

Current standards for SCC diagnosis and treatment

Jemima Mellerio

St John's Institute of Dermatology

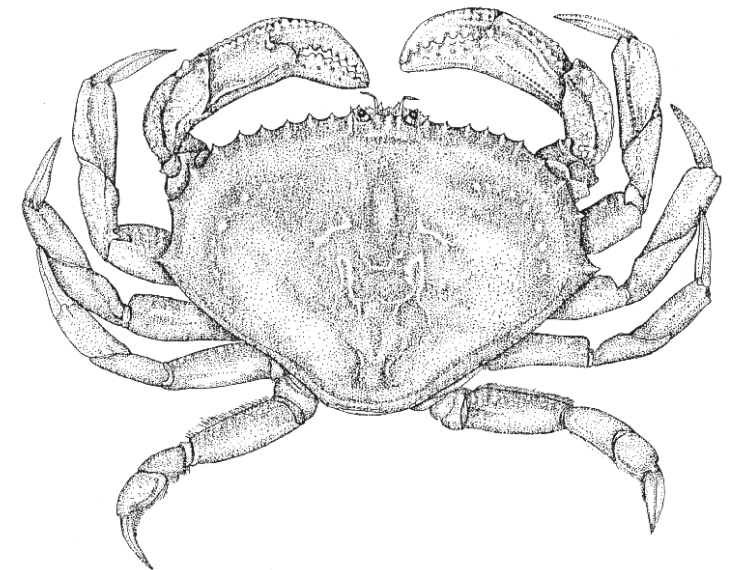
Guy's and St Thomas' NHS Foundation Trust

London



Squamous cell carcinoma in EB

- Predominantly in severe RDEB
 - Occur early in life
 - Multiple primary tumours
 - Behave aggressively
 - Arise at sites of repeated injury and scarring
- Other types but later onset (Kindler, other RDEB, DDEB, JEB)
- Multifactorial aetiology
 - e.g. fibrosis, inflammation, colonization, innate immunity



Squamous cell carcinoma in EB

Fine et al. *J Am Acad Dermatol* 2009

Cumulative risk of at least one SCC:

7.5% by 20 years

68% by 35 years

80% by 45 years

90% by 55 years

Cumulative risk of death if have had SCC:

57% by 35 years

87% by 45 years

Most die within **5 years** of a 1st SCC

Kim et al. *Acta Derm Venereol* 2018

17/49 RDEB had SCC

11 RDEB-S:

Cumulative risk of at least one SCC:

26% by 20 years

76% by 35 years

Cumulative risk of SCC-related death:

30% by 25 years

84% by 34 years

Median survival from 1st SCC **4 years**

Squamous cell carcinoma in EB

Robertson et al. *Acta Derm Venereol* 2021

28-year experience of EB SCC

221 tumours in 44 patients

31 RDEB-S:

Median age 29.5 y (13-52)

