

# 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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<b>Registration date</b> 02/07/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 12/12/2024	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English Summary

### 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

### Contact name

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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 hypothesis**

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

## Condition

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  $\geq 65$  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  $\leq$  four months
  - Perineural invasion (nerve diameter  $\geq 0.1$  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  $\pm 3.36$  and  $\pm 2.68$  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, 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

## **Overall study end date**

01/01/2031

# **Eligibility**

## **Participant 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 ( $\geq 1$  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

**Participant 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

**Recruitment start date**

31/07/2024

**Recruitment end date**

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

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## **Sponsor information**

### **Organisation**

Cardiff University

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### **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](mailto:SCCAFTER@cardiff.ac.uk).

**IPD sharing plan summary**

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>	version 1.1	18/03/2024	01/07/2024	No	No