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17-20 September 2024

PreCongress day: 16 September

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Non-Melanoma Skin Cancer

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Introduction

- NMSC Melanoma 5%
- BCC (75%)
- SCC (20%)
- Merkel Cell(1%)
- {Adnexal}/{Sarcoma} others
- High levels in Head and Neck and are increasing in Incidence
- A great opportunity for OMF Surgeons

- UK 230,000 cases NMSC/year
- 90% of all skin cancers are NMSC
- 57% males 43% females
- Age Incidence rates Highest in > 90yr olds
- Trends UK since1990s, incidence rates have increased by 169%
- Last decade, rates have increased 42%
- Mortality > 720 deaths from NMSC UK each yr
- <1% of all cancer deaths
- Projections Incidence up to 400,000 per year

Cancer Research UK. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/non-melanoma-skin-cancer

Causes of Non-Melanoma Skin Cancer (NMSC)

- Ultraviolet (UV) Radiation: Sunlight / Tanning Beds
- Skin Type Fair Skin; Red or Fair Hair
- Genetic Factors
  - Family History
  - Previous Skin Cancer
- Other Factors
  - Chronic Wounds / Inflammation
  - Weakened Immune System
  - Human Papillomavirus (HPV)

Genetics of NMSC:

Key Genetic Mutations

- TP53: Mutations in this tumor suppressor gene are common in NMSC
- PTCH1/2 SUFU : Mutations in these genes are linked to basal cell carcinoma (BCC)
- CDKN2A: Alterations in this gene are associated with squamous cell carcinoma (SCC)

Genomic Instability

-DNA Repair Deficiency: Defects in DNA repair mechanisms genomic instability and cancer

Epigenetic Changes

- Methylation: Abnormal DNA methylation patterns can contribute to NMSC development

Inherited Syndromes

- Gorlin Syndrome: Caused by mutations in the PTCH1 gene, increasing the risk of BCC
- Xeroderma Pigmentosum: A condition with defective DNA repair -high risk of skin cancers

Tumor Microenvironment

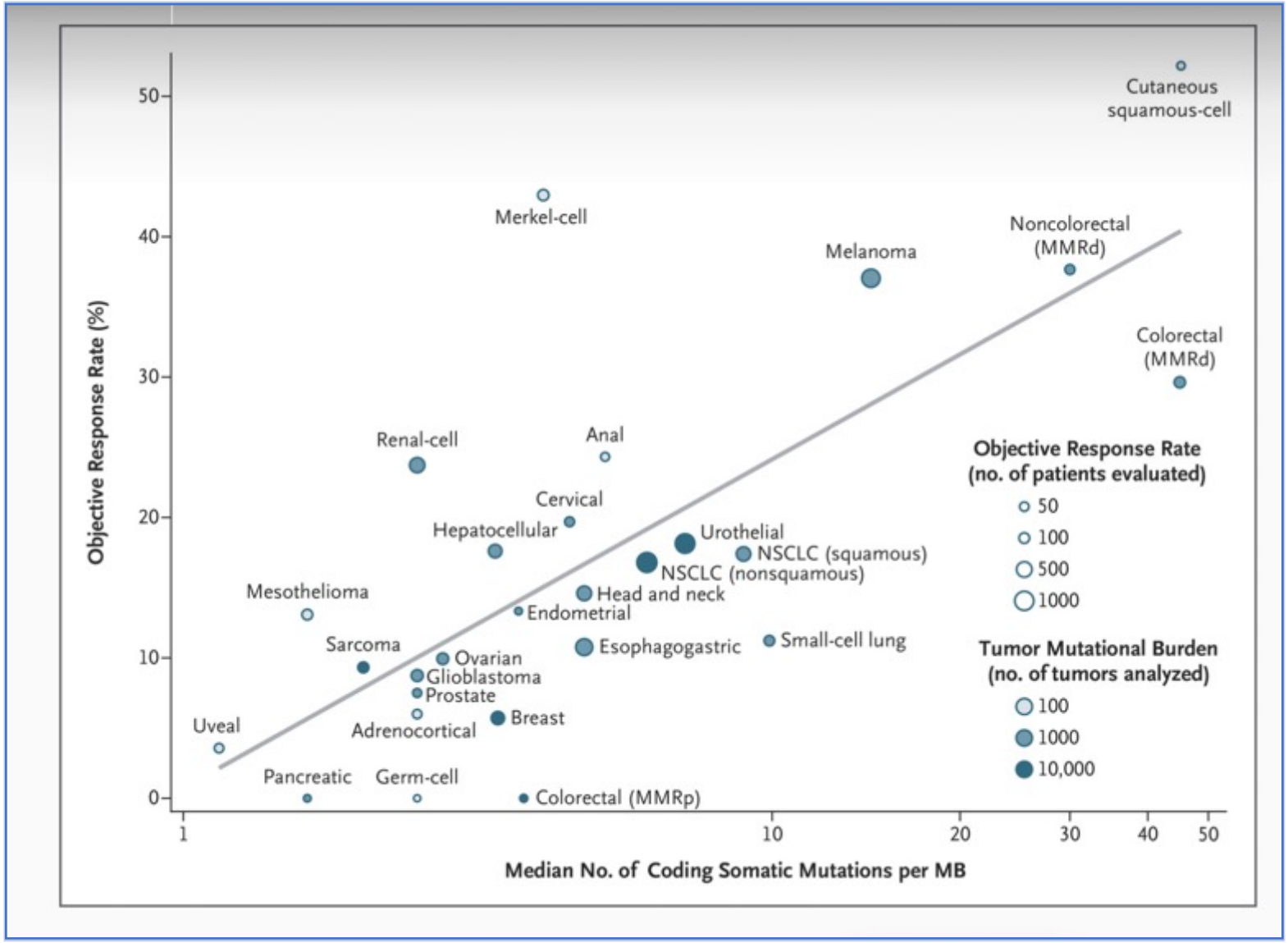
- Immune Response: Genetic factors influencing the **immune response** can affect NMSC progression