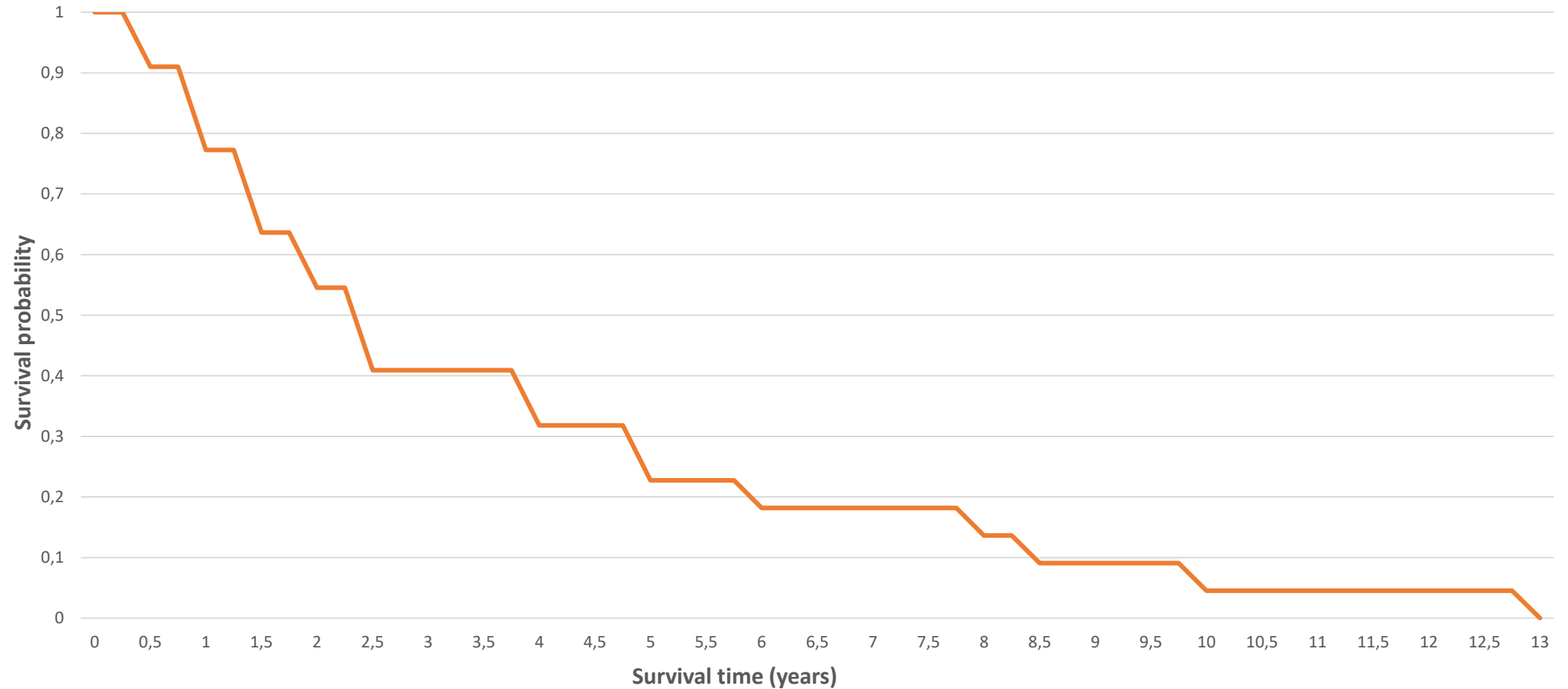
13 other EB types (DEB, JEB, KEB):

Median age 47.1 y (30-89)

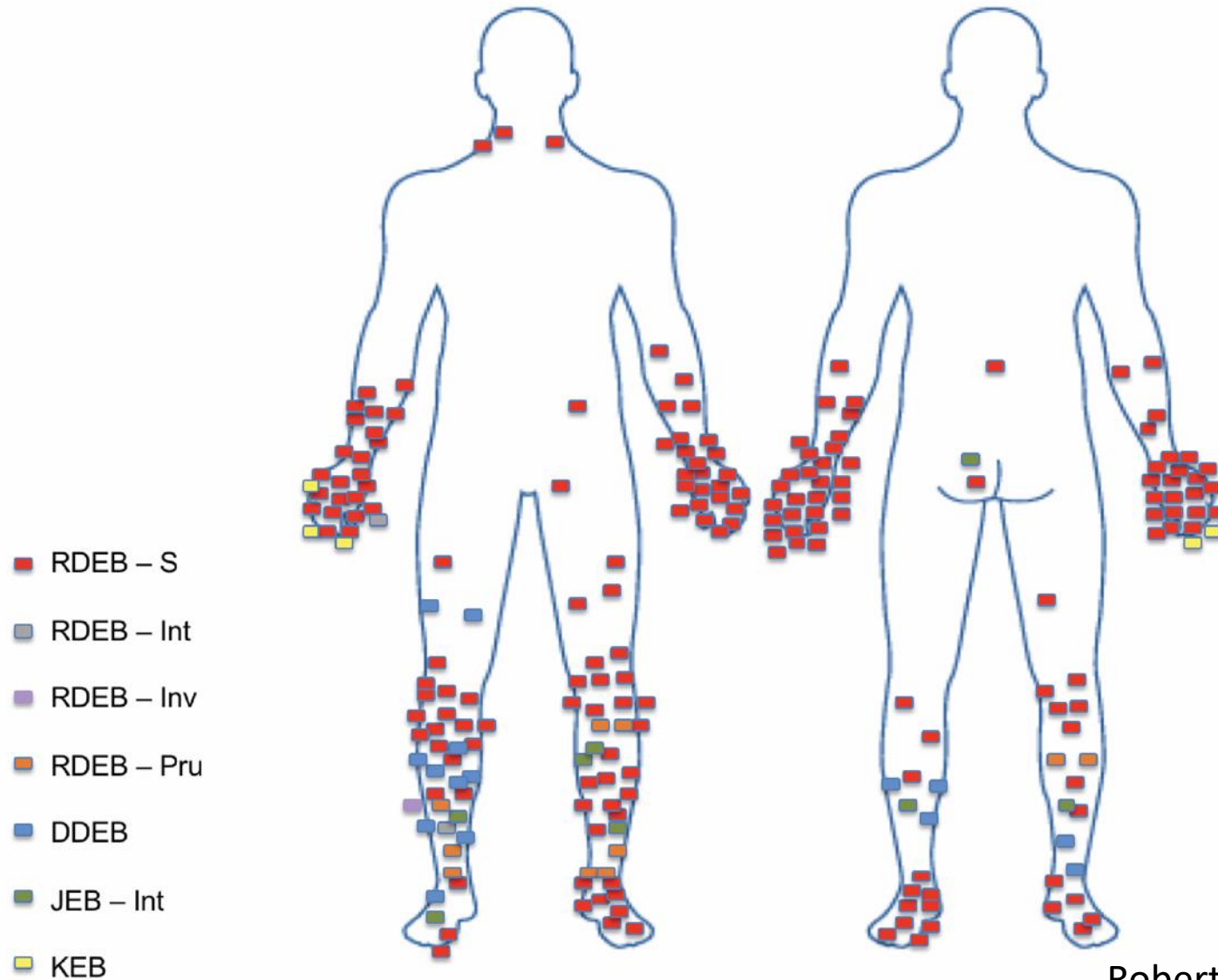
Mean number of primaries 5.8 (1-44)

RDEB-S median survival from 1st SCC **2.4 y** (0.5-12.6)

Squamous cell carcinoma in EB



SCC in EB: Natural history

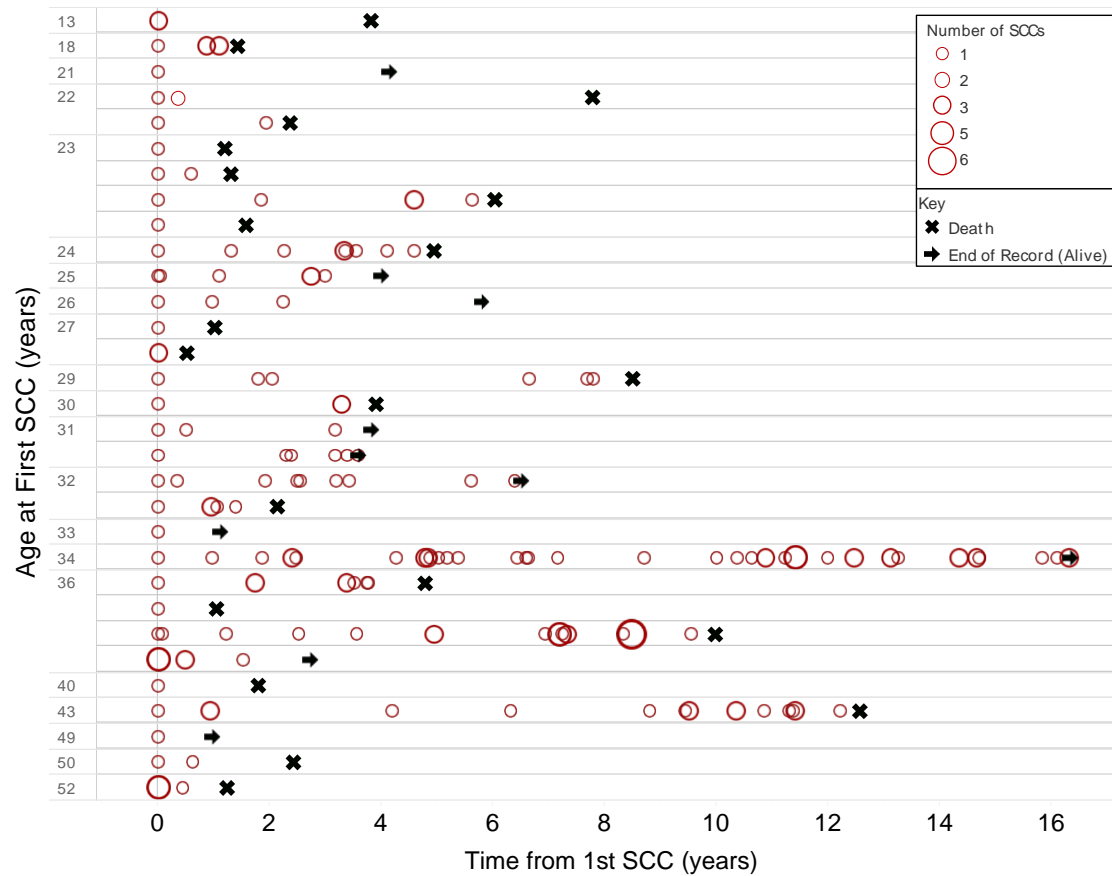


SCC in EB: Natural history

- Areas of recurrent wounding and scarring
- Multiple primaries
- Behave aggressively despite complete excision

SCC in EB: Natural history

- Crescendo effect of new cancers



SCC in EB: Guidelines

- Open access
- Downloadable from DEBRA International website
www.debra-international.org

SYSTEMATIC REVIEW

BJD
British Journal of Dermatology

Management of cutaneous squamous cell carcinoma in patients with epidermolysis bullosa: best clinical practice guidelines

J.E. Mellerio,^{1,2} S.J. Robertson,³ C. Bernardis,⁴ A. Diem,⁵ J.D. Fine,⁶ R. George,⁷ D. Goldberg,⁸ G.B. Halmos,⁹ M. Harries,¹⁰ M.F. Jonkman,¹¹ A. Lucky,¹² A.E. Martinez,² E. Maubec,¹³ S. Morris,¹⁰ D.F. Murrell,¹⁴ F. Palisson,¹⁵ E.I. Pillay,¹ A. Robson,¹⁶ J.C. Salas-Alanis¹⁷ and J.A. McGrath¹⁸

Mellerio *et al.* *Br J Dermatol* 2016; 174: 55-67

SCC in EB: Surveillance and monitoring

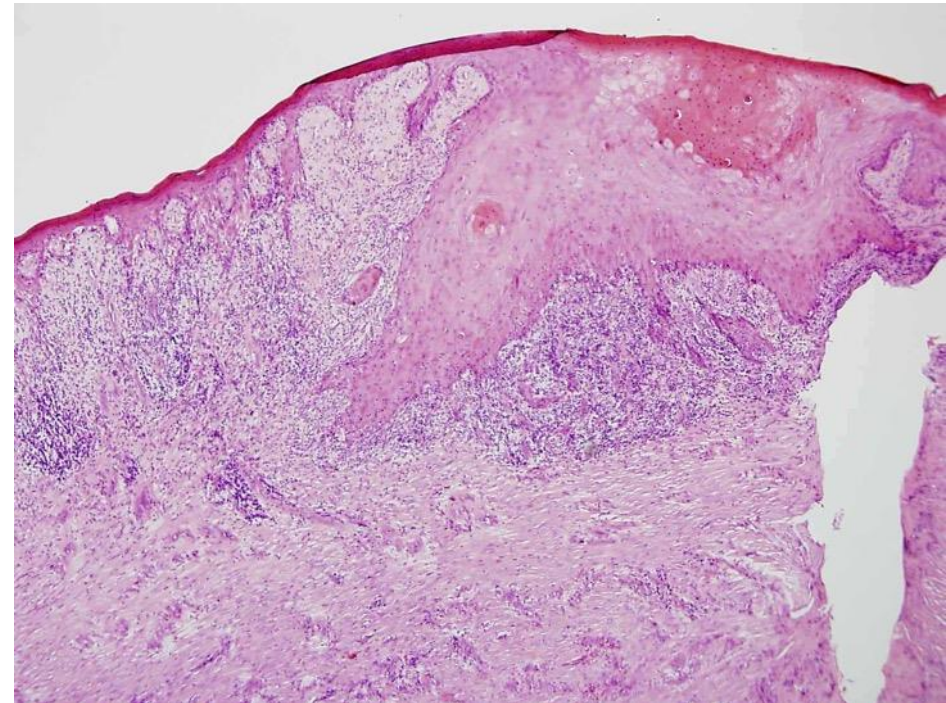
- Non-healing
- Exophytic
- Hyperkeratotic
- 'Feels different'

SCC in EB: Surveillance and monitoring

- Discuss with parents/caregivers and patients from childhood/adolescence
- RDEB-S every 3-6 months from 10 years
- Other at-risk types every 6-12 months from 20 years
- High degree of suspicion at all times
- 3-monthly follow-up after SCC diagnosed

SCC in EB: Diagnosis

- Biopsy: several punch biopsies
- Pathologist with experience of EB SCCs if possible
- Discussion with multidisciplinary team

