

SCC–AFTER eligibility criteria

Participants are eligible for the trial if they meet all of the following inclusion criteria and none of the exclusion criteria apply. All queries about participant eligibility should be directed to the CTR Trial Team before randomisation.

Inclusion criteria

1) High-risk primary cSCC (T2b/T3 by BWH staging criteria) excised with histologically clear peripheral and deep margins (≥ 1 mm by RCPATH criteria). Surgical excision margins should be consistent with BAD guidelines (peripheral and deep) and will be recorded.

If, after surgical excision with curative intent (either wide local excisions with predetermined margins or Mohs micrographic surgery) the deep histological margin is < 1 mm, the patient is eligible if ALL of the following are met:

- For scalp cases only: the galea aponeurotica (or galeal aponeurosis) must be resected with no evidence of tumour infiltration. If infiltration of the galea is present, the deep histological excision margin must be ≥ 1 mm).
- All cases: the MDT is in agreement that surgical treatment is complete;
- All cases: the pathological size of the deep margin is recorded

2) Time since excision surgery < 3 months (< 4 months acceptable only if necessary).

3) ECOG performance status of 0, 1, 2, or 3 at enrolment (Appendix 1).

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.

* Patients should be provided with additional support and adjustments where needed (e.g., layering of information, involvement of a family member/friend as a support person, provide witnessed informed consent if unable to confirm informed consent in writing).

Note: this will include those patients who are elderly, frail and have multiple long-term chronic conditions who are a group at particular risk for cSCC. It will also include immunocompromised patients who are excluded from most clinical trials but have high rates of cSCC.

Exclusion criteria

1) Any current clinicopathological evidence of loco-regional recurrence of the index tumour.

2) Previous (within 2 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 to 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.

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.***

**Please consider discussing all patients with multiple cSCC draining to the same nodal basin as the index cSCC with the SCC–AFTER trial team including those within the last 3 years.

***Please discuss patients with malignancy of concern with the SCC–AFTER trial team

SCC-AFTER Screening Log Decision Tree

"Is the patient high-risk primary cSCC as per BWH classification?"

Definition of high-risk cSCC= T2b/T3 by BWH with 2 or more of the following 4 risk factors ("3D and P": 1) Diameter 20mm or greater; 2) Depth of invasion: either > 6mm OR beyond subcutaneous fat (NB even if both are present, this counts as only one factor); 3) Differentiation poor (G3); 4) Perineural invasion in nerve diameter 0.1 mm or greater). T2b = 2 or 3 high risk features. T3 = all 4 risk features or bone invasion.