Yarchoan NEMJ 2017

Tumor Mutational Burden and Response Rate to PD-1 Inhibition

cSCC is highly Immunogenic

PDL-1 highly expressed



Common Immunotherapy Drugs for NMSC

- Cemiplimab (Libtayo)
  - Type: Anti-PD-1 antibody
  - Use: Approved for advanced cutaneous squamous cell carcinoma (CSCC) not curable by surgery or radiation
- Pembrolizumab (Keytruda)
  - Type: Anti-PD-1 antibody
  - Use: Effective in treating advanced CSCC and Merkel cell carcinoma (MCC)
- Avelumab (Bavencio)
  - Type: Anti-PD-L1 antibody
  - Use: Used for advanced MCC.
- Nivolumab (Opdivo)
  - Type: Anti-PD-1 antibody
  - Use: Investigated for use in advanced NMSC.
- Ipilimumab (Yervoy)
  - Type: Anti-CTLA-4 antibody
  - Use: Sometimes used in combination with other immunotherapies for advanced skin cancers

Features of Aggressive NMSC

- Local Invasion
- Cranial Nerve involvement VII V
- Vital Structures Eyes, Nose, Skull Base, Bone
- Parotid Gland
- Loco-Regional Lymph nodes
- Distant Metastasis

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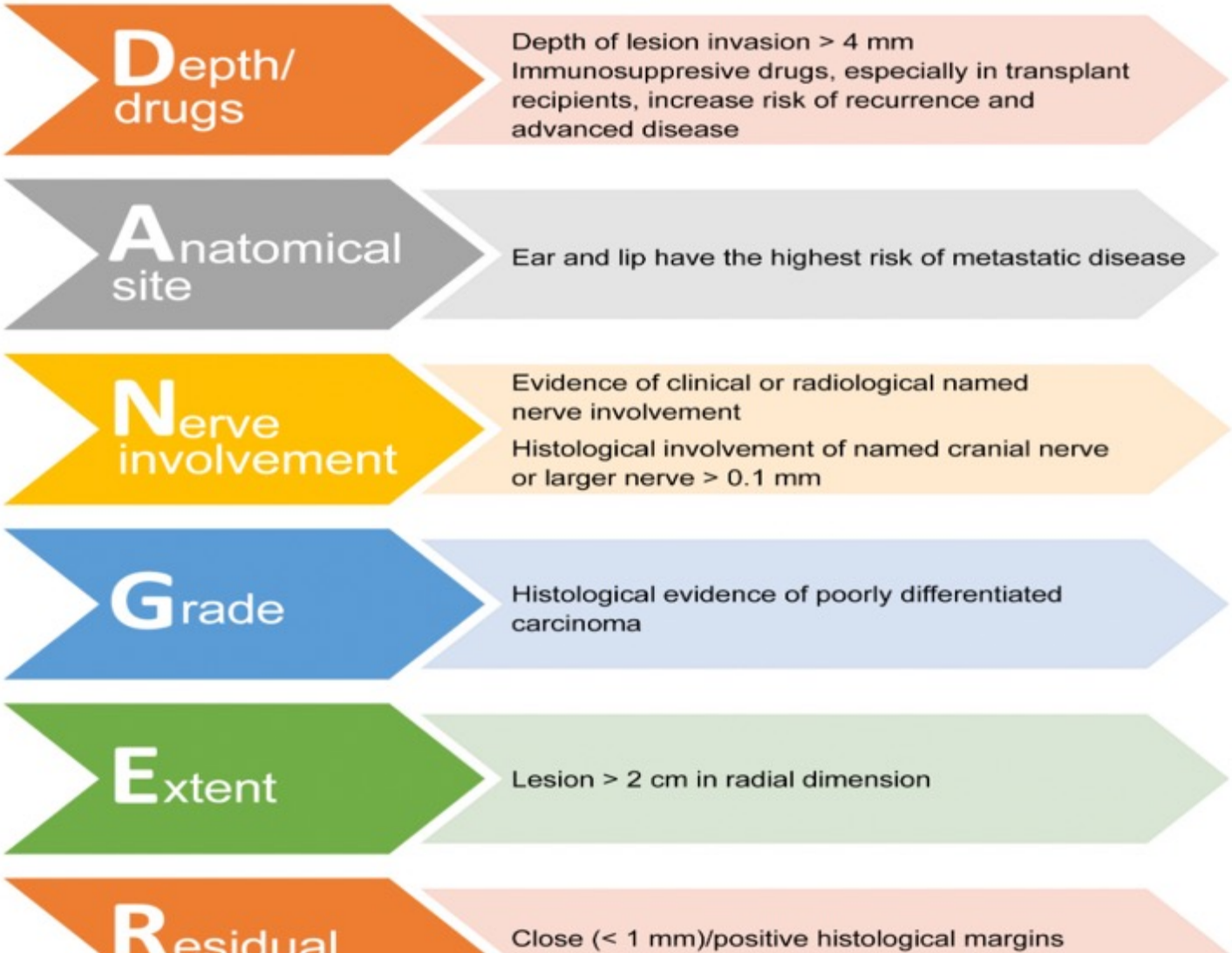
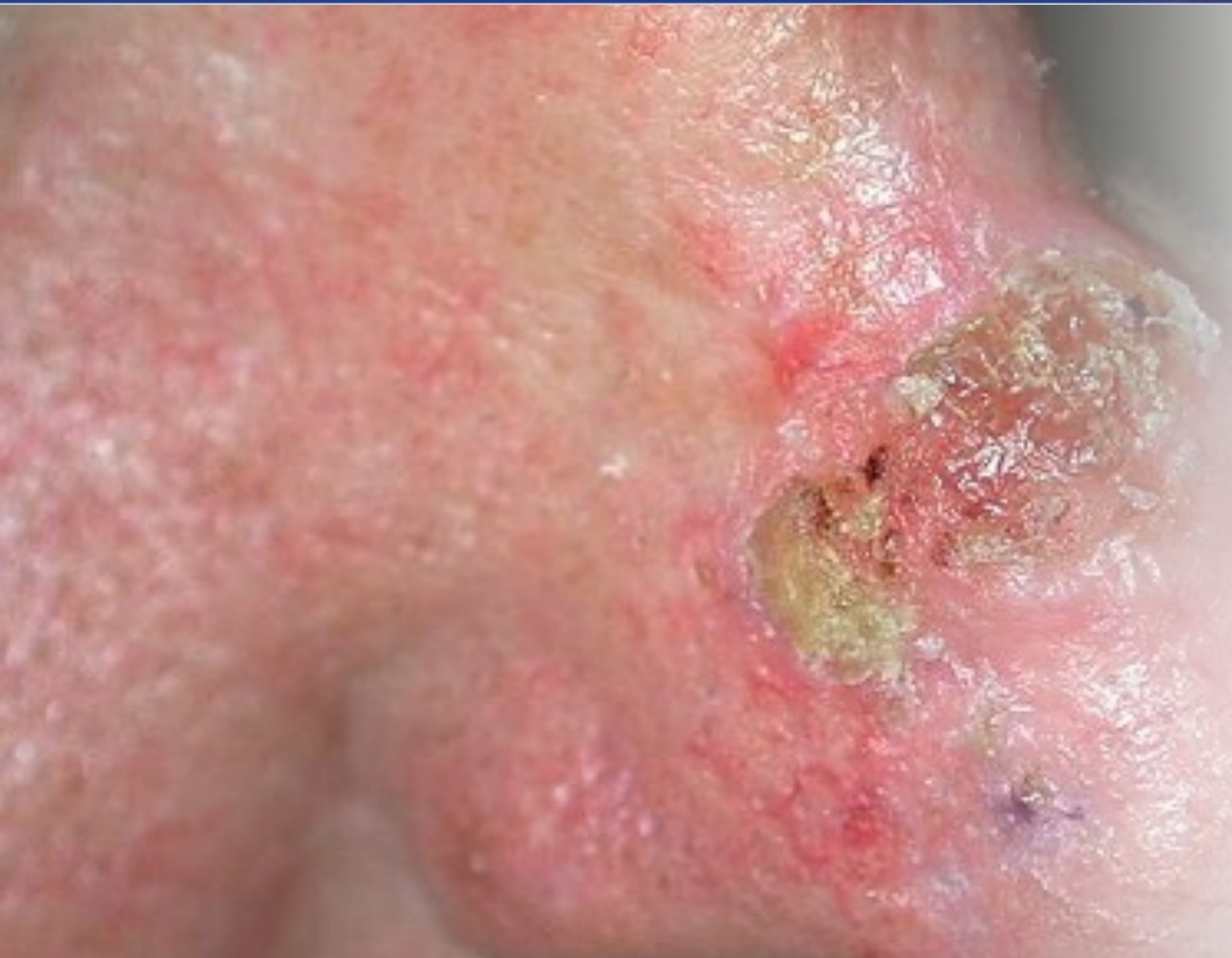
1 The DANGER framework used to identify high risk primary cutaneous lesions