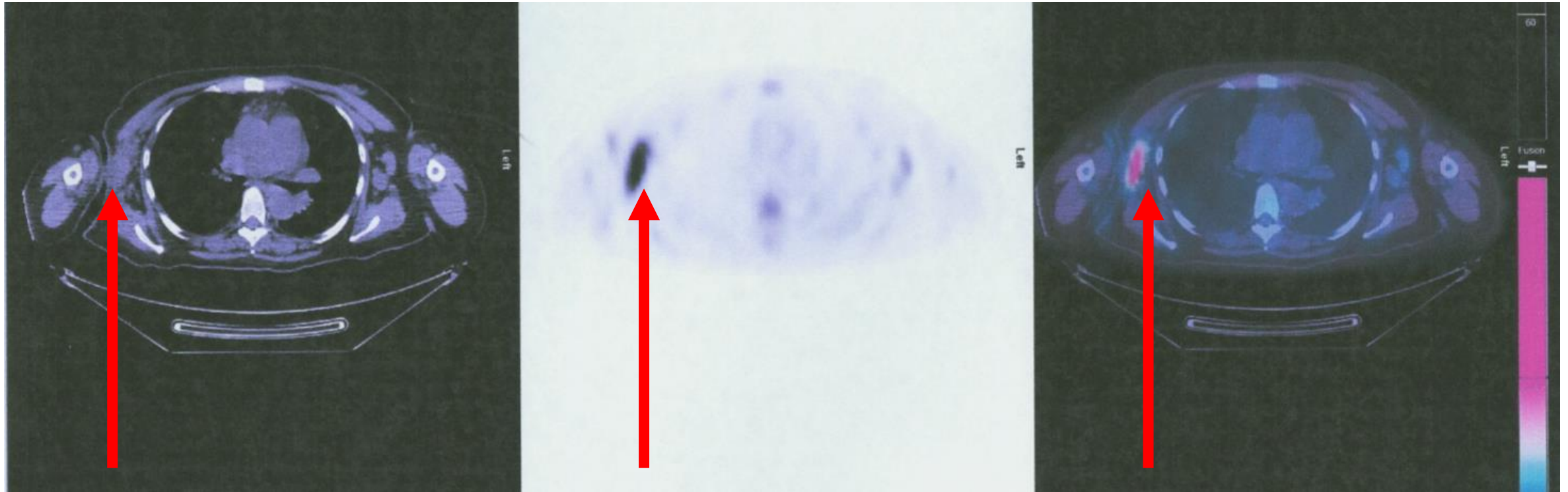


SCC in EB: Staging

- Fine needle aspiration of palpable regional lymph nodes
- Ultrasound-guided lymph node biopsy
- Role for sentinel lymph node biopsy?
- Offer regional lymph node clearance if positive
- CT or MRI if ≥ 5 cm diameter or underlying structures to assess pre-op

SCC in EB: Staging

- FDG-PET/CT scan if $\geq 5\text{cm}$ diameter or suspicion of spread



SCC in EB: Treatment

- Wide local excision is treatment of choice
- Amputation if extensive or anatomical constraints
- Regional LN clearance if positive
- Role of Mohs micrographic surgery?
- *In situ* disease: ? Imiquimod, topical 5-fluorouracil or photodynamic therapy



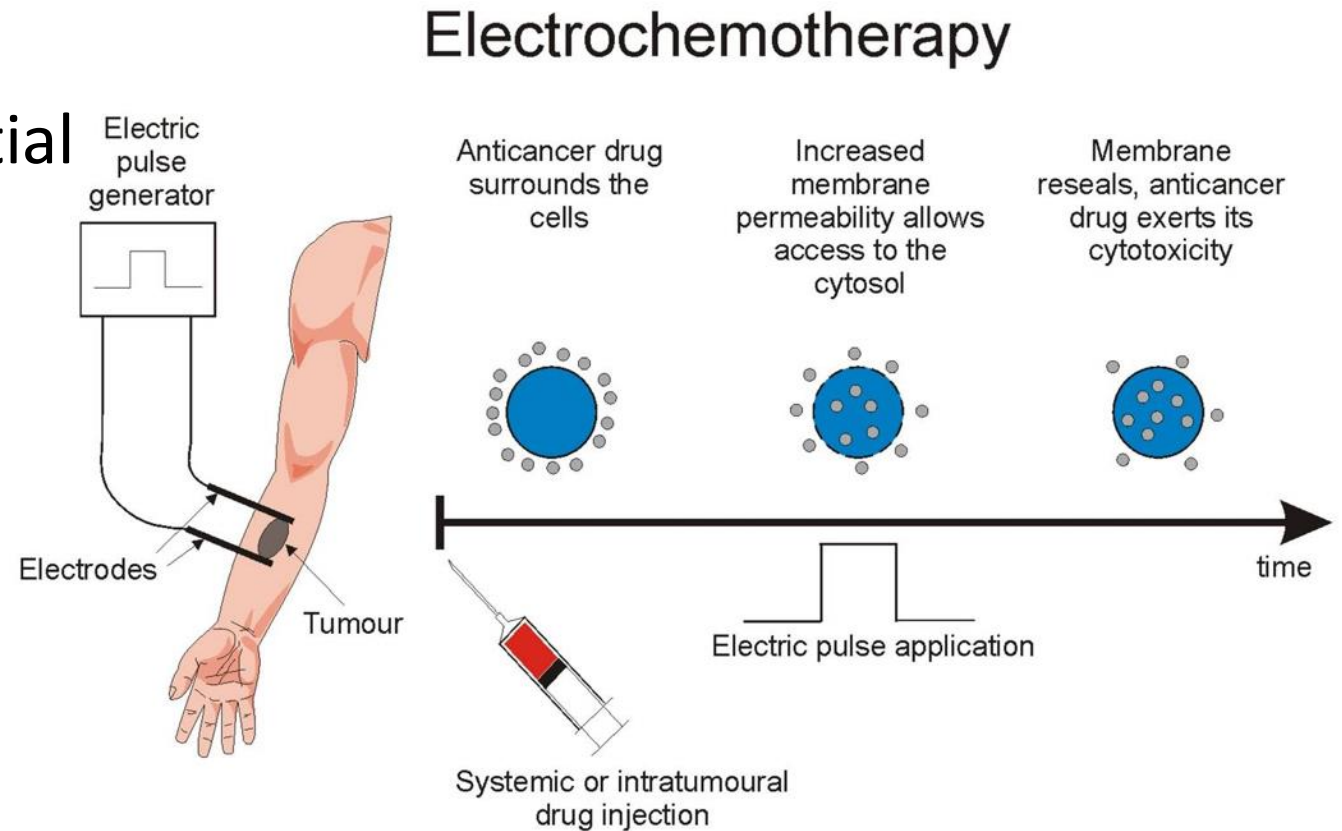
SCC in EB: Adjuvant treatment

- Radiotherapy
 - Local, regional or distant spread
 - Give in smaller fractions to limit skin damage
- Conventional chemotherapy
 - Cisplatin, 5-fluorouracil
 - Generally poor responses and significant toxicity

SCC in EB: Adjuvant treatment

- Electrochemotherapy

- IV bleomycin
- Case reports showing partial or complete responses
- Pain and sepsis

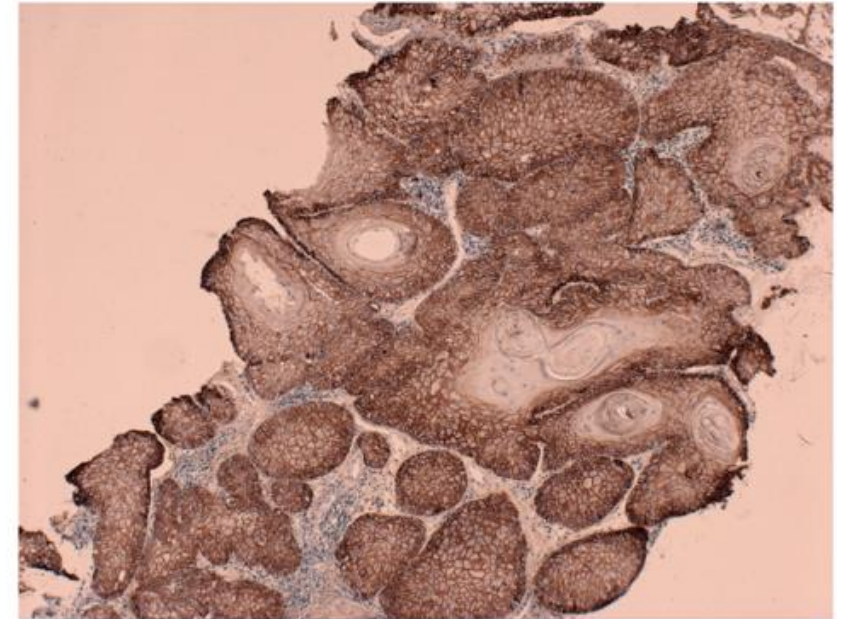
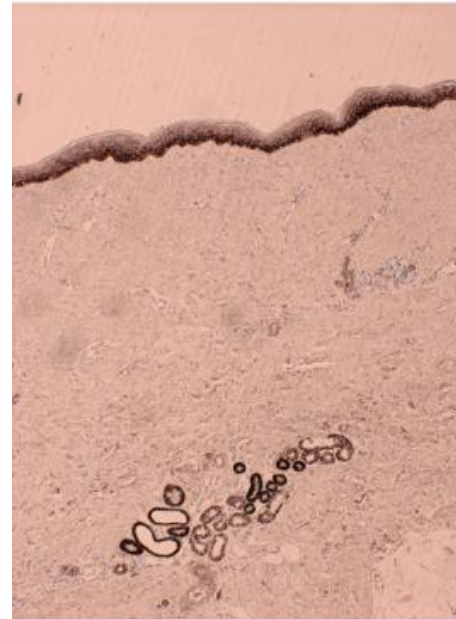


