ISRCTN54806122 https://doi.org/10.1186/ISRCTN54806122

The SCC-AFTER research study aims to find out whether it is better to use radiotherapy or not to prevent high-risk skin cancer from coming back after it has been removed by surgery

Submission date 04/06/2024	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 02/07/2024	**Overall study status** Ongoing	
Last Edited 23/05/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Some squamous cell cancers are called ‘high-risk’, meaning that there is a higher chance that they could come back after surgery compared to other skin cancers. Around 3 out of 10 people with high-risk skin cancer may experience their cancer coming back within 3 years of the surgery. Radiotherapy (x-ray treatment) is sometimes given to people with high-risk skin cancer after surgery to try and reduce the chances of the cancer coming back. This is called ‘post-operative’ or ‘adjuvant radiotherapy’. It is given to the area of the skin where the cancer was removed. It works by using X-rays to destroy any cancer cells that might be left behind in that area. However, there is no certainty that radiotherapy does stop high-risk skin cancers from coming back. The alternative to radiotherapy is to start a close clinical follow-up to monitor if the skin cancer shows signs of coming back and to treat it if it does. This study aims to find out whether using radiotherapy in people who have had high-risk squamous cell cancer removed by surgery reduces the chances of their skin cancer coming back, or whether radiotherapy is not necessary and only close clinical follow-up is required. The study will also find out what impact it has on quality of life.

Who can participate?
People aged 18 years old and over who have had this type of high-risk skin cancer removed with surgery

What does the study involve?
The study will have two groups of patients:
Radiotherapy and close clinical follow-up:
• Will receive treatment with radiotherapy every weekday for 2-6 weeks, starting within 4 months of the surgery that removed the cancer.
• Will be followed up closely for 3 years to see if the skin cancer shows signs of returning.
• Will be unlikely to have radiotherapy again in the future if the skin cancer does return to the same place.

Close clinical follow-up:
• Will be followed up closely for 3 years to see if the skin cancer shows signs of returning.
• May be able to have radiotherapy in the future if the skin cancer does return to the same place.

There is a linked study that wants to find out more about how patients feel about taking part in the trial. It will involve somebody asking patients questions about their experience and these will be recorded.

What are the possible benefits and risks of participating?
Possible benefits of Radiotherapy followed by close clinical follow-up:
• Radiotherapy may lower the risk of a patient's cancer coming back.

Possible benefits of Close clinical follow-up:
• Patients will not need to attend for daily radiotherapy or experience the side effects that may come with radiotherapy.
• Radiotherapy has not been proven to lower the risk of a patient's cancer coming back.
• Patients may be able to have radiotherapy at a later date if their cancer does come back.

Possible risks of Radiotherapy followed by close clinical follow-up:
• Radiotherapy has not been proven to lower the risk of a patient's cancer coming back.
• Patients would not be able to have further radiotherapy in the same area if the cancer comes back in the same place and would therefore need different treatment.
• Radiotherapy is generally very well tolerated, however, there are possible short-term and long-term side effects from radiotherapy:
Short term: Skin redness, irritation, itching, flaking, peeling, scaling and dryness in the treatment area. The skin may scab over or break down in the treatment area. General tiredness during the treatment period. Some side effects can be specific, such as potential interactions with other medicines a patient may take or with a pacemaker. This may affect the radiotherapy. These will be discussed with the medical team.
Long-term: Permanent skin texture changes in the treatment area are possible and include thicker or thinner skin, skin colour change and rarely a more long-term non-healing ulcer that may require further treatment such as dressings or surgery. If radiotherapy is given to an area on the body where hair grows such as the scalp, it can sometimes cause permanent hair loss.

Possible risks of Close clinical follow-up:
• The cancer may come back even though a patient has had surgery and may require further treatment, such as surgery or radiotherapy.

Where is the study run from?
The study is being co-ordinated by the Centre for Trials Research on behalf of Cardiff University.

