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SPOT-IT: prevention of the cutaneous squamous cell carcinoma in immunosuppressed patients using topical treatment

Submission date
25/06/2025

Recruitment status
Recruiting

Registration date
09/09/2025

Overall study status
Ongoing

Last Edited
09/09/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Cutaneous squamous cell carcinoma (cSCC) is one of the commonest skin cancers, with numbers increasing by 5% every year in the UK. Immunocompromised people have a much higher risk of developing cSCC, and some will develop many cSCCs requiring multiple surgical operations that can be cosmetically disfiguring as they affect the face or head. cSCC prevention is therefore especially important for people with a weakened immune system, such as those who have received organ transplants, who need to take lifelong immunosuppressive medications. They have the highest risk for new cSCC, about 100-fold greater than individuals who have a normal immune system. However, there has been little research into how to prevent cSCC from developing in people with weakened immune systems. A study in Australia in the 1990s showed that daily sunscreen can also reduce cSCC numbers in people with normal immune systems, and the current standard of care for patients with a previous cSCC is to apply daily sunscreen. cSCC may develop from areas of sun-damaged skin called actinic keratoses (AK), and treatment of AK may also help prevent cSCC. There are several treatments available for AK, but the most effective is 5-fluorouracil 5% cream (5FU), which is a form of topical chemotherapy. Studies in people with normal immune systems have shown that treating AK with 5FU cream (applied twice a day for four weeks) will reduce the chance of cSCC developing by 75% over the next year. This has not been conclusively tested in people with weakened immune systems and has never been directly compared with sunscreen alone. Also, this treatment is difficult to tolerate, causing red skin with pain, weeping/crusting and a distressing appearance that may last up to 6 weeks. Recently, it was shown that combining 5FU with a vitamin D ointment called calcipotriol (5FU+CAL) boosts the effectiveness of 5FU such that only a 4 to 6-day treatment course is needed, with side effects such as redness/crusting settling within 2 weeks. Patients who have used this treatment have found it more tolerable, but there are no large studies investigating how effective the combination treatment is. The researchers surveyed 32 organ transplant patients who had used both the 5FU cream alone and the 5FU+CAL combination; 81% found the combination as effective as 5FU at clearing AK, and most preferred it. None experienced any problems with the 5FU+CAL combination. The purpose of the study is to compare whether topical 5FU cream (applied twice daily for 4 weeks sequentially to each of the three selected intervention zones and repeated annually for 3 years) is more effective than standard of care

(this means advice to apply sunscreen daily and to have regular monitoring) in preventing cSCC. The study will also look at whether combination topical 5FU+CAL (applied twice daily for 6 days, followed by a 1-day treatment break sequentially to each of the three selected intervention zones and repeated annually for 3 years) is more effective in preventing cSCC than standard of care and, if it is, whether it is as effective as 5FU cream alone.

Who can participate?
Patients with a weakened immune system (for any reason) will be identified from the dermatology outpatient clinics they are already regularly attending.

What does the study involve?
Participants should have had at least one previous cSCC skin cancer treated. All patients in the study will be advised to apply daily sunscreen and will be monitored by the study team at the same timepoints during the study. The topical treatment (5FU alone or 5FU+CAL combination treatment) will be repeated each year for 3 years, and the time it takes to develop a new cSCC will be recorded over the 3-year trial treatment and up to 4 years of follow-up. Participants will also be asked about their experience of side effects, including pain, redness, quality of life and how acceptable the treatments are.

What are the possible benefits and risks of participating?
Benefits: It is hoped that the study treatment may slow down or clear the actinic keratoses and prevent the development of new skin cancers. However, there is no guarantee of this, and it is unknown which, if any, of the three treatment options is better than the other.
The information from this study will help doctors learn more about treatments to prevent the development of cSCC. It is possible that participants may not experience any direct health benefits during or following completion of this study. However, they will be contributing to research that may benefit future patients with a similar skin problem.

Risks: Like all medicines, the topical creams used in this study can cause side effects. For most people, however, they are manageable with the support of the clinical team. All side effects are reported to the research team at Cardiff University, who will closely monitor problems that might develop. Similarly, all side effects and benefits are confidentially reviewed by an independent group of people who are not involved with the study. This is to ensure that any problems are rapidly identified and acted upon.

