutritional purposes are eligible)
12. Any other situation, which in the opinion of the local PI, makes the patient an unsuitable candidate for this trial (eg with profusely bleeding tumours where the PI has concerns about randomisation to paclitaxel/carboplatin arm where there is risk of aggravation of bleeding due to higher risk of thrombocytopenia)

Date of first enrolment
14/06/2016

Date of final enrolment
16/01/2024

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Velindre Cancer Centre
Velindre Road
Cardiff
United Kingdom
CF14 2TL

Study participating centre
Bristol Haematology and Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Sponsor information

Organisation
Velindre NHS Trust

ROR

https://ror.org/05ntqkc30

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Trial data is the property of the trial Sponsor and will therefore will only be made available upon completion of a formal application outlining the intended use of the data. Applications will be reviewed by the TMG and TSC before data can be released.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	Embedded qualitative study	23/09/2024	24/09/2024	Yes	No
Other publications	Longitudinal interview study of participants' experiences of the SCOPE2 trial	26/02/2025	05/03/2025	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes