

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	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 26/10/2016	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 05/03/2025	Condition category Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

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>

Study website

<https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/scope2>

Contact information

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Public

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Scientific

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Additional identifiers

EudraCT/CTIS number

2015-001740-11

IRAS number

169633

ClinicalTrials.gov number

NCT02741856

Secondary identifying numbers

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

Secondary study design

Randomised parallel trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

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 measure

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

Secondary outcome measures

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

Overall study start date

14/06/2014

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) ≤ 13 cm. The primary tumour should also be ≤ 10 cm.
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 $\geq 40\%$ 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) $\geq 1.5 \times 10^9/L$
 - 12.2. Platelets $\geq 100 \times 10^9/L$
 - 12.3. Serum bilirubin $\leq 1.5 \times \text{ULN}$
 - 12.4. ALT / AST $\leq 2.5 \times \text{ULN}$
 - 12.5. ALP $\leq 3 \times \text{ULN}$
 - 12.6. Glomerular filtration rate ≥ 40 mls/min using locally agreed methodology.
 - 12.6.1. If GFR ≥ 60 mls/min by Cockcroft-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 ≤ 10 cm defined by CT, EUS and/or PET. This includes ≤ 8 cm 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

Age group

Mixed

Lower age limit

16 Years

Sex

Both

Target number of participants

Planned Sample Size: 430; UK Sample Size: 430

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 >2 cm 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

England

United Kingdom

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

Sponsor details

Velindre Road
Cardiff
Wales
United Kingdom
CF14 2TL

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/05ntqkc30>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Data from all sites will be analysed together and published as soon as possible after receiving the primary end points (expected in 14/03/2024). The TMG will form the basis of the writing committee and advise on the nature of publications, subject to the Sponsor’s requirements.

Intention to publish date

31/12/2026

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