

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

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Registration date 02/07/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 23/05/2025	Condition category Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

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

Contact information

Type(s)

Public, Scientific

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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 < 3 months

- o Three to \leq four months
 - Perineural invasion (nerve diameter ≥ 0.1 mm)
 - 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 (≥ 1 mm 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**

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Study participating centre**Kings Mill Hospital**

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Study participating centre**Velindre Cancer Centre**

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Study participating centre**Nottingham University Hospitals NHS Trust - City Campus**

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Study participating centre
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Study participating centre
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Study participating centre

East Lancashire Hospitals NHS Trust

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Study participating centre

Maidstone & Tunbridge Wells NHS Trust Hq

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Study participating centre

Churchill Hospital

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Study participating centre

Barts and the London NHS Trust

Alexandra House
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Sponsor information

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Sponsor details

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Sponsor type

University/education

Website

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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