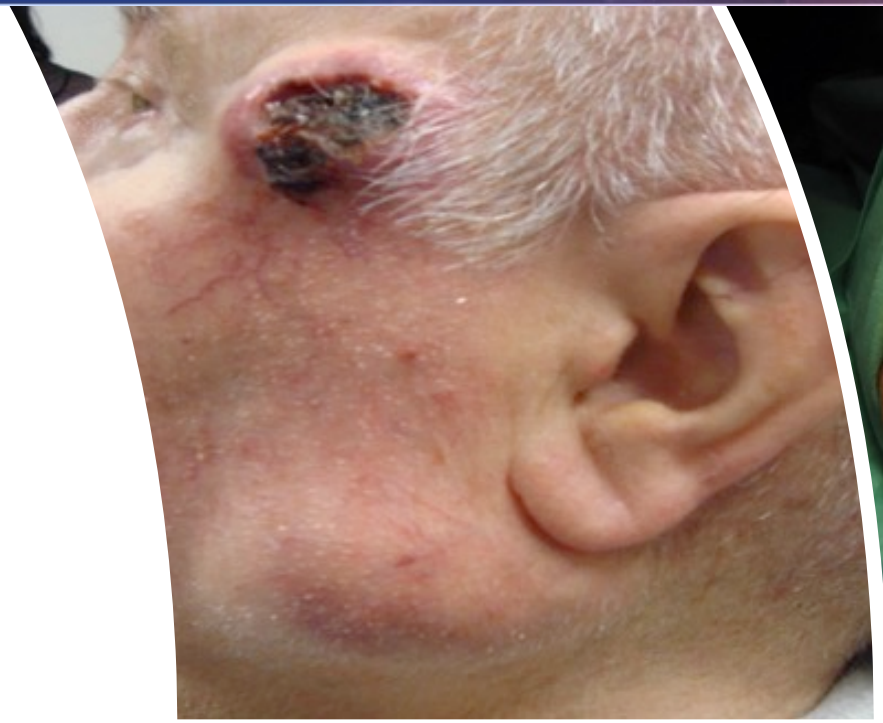


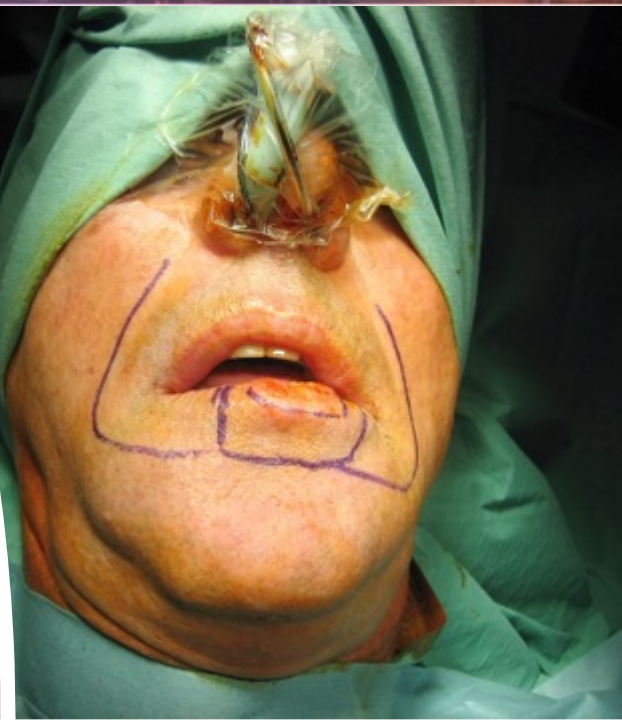
The Good

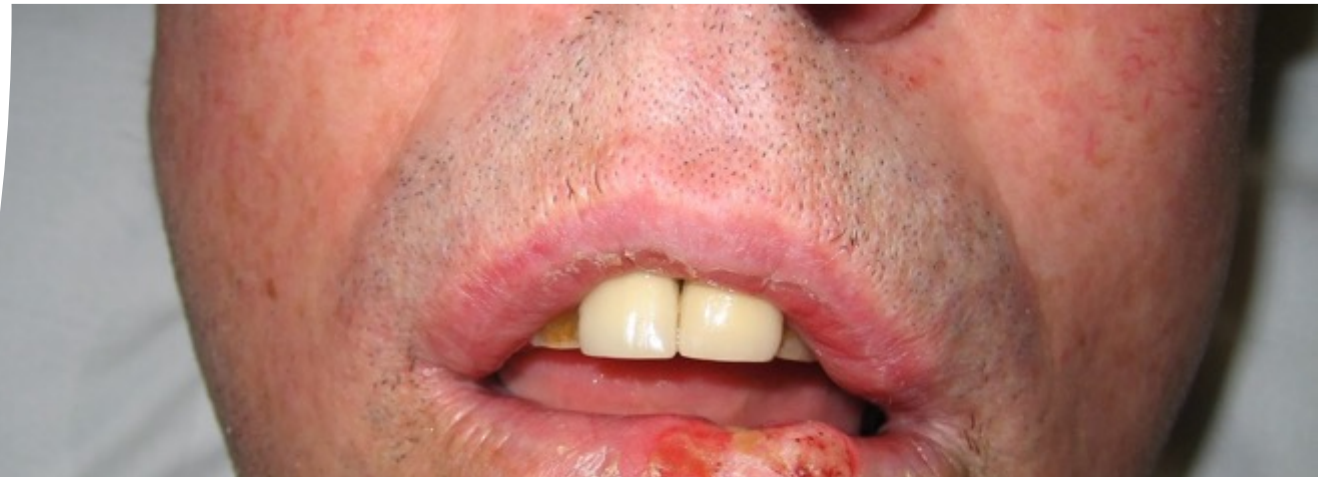
- Local Disease with no nodal extension
- Prognosis good with excision margins
- Local Recurrence 2-5%

The Bad

- Multi focal disease
- Nodal extension
- Parotid and Facial Nerve Involvement
- Perineural Spread
- Critical Structures
  - Oral Sphincter, Eye , Nose

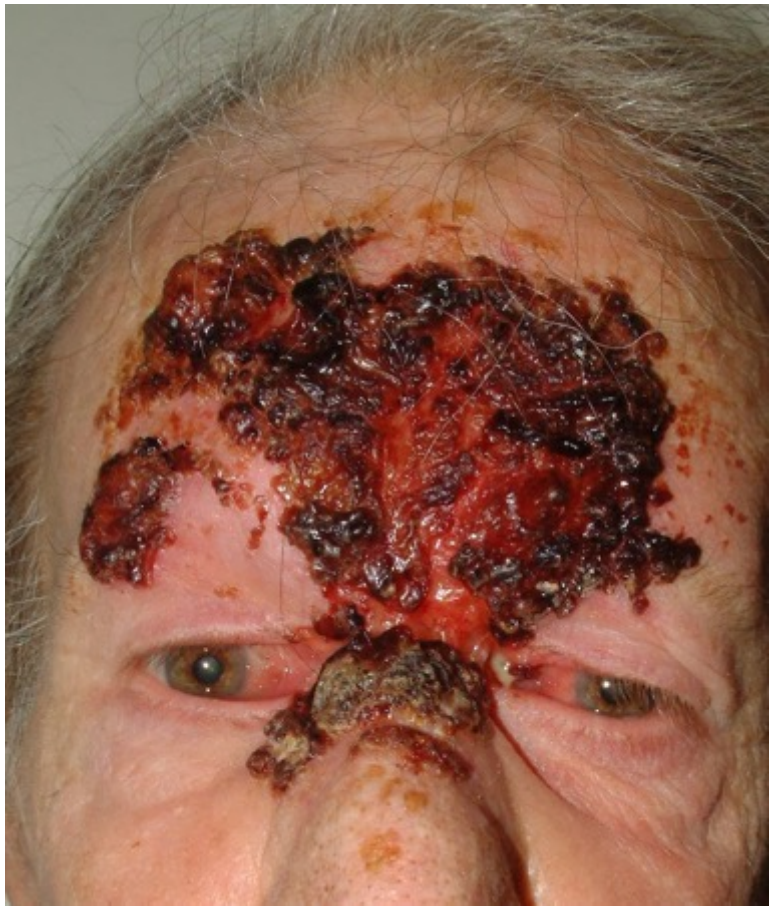


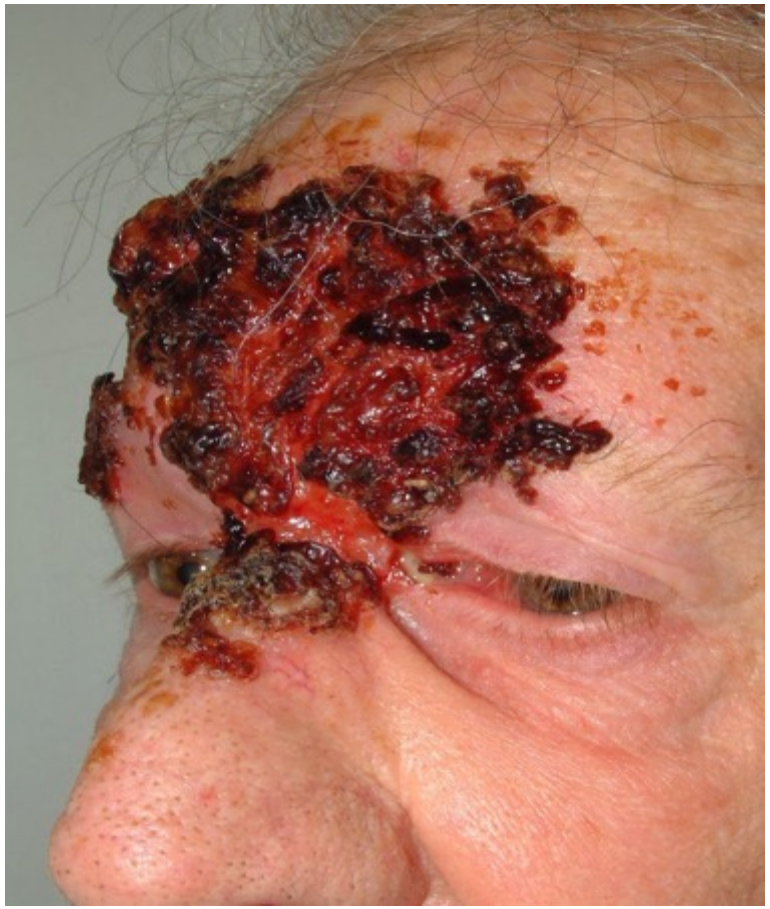


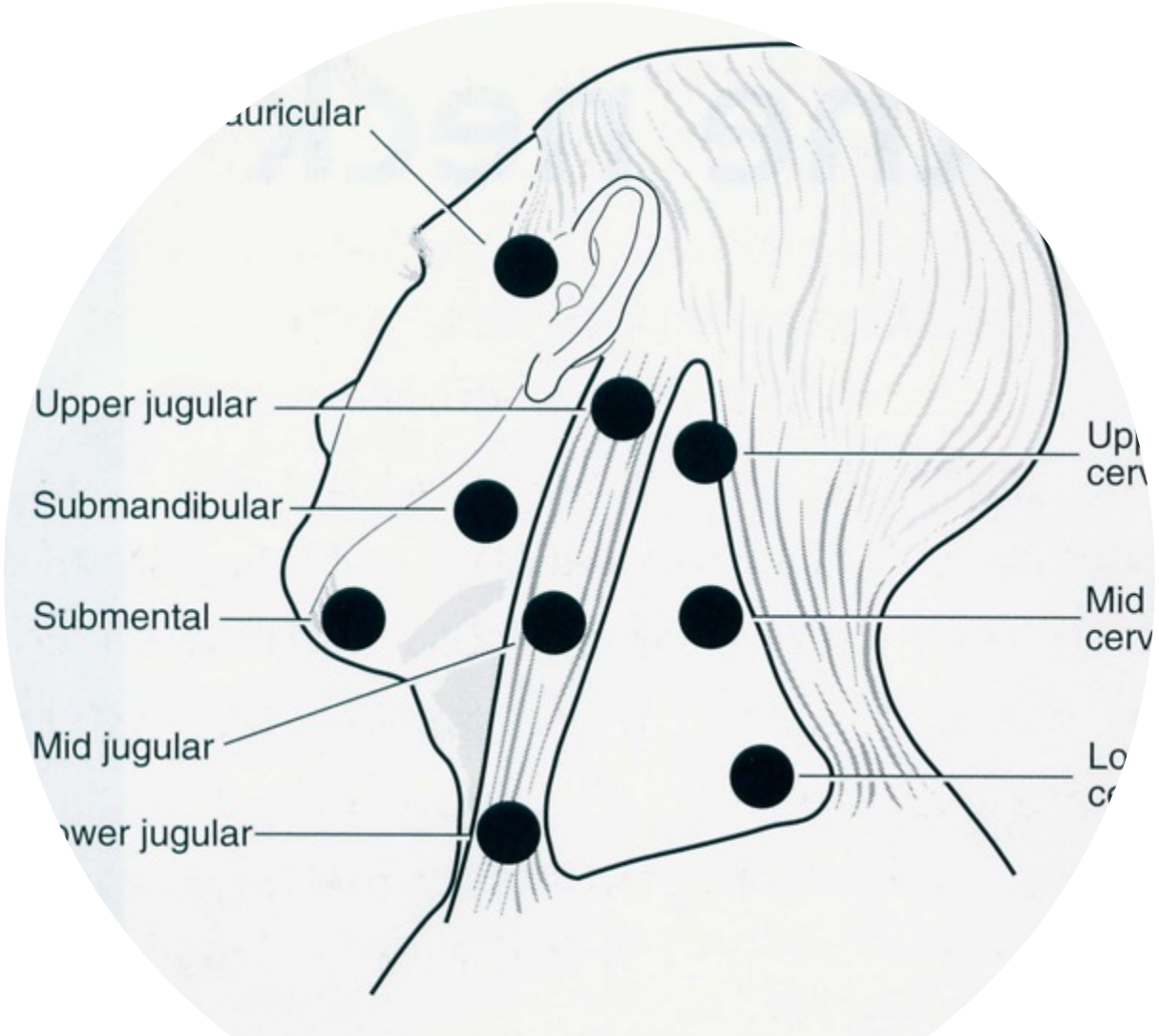


The Ugly

- Widespread Malignancy
- Cranial Extension
- Neglect
- Poor general health
- Psychological Issues
- Team resource







Parotid and Neck in cSCC

- Survival is related to Neck Disease
- Parotid first echelon nodal bed
- Any regional metastasis to the neck when compared to parotid alone conferred **worse** DSS and OS
- Regional metastasis of HNcSCC to the neck confers **worse** outcomes compared to metastasis to the parotid alone.