When is the study starting and how long is it expected to run for?
January 2024 to January 2031

Who is funding the study?
National Institute for Health and Care Research (NIHR)

Who is the main contact?
SCCAFTER@cardiff.ac.uk

Study website

https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/scc-after

Contact information

Type(s)
Public, Scientific

Contact name
Ms Ann White

ORCID ID
https://orcid.org/0000-0001-7317-6304

Contact details
Centre for Trials Research (CTR) – Cancer Group
College of Biomedical & Life Sciences
Cardiff University
6th Floor, Neuadd Meirionnydd
Heath Park
Cardiff
United Kingdom
CF14 4YS
+44 (0)2920687465
SCCAFTER@cardiff.ac.uk

Type(s)
Principal Investigator

Contact name
Prof Catherine Harwood

ORCID ID
https://orcid.org/0000-0002-1375-0965

Contact details
The Royal London Hospital
Barts Health NHS Trust
London
United Kingdom
E1 1BB
+44 (0)20 7882 2332
SCCAFTER@cardiff.ac.uk

Type(s)
Principal Investigator

Contact name
Prof Agata Rembielak

ORCID ID

https://orcid.org/0000-0003-2351-7179

Contact details
The Christie NHS Foundation Trust
Wilmslow Road
Manchester
United Kingdom
M20 4BX
+44 (0)161 446 8583
SCCAFTER@cardiff.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
331136

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SPON1924-22, IRAS 331136, CPMS 62841

Study information

Scientific Title
Adjuvant radiotherapy in patients with high-risk primary cutaneous Squamous Cell Carcinoma AFTER surgery (SCC-AFTER): an open-label, multicentre, two-arm phase III randomised trial

Acronym
SCC-AFTER

Study objectives
Following complete excision of high-risk primary cutaneous squamous cell carcinoma (HR cSCC) is adjuvant radiotherapy (ART) plus standard clinical follow up superior in reducing loco-regional recurrence compared with standard clinical follow up alone?

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 11/04/2024, East of England - Essex Research Ethics Committee (2 Redman Place, London, EC20 1JQ, United Kingdom; +44 (0)207 104 8106; Essex.REC@hra.nhs.uk), ref: 24/EE/0049

Study design
Multicentre interventional open-label two-arm Phase III randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Adjuvant radiotherapy in patients with high-risk primary cutaneous Squamous Cell Carcinoma AFTER surgery

Interventions
This study aims to find out whether using radiotherapy in people who have had high-risk skin cancer removed by surgery reduces the chances of their skin cancer coming back, or whether radiotherapy is not necessary and only close clinical follow-up is required. This is an open-label, multicentre, two-arm, phase III randomised control trial to evaluate superiority, cost-effectiveness, and effects on quality of life (QoL) of adjuvant radiotherapy (ART) in completely resected high-risk (BWH T2b/3) primary cutaneous squamous cell carcinoma (cSCC).

Patients will be randomised to either the ART followed by close clinical follow-up (ART arm) or close clinical follow-up only (comparator arm and current standard care). Patients will be assessed following UK guidance at baseline, mid-ART (ART arm only), 4 monthly for 2 years, then 6-monthly for year 3. During the follow-up period, QoL and Health Economics (HE) will be assessed twice for year 1, and annually in years 2 and 3. Progression and survival data will be collected throughout the trial.

Participants will be randomised using unweighted minimisation with a 20% random element. The stratification/balancing variables are detailed below.
STRATIFICATION/BALANCING VARIABLES
The balancing factors will be:
• Age
o Less than 65
o >=65 to <80
o 80 or over
• Stage of cancer BWH classification
o T2b
o T3
• Immunocompromised
o Yes
o No
• Time since surgery (months)
o < Three months

o Three to ≤ four months
• Perineural invasion (nerve diameter >=0.1mm)
o Yes
o No
Each factor will have equal weighting.

An internal pilot targeting the recruitment of 100 patients within the first 12 months will determine feasibility. Two interim analyses after 77 and 115 events (600-760 randomised) trigger early stopping if the log-rank statistic is larger than +/- 3.36 and +/- 2.68 respectively. Stopping for efficacy means fewer participants and shorter follow-ups. Otherwise, the trial will be analysed when at least 194 events have been reported.

A Quintet Recruitment Intervention (QRI) and INCLUSION Study Within a Project (SWAP) are integrated within the trial to optimise recruitment and inclusion of people with multiple long-term conditions, safeguard informed consent, address clinician equipoise, and identify organisational barriers.

