# Rhenium-188 skin cancer therapy: two-year efficacy and safety from a prospective multicenter phase IV study with dermatology-directed assessment of skin findings: (EPIC-Skin Trial)

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## 1 Background

Non-melanoma skin cancers (NMSC) are the most common malignancies worldwide. While surgical excision, including micrographic surgery, achieves clearance rates exceeding 95%, treatment may be associated with disfigurement, functional morbidity, or may not be appropriate in cases of multiple lesions, anatomically difficult locations, due to patient comorbidities or preference. Epidermal radionuclide therapy with rhenium-188 has been in clinical use since 2008, with retrospective series, pooled analyses, and prospective studies reporting high local control and favourable cosmetic outcomes in lesions <3 mm deep [1]. Building on these data, the present analysis revisits twenty four-month outcomes from a prospective multicentre phase IV study and incorporates an independent, dermatology-directed assessment to refine interpretation of treatment-related skin findings and healing trajectories.

## 2 Methods

This prospective, multicentre, single-arm phase IV study enrolled 187 adults with 1-3 biopsy-proven basal cell carcinoma or squamous cell carcinoma lesions ≤3 mm deep and ≤8 $cm^2$. Patients received a single outpatient treatment with rhenium-188 epidermal radionuclide therapy delivering 50 Gy to the deepest point of the lesion. Efficacy was assessed using modified Response Evaluation Criteria in Solid Tumors (RECIST) criteria after 12 months, with the planned primary endpoint, measuring complete response scheduled for 24 months. Adverse events were prospectively collected using CTCAE v5.0 and coded with MedDRA. Adverse events of interest included radiation dermatitis, skin ulceration, alopecia, skin induration, hypopigmentation, hyperpigmentation, and telangiectasia. An independent, dermatology-directed panel, comprising four physicians not involved as study investigators, was convened to review standardized clinical photographs to contextualise skin findings and healing patterns.

## 3 Results

### Demographics

**187 patients**
**Enrolled in study**
(Age: Median 71.5 years (range: 27-95 years))

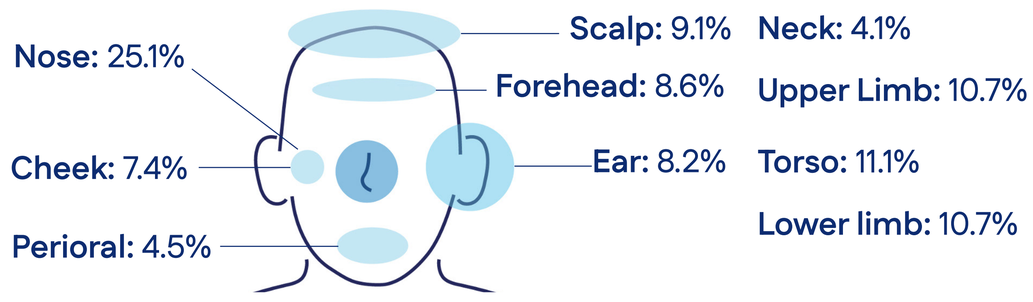
**171 tumours**
**From 130 patients**
with 24-month follow-up

**BCC and/or SCC:**
1-8$cm^2$; ≤3mm deep.

**Fitzpatrick Type:**
I (23%); II (56.7%); III (18%); IV (1.7%), (0%), VI (0.6%)

### Lesion Characteristics

**Rhenium-SCT single-session 50Gy treatment to depth of tumour**




### 24 Month Outcomes

**Table 1: Primary endpoint in the EPIC-Skin trial.** Modified visual RECIST response categories for ITT patient tumours, based on 171 evaluable tumours in 130 patients with 24m follow up. Missing data are not imputed.

| Category | All Tumours | BCC Tumours | SCC Tumours |
|---|---|---|---|
| Complete response | 162/171 (94.7%*) | 123/131 (93.9%) | 39/40 (97.5%) |
| Partial response | 6/171 (3.5%) | 6/131 (4.6%) | 0/40 (0.0%) |
| Stable disease | 2/171 (1.2%) | 1/131 (0.8%) | 1/40 (2.5%) |
| Progressive disease | 1/171 (0.6%) | 1/131 (0.8%) | 0/40 (0.0%) |

*Global EPIC-Skin longitudinal response analyses are undergoing final harmonisation and validation ahead of manuscript submission.

**Primary Efficacy Endpoint**
94.7% complete response rate

**Cosmesis**
8.5/10 Patient-rated mean
7.9/10 Clinician rated mean

**QoL**
+7.92 improvement in SKINDEX-16 scores from baseline

**Safety**
Manageable safety profile consistent with conventional radiotherapy

### Typical Healing Trajectory

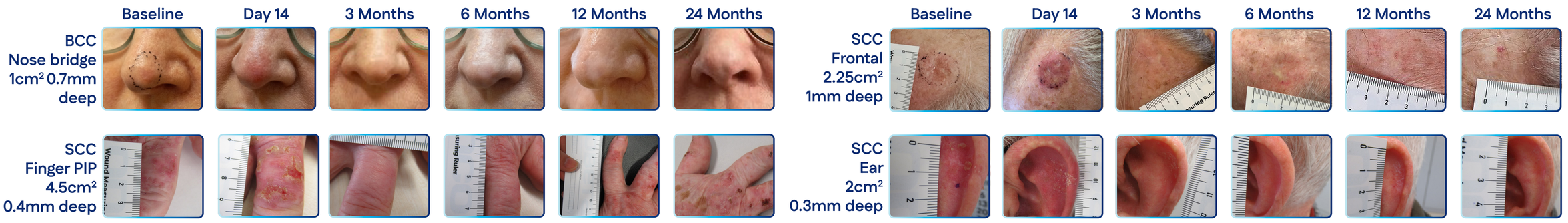



Fig. 1. Example healing profiles in EPIC-Skin over 24m follow-up.

### Local Skin Reactions

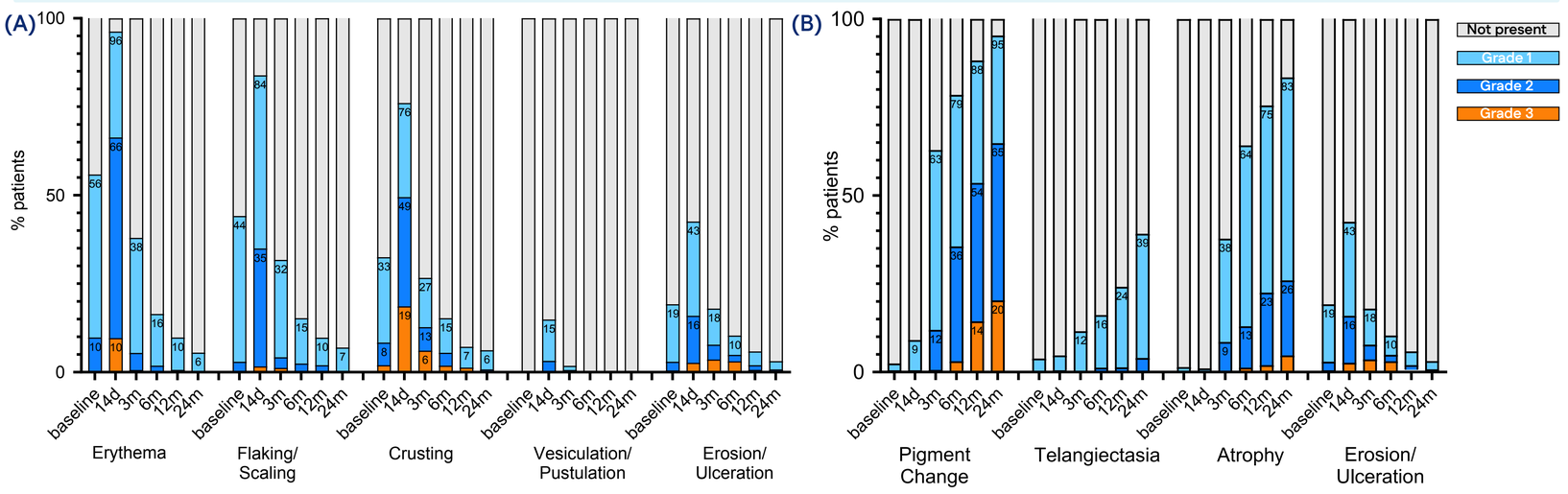



**Fig 2. Distribution of graded local skin reactions following treatment.** Assessments were performed at the lesion level using four independent dermatology raters who graded early local skin reactions (A) and late local skin reactions (B) on a 0–3 scale. Median lesion-level scores across raters were categorized as Grade 1 (0.5–1), Grade 2 (1.5–2), or Grade 3 (2.5–3) and summarized descriptively. Sensitivity analyses limited to lesions with high inter-rater agreement or limited to lesions with 24m of followup demonstrated results consistent with the primary analysis (data not shown).

## 4 Conclusions

Treatment of NMSCs with Rhenium-188 epidermal radioisotope therapy achieved a complete response rate of 94.7% at 24 months post-treatment. Acute local skin reactions were consistent with expected radiation-related effects, were predominantly mild to moderate in severity. Local skin reactions returned to below baseline by 3 months and generally resolved within 12 months. Late local skin reactions were primarily pigmentary alterations and atrophy, typically mild to moderate in severity.

These findings demonstrate the high clinical benefit of Rhenium-188 treatment and support the need for transparent discussion with patients regarding expected skin changes as part of shared decision-making when considering treatment options.

**References:** [1] Giuseppe Cardaci, MBBS,a Siddhartha Baxi, MBBS,b Saima Vohra, PhD,c Cody Allison, PhD,d Angela Hong, MBBS,e,f Nicola Mulholland, MBBS,g Mike Sathekge, MBChB, PhD,h Kgomotso Mokoala, MBChB,h Martin Heuschkel, Dr. med.,i Julia Tietze, Dr. med.,j Siroos Mirzaei, FANM,k and Gerhard Dahlhoff, Dr. med.l,, (2025), Efficacy, Safety, and Patient Reported Outcomes of Rhenium-Skin Cancer Therapy for Non Melanoma Skin Cancer: 1-Year Results from the EPIC-Skin Study, Advances in Radiation Oncology, 101802. Rhenium-Skin Cancer Therapy (SCT) for the Treatment of Non-Melanoma Skin Cancer. (EPIC-Skin); ClinicalTrials.gov ID NCT05135052

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