SCOPE1 and SCOPE2 Trials of Definitive Chemoradiotherapy for Oesophageal Cancer

Translational Research project call

On behalf of the SCOPE1 and SCOPE2 trialists of definitive chemoradiotherapy for Oesophageal cancer, the CRUK Centre for Trials Research Cardiff, Velindre University NHS Trust (Sponsor), NCRI Upper GI study group and CTRad, we would like to engage the scientific community in developing our translational research proposals for samples from the SCOPE1 and SCOPE2 phase II/III trials.

- **SCOPE1** was a phase II trial which randomised patients with locally advanced oesophageal cancer to definitive chemo-radiotherapy with cisplatin and capeciteabine +/- cetuximab. The study accrued 259 pts between February 2008 and February 2012. The primary analysis paper is available here: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(13)70136-0/fulltext
  Long term follow-up results are available here: https://www.nature.com/articles/bjc201721

- **SCOPE2** is an ongoing randomised phase II/III trial of definitive chemo-radiotherapy exploring two randomised questions: 1. The role of radiotherapy dose escalation, and 2. the role of PET imaging during neoadjuvant chemotherapy to inform treatment switch. The study has so far randomised 331 of a planned 395 patients, is open in 33 hospitals across the UK, and is due to close to recruitment in May 2023. More information about the study is available here: https://www.clinicaloncologyonline.net/article/S0936-6555(22)00170-4/fulltext

From the SCOPE1 trial we have initiated a piece of collaborative translational research with Simon Lord (Oxford) and Russell Petty (Dundee) using sections from the pre- and post-treatment tumour biopsy FFPE samples from 211 patients. Here, we shall look to identify whether EGFR copy number analysis can identify a sub-group that may benefit from cetuximab. This work should report in Q4 2022 and explores the development of a gene expression signature for radiation sensitivity as well as exploring EGFR pathways in relation to the use of cetuximab.

The remaining SCOPE1 samples available for use break down as follows (please note, the amount available may be variable). Each column represents the number of patients' worth of samples:

Baseline Tissue alone	Post treatment tissue alone	Paired pre- & post-treatment tissue	Full set of bloods (pre & post plasma & serum)	Pre & post plasma (excl. full sets)	Pre & post serum (excl. full sets)	Pre plasma & serum (excl. full sets)	Post plasma & serum (excl. full sets)	Pre plasma	Pre serum	Post plasma	Post serum
25	63	123	96	8	3	67	19	184	173	124	118

We are planning to collect the FFPE samples from SCOPE2 prior to the end of the trial and are seeking collaborative proposals with or without funding which may use any of the SCOPE1 or 2 samples sets.

We anticipate collecting a large number of FFPE samples from SCOPE2 including pre-treatment biopsies and 24 week biopsies, with estimated numbers of samples as follows:

Diagnostic tissue	Week 24 tissue
~320	~240

In relation to the collaboration with Simon Lord, we have already proposed a validation of the signature work from SCOPE1 as described below:

> We hypothesise that a gene expression signature can accurately predict survival in patients undergoing chemoradiotherapy for squamous oesophageal cancer. We have already carried out RNASeq of the SCOPE-1 samples and in collaboration with the Buffa Computational Biology Group at the University of Oxford we are currently using machine learning classifier techniques to conduct discovery analyses of novel transcriptomic signatures that predict outcome. Using the SCOPE-2 samples, we shall look to validate this signature. The line of site would be to take this signature into a prospective clinical trial to assess its value in selecting patients for primary chemoradiotherapy versus surgery.

We would appreciate receiving Expressions of Interest, maximum 2 pages (not including appendix) emailed to SCOPE2@cardiff.ac.uk by the **23rd of September 2022**, to include:

- Project lead (we encourage early career researchers with mentors)
- Project team and expertise, detailing your track record of research in this area
- Description of project plan
- Lay summary of project plan
- Description of any preliminary data
- Number of samples required and amount of material needed from each sample
- Planned source of funding (depending upon proposals this may be a joint effort with other groups)
- Appendix:
    - relevant published papers to support the work (max 3)
    - short CV of project lead (2-page max)

Projects considered of adequate interest will be invited to an open discussion in October, which will be a hybrid event, hosted by the CRUK Centre for Trials Research in Cardiff. Extra weighting will be given to study concepts that engage with the clinical randomisations but these are not essential.

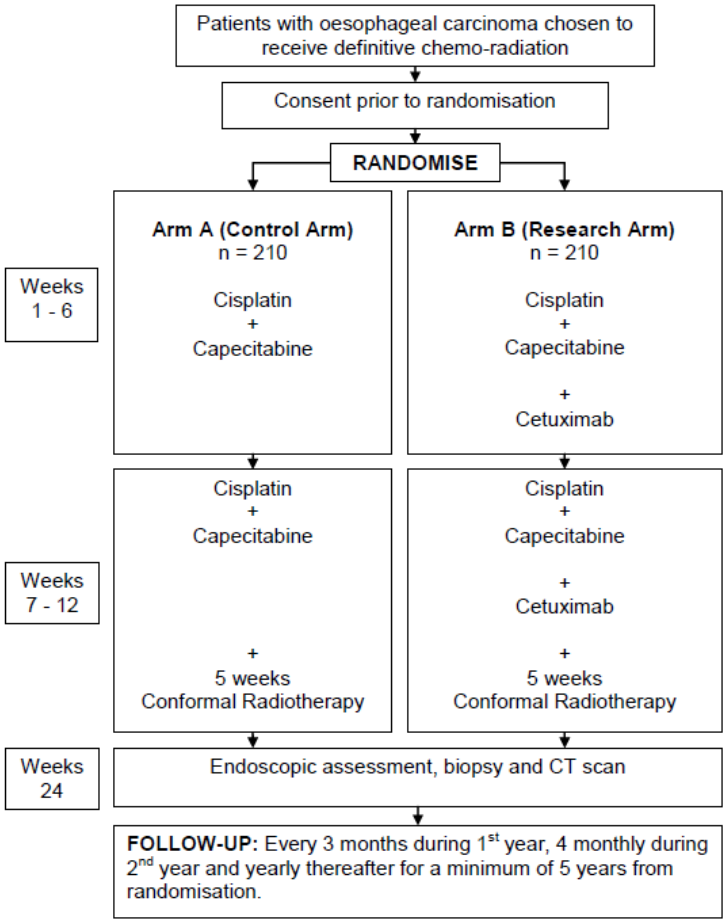
Please forward questions for the team to SCOPE2@cardiff.ac.uk.

Appendix 1 Further information about SCOPE1

A randomised phase II/III multicentre clinical trial of definitive chemoradiation, with or without cetuximab, in carcinoma of the oesophagus.

SCOPE1 was a trial for patients with non-metastatic cancer of the oesophagus who had been chosen to receive chemo-radiotherapy. The aim was to determine whether the addition of the monoclonal antibody cetuximab (Erbitux™) improved patient survival compared to standard chemo-radiation alone.

SCOPE1 was funded by Cancer Research UK and sponsored by Velindre University NHS Trust, with the cetuximab provided by Merck.



Appendix 2 Further information about SCOPE2

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

SCOPE2 is for patients with non-metastatic cancer of the oesophagus who are treated with chemo-radiotherapy (with a RT dose of either 50 or 60Gy). The trial is funded by Cancer Research UK and sponsored by Velindre University NHS Trust.