Diociaiuti et al. *JEADV* 2016;30:1195-6

Bartolo et al. *Dermatol Ther* 2020;33:e14093

SCC in EB: Adjuvant treatment

- **Cetuximab**
 - Monoclonal EGFR inhibitor
 - Weekly IV infusions
 - Variable clinical response



EGFR

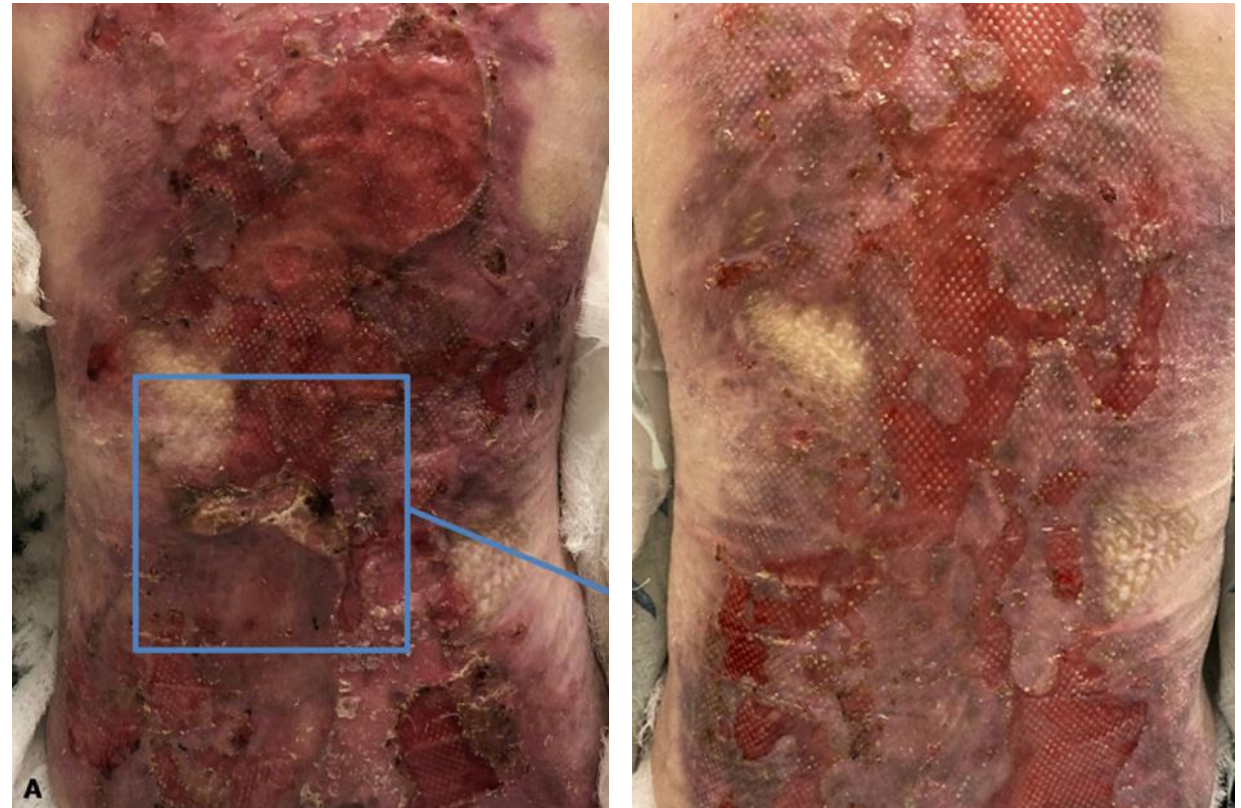
SCC in EB: Adjuvant treatment

- Checkpoint inhibitors: anti-PD-1 or PD-1R
- **Pembrolizumab**
 - PD-1 inhibitor
 - IV every 3 or 6 weeks
- **Nivolumab**
 - PD-1 inhibitor
 - IV every 2 or 4 weeks
 - Phase II clinical trial for locally advanced or metastatic SCC of the skin