Where is the study run from?
Cardiff University, UK

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

Who is funding the study?
Cancer Research UK

Who is the main contact?
SPOT-IT@cardiff.ac.uk

Plain English summary under review with external organisation

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008229

Protocol serial number
SPON2010-25

Study information

Scientific Title
SPOT-IT: cutaneous SCC Prevention using tOpical Therapy in Immunosuppressed patienTs

Acronym
SPOT-IT

Study objectives
• To establish whether 5% 5-Fluorouracil (5FU) topical treatment (comparator: standard of care sunscreen + surveillance) is effective in prevention of cutaneous SCC (cSCC) in

immunosuppressed individuals in terms of time to new cSCC development within intervention zones (Phase III)

• To establish whether 5FU and calcipotriol ointment (5FU+CAL) combination therapy (comparator: 5% 5-Fluorouracil (5FU) topical treatment) is effective in prevention of cutaneous SCC (cSCC) in immunosuppressed individuals in terms of time to new cSCC development within intervention zones (embedded Phase II trial)

• To establish whether combination 5FU and calcipotriol ointment is superior to standard of care in prevention of cSCC within intervention zones in immunosuppressed individuals
• To evaluate the impact of treatment on subsequent cSCC accrual within and outside intervention zones
• The time to any new primary cSCC outside intervention zones
• The time to and accrual of other non-cSCC skin cancers within and outside intervention areas
• To evaluate the time to onset, severity and time to resolution of local skin toxicity associated with each topical treatment
• To assess other adverse events
• To evaluate whether 5FU+CAL combination therapy had higher acceptability and lower severity of local skin toxicity compared with 5FU monotherapy
• To evaluate participants' experience and preference for each topical treatment and its effects on quality of life
• To assess the cost-effectiveness of each topical treatment based on the incremental cost per quality-adjusted life year gained

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 21/08/2025, North West - Haydock Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8029; haydock.rec@hra.nhs.uk), ref: 25/NW/0207

Study design
Randomized controlled study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Cutaneous Squamous cell carcinoma (SCC) is a type of skin cancer. Some SCC may develop from areas of sun-damaged skin called actinic keratoses (AK), which arise on skin areas exposed to sunlight.

Interventions
SPOT-IT Participants will be randomised to one of the following trial treatments:
Sunscreen + surveillance: Sunscreen with sun protection factor (SPF) 50+ will be applied daily as per the PI's recommendations and the participant's requirements. In this trial, sunscreen is not defined as an IMP.

5FU monotherapy: SPOT-IT Participants allocated to the 5FU monotherapy arm will be asked to apply a thin layer of 5FU cream to the affected area twice a day for 4 weeks sequentially to each of the three intervention zones.

Participants will be asked to follow the treatment schedule in the following order:
Neck, shawl, ± non-hair bearing scalp for 4 weeks (weeks 1-4)
Face and ears for 4 weeks (weeks 5-8)
Upper limbs for 4 weeks (weeks 9-12)
The 5FU will be applied for a total of 12 weeks without any break between the intervention zones above.

If the participant has no hair at their temples beyond hairline recession, this area should be treated as part of their face. If an AK occurs on the parting area of the hair, it is recommended to treat this area with 5FU as intervention zone no. 1. In either case, treatment will be discussed and agreed, by participants and PI. This schedule will be repeated annually for 3 years and on day 1 of Years 2 and 3 (± 6 weeks window). The total dose of 5FU should not be greater than an area of 500cm2 (23x23cm) at a time.

5FU + CAL combination: Trial participants randomised to the 5FU+CAL arm will be required to apply a thin layer of 5FU cream to the intervention zone(s) and left to absorb (5 minutes). Calcipotriol ointment should then be applied to the same intervention zone(s) in the same quantity. This combination should be applied twice a day for 6 days, followed by a 1-day treatment break, sequentially to each of the intervention zones. This schedule will be repeated annually for 3 years. The maximum weekly dose of CAL ointment is 100g and should not be exceeded, as hypercalcaemia may occur. Participants will be asked to follow the following order:
1. Neck, shawl, ± non-hair bearing scalp for 6 days, followed by a 1-day break
2. Face and ears for 6 days, followed by a 1-day break
3. Upper limbs for 6 days

If the participant has no hair at their temples beyond hairline recession, this area should be treated as part of their face. If an AK occurs on the parting area of the hair, it is recommended to treat this area with 5FU as intervention zone no. 1. In either case, treatment will be discussed and agreed, by participants and PI.