Intervention Type
Procedure/Surgery

Primary outcome measure
Loco-regional recurrence (LRR)-free survival time, time to LRR is defined as the time from randomisation to date of clinical detection of what is subsequently confirmed to be local, regional, or loco-regional recurrent disease, measured using physical examination at a skin clinic at 4, 8, 16, 12, 24, and 36 months following randomisation until the end of the study

Secondary outcome measures
1. Quality of life (QOL) measured using EORTC QLQ C30, skin-specific Skin Cancer Index, Picker Patient Experience 15 questionnaire and EQ-5D at 4, 12, 24, and 36 months post-randomisation
2. Distant metastasis-free survival, defined as days from randomisation to the date of distant metastasis or death from any cause, measured using data reported by completion of recurrence CRF from randomisation until the point of recurrence is confirmed or death
3. Overall survival, defined as days from randomisation to death for any reason, measured using data reported by completion of a death CRF at the date of death
4. Safety/toxicity as assessed by common terminology criteria for adverse events (CTCAE) V5.0 scoring system and serious adverse events, including patient-reported outcomes version of the CTCAE, measured using adverse event CRFs at 4, 8, 16, 24, 26 months post-randomisation
5. Cost-effectiveness measured using health utility using EQ-5D-5L and recording health resource use at 4, 12, 24, and 36 months post-randomisation. The primary economic outcome is cost per quality-adjusted life year (QALY). The secondary economic outcome is resource use and costs.

Overall study start date
01/01/2024

Completion date
01/01/2031

Eligibility

Key inclusion criteria

1. High-risk primary cSCC (T2b/T3 by BWH staging criteria) excised with adequate peripheral and deep surgical margins (according to BAD guidelines) with histologically clear margins (≥1mm by Royal College of Pathology criteria
2. Time since excision surgery < 3 months (<2 months is preferred)
3. ECOG performance status of 3 or less at enrolment
4. Aged 18 years or older at time of consent
5. Fit for ART and able to attend radiotherapy outpatient appointments
6. Life expectancy >6 months
7. Informed Consent obtained* which must be prior to any mandatory study-specific procedures, sampling, and analyses

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
840

Key exclusion criteria
1. Any current clinicopathological evidence of loco-regional recurrence of the index tumour
2. Previous (within 3 years) or current non-index primary cSCC in skin drained by the same lymph node basin
3. cSCC on anatomical sites which interfere with suitability for ART (such as vermilion lip, eyelids, breast, anogenital area)
4. Patients with evidence of regional or distant disease at time of primary cSCC diagnosis
5. Previous radiotherapy in the same area
6. Patients with reproductive potential who are not willing to use contraception for the duration from trial consent until the last dose of radiotherapy if they are randomised to the ART arm
7. Unable to lie still unattended for the duration of ART (estimated to be around 5 minutes)
8. Participation in another interventional clinical study that may affect the recurrence of cSCC (primary endpoint)
9. History of another malignancy where metastasis could cause diagnostic uncertainty or patients receiving active systemic anti-cancer treatment (excluding hormonal treatment for prostate or breast cancer) or radiotherapy

Date of first enrolment
31/07/2024

Date of final enrolment
14/06/2027

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
The Christie
550 Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

Study participating centre
Kings Mill Hospital
Sherwood Forest NHS Trust
Mansfield Rd
Sutton-in-Ashfield
United Kingdom
NG17 4JL

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

Study participating centre
Nottingham University Hospitals NHS Trust - City Campus
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Tayside
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Clatterbridge Cancer Centre
Clatterbridge Hospital
Clatterbridge Road
Wirral
United Kingdom
CH63 4JY

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Barking, Havering and Redbridge University Hospitals NHS Trust
Queens Hospital

Rom Valley Way
Romford
United Kingdom
RM7 0AG

Study participating centre
East Lancashire Hospitals NHS Trust
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre
Maidstone & Tunbridge Wells NHS Trust Hq
Maidstone Hospital
Hermitage Lane
Maidstone
United Kingdom
ME16 9QQ

Study participating centre
Churchill Hospital
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
Barts and the London NHS Trust
Alexandra House
The Royal London Hospital
Whitechapel
London
United Kingdom
E1 1BB

Sponsor information

Organisation
Cardiff University

Sponsor details
McKenzie House
8th Floor
30-36 Newport Road
Cardiff
Wales
United Kingdom
CF24 0DE
+44 (0)29 2087 9130
resgov@cardiff.ac.uk

Sponsor type
University/education

Website
https://www.cardiff.ac.uk/

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in peer-reviewed scientific journals, conference presentation, publication on website and submission to regulatory authorities.

Intention to publish date
31/12/2030

Individual participant data (IPD) sharing plan
The final datasets generated and analysed during the trial will be available upon request directly from the sponsor subject to review using SCCAFTER@cardiff.ac.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	18/03/2024	01/07/2024	No	No