SCC in EB: Adjuvant treatment

- Checkpoint inhibitors: anti-PD-1 or PD-1R
- **Cemiplimab**
 - PD-1 inhibitor
 - FDA and EMA approved for advanced cutaneous SCC
 - IV every 3 weeks



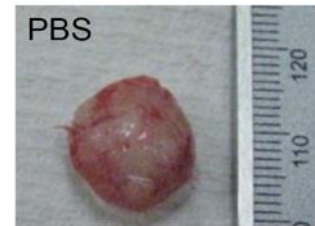
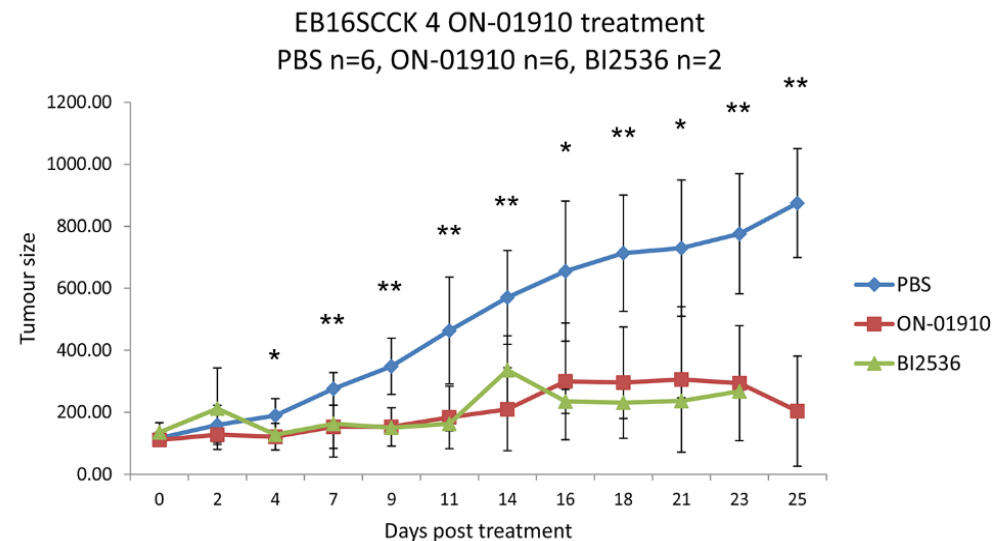
SCC in EB: Adjuvant treatment

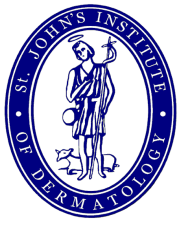
- Checkpoint inhibitors: anti-PD-1 or PD-1R
- **Cemiplimab**
 - PD-1 inhibitor
 - FDA and EMA approved for advanced cutaneous SCC
 - IV every 3 weeks



SCC in EB: Adjuvant treatment

- Polo-like kinase inhibitor
- **Rigosertib**
 - IV or oral
 - Phase II clinical trial underway for RDEB SCCs





SCC in EB: Prevention

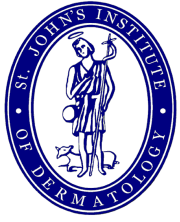
- Systemic retinoids
 - Tolerated in EB
 - No clinical trials of efficacy
 - When to start?
 - Potential for rebound?
- ?Metformin
 - Enhanced respiration and glycolysis gene expression analyses in RDEB SCC cells
 - Anti-neoplastic effect *in vitro* and *in vivo* with metformin



SCC in EB: End of life care

- Involvement of palliative care services early
- Patient and family at the centre of decision-making
 - Pain control
 - Wound management
 - Psychological support
 - Support with personal care





SCC in EB: Summary

Major issue especially severe RDEB

Other EB types also at risk

Aggressive, multiple primaries, poor life expectancy

Diagnostic difficulties of cancer vs normal EB wounds

Surgery remains gold standard but may not be possible

Clinical trials of newer therapies logistically challenging

Knowledge of mechanisms as a key to new therapies

Repurposing of other cancer treatments