Participants in the 5FU monotherapy arm or in the 5FU + CAL combination arm will be instructed to apply sunscreen at least 1 hour after the morning treatment with 5FU or 5FU + CAL if engaging in outdoor activities.

Follow-up: After trial treatment and clinical assessments in Year 3, or earlier if treatment is discontinued before Year 3, participants will be followed up until the closure of the trial or up to 4 years, depending on the date of the participant's enrolment into the trial.

Randomisation: Eligible patients will be randomised via the trial SPOT-IT web-based system to one of the three trial arms above. All screening data must be available and entered onto REDCap before randomisation. When the randomisation is completed, the system will confirm whether the participant has been allocated to the Standard of care (sunscreen + surveillance), 5FU monotherapy or 5FU+CAL combination arm. All data entry will be via Electronic Data Capture (EDC).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
5FU [5-Fluorouracil] , CAL [Calcipotriol]

Primary outcome(s)
Time from randomisation to new primary cSCC arising in any of the three selected intervention zone(s): 1) neck, shawl, ± non-hair bearing scalp; 2) face and ears; 3) upper limbs measured using data recorded from randomisation to the time when a new primary cSCC is observed

Key secondary outcome(s))
1. More effective treatment will be assessed in terms of time to new cSCC development within intervention zones from randomisation.
2. The impact of treatment of subsequent cSCC within and outside the intervention zone(s) will be evaluated in terms of time to onset and number of cSCC and non-cSCC skin cancers.
3. Local skin toxicity associated with each topical treatment from time to onset to resolution will be assessed through the collection of AEs, radiotherapy details, and concomitant medications as reported by clinicians on CRF and by participants on logbooks.
4. Participants' experience and preference for each topical treatment will be assessed through logbooks throughout the trial and quality of life (QoL) questionnaires on Day 1 and month 4 of each treatment year, and at least annually for up to 4 years of follow-up.
5. Treatment's effect on quality of life will be assessed through clinical reported clinical frailty on Day 1 of treatment in Y2-3 and at least annually for up to 4 years follow-up.
6. Cost-effectiveness of each topical treatment will be assessed through the QoL questionnaire and Resource use questionnaire on Day 1 and month 4 of each treatment year, and at least annually for up to 4 years of follow-up.

Completion date
31/12/2031

Eligibility

Key inclusion criteria
To be eligible for participation in this trial, the patient must:
1. Have a diagnosis of immunodeficiency being either organ or stem cell transplant recipient; haematological malignancy; long-term immunosuppressive medication for immune mediated inflammatory condition; living with human immunodeficiency virus infection (HIV)
2. Have history of at least one cSCC in the last 5 years
3. Be willing and able to provide written informed consent for the trial
4. Be willing and able to adhere to study procedures
5. Age 18 years or over on day of signing consent
6. For Organ Transplant Recipients (OTR): have stable transplanted organ function (transplant duration > 2 years) for at least 3 months prior to enrolment in the trial
7. No change in immunosuppressive medication in 3 months prior to enrolment in the trial

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Is unsuitable for treatment with topical 5FU or calcipotriol e.g. previously intolerant
2. Known disorders of calcium metabolism, including hypercalcaemia, or any condition that may predispose to elevated serum calcium levels
3. Known DPD (dihydropyrimidine dehydrogenase) deficiency
4. Severe renal or liver impairment
5. Has used topical 5FU or calcipotriol or other actinic keratosis (AK)-field treatment in the planned treatment zone within 8 weeks prior to enrolment in the trial
6. Has started treatment with mTOR inhibitors or systemic retinoids within 6 months prior to enrolment
7. Is participating in a clinical study with other Investigational Medicinal Products
8. Is pregnant or breastfeeding or planning to conceive or fathering children within the projected duration of the trial

Date of first enrolment
01/02/2026

Date of final enrolment
31/01/2030

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Cardiff University
Centre for Trials Research
6th Floor, Neuadd Meirionnydd
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CF14 4YS

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Research organisation

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from SPOT-IT@cardiff.ac.uk. As per the CTR SOP on data release, applicants interested in requesting data will submit a CTR data sharing request form, which will be reviewed by CTR key personnel (e.g. statistician, study lead, director, and sponsor) and/or peer-reviewed by the relevant team (TSC, IDMC, funder). If the request is accepted, an agreement between the trial sponsor and the applicant will be issued before the delegated members of the CTR staff release the data in the format agreed in the contract.

IPD sharing plan summary
Available on request