Sydney Unit

n= 535 cSCC

Long follow up

Parotid Staging parotid positive only ? neck mets?

Neck Disease -Overall Survival and Disease Specific Survival reduced with neck metastasis

Follow up and Survival

Management Strategies

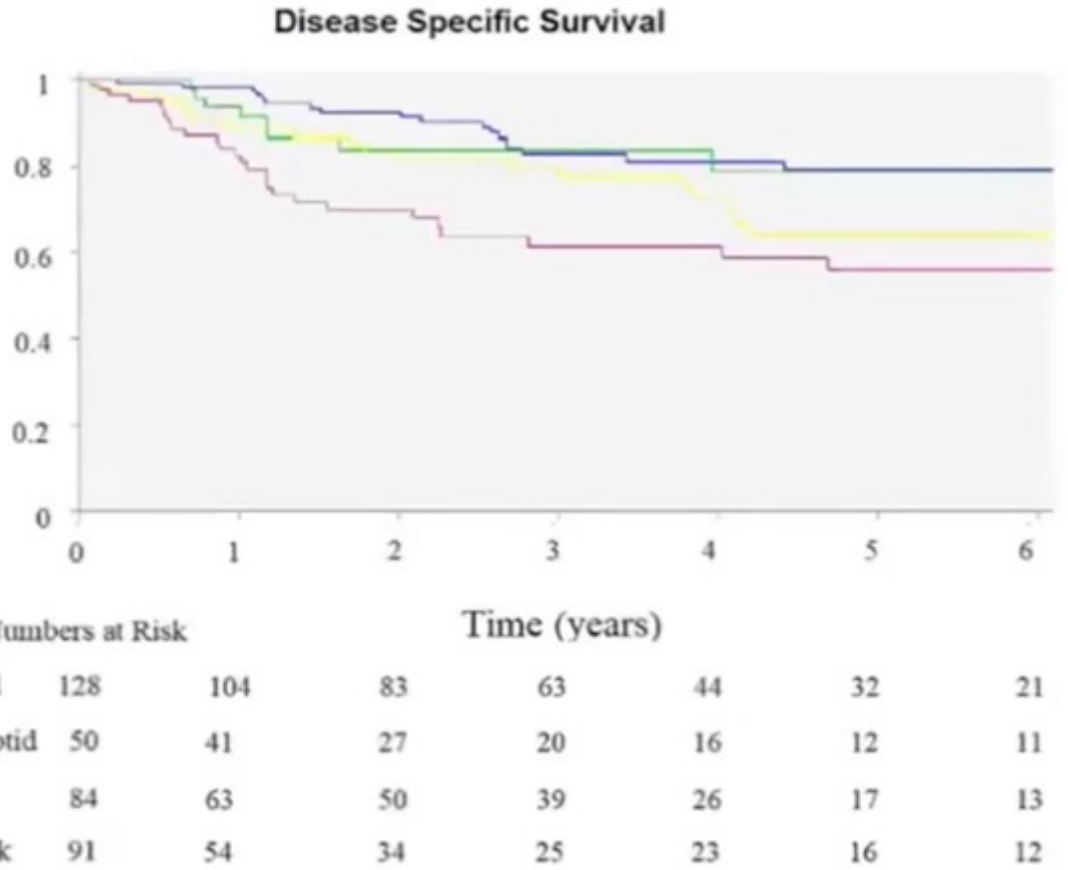
HEAD & NECK
JOURNAL OF THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK

ORIGINAL ARTICLE

The significance of regional metastasis location in head and neck cutaneous squamous cell carcinoma

Craig P. Mooney MBBS, Jonathan R. Clark MBBS, MD, FRACS, Kerwin Shannon MBBS, FRACS, Carsten E. Palme MBBS, FRACS ... See all authors

First published: 21 May 2021 | https://doi.org/10.1002/hed.26744 | Citations: 5



- Develop Neck protocols
- Extra capsular Spread ECS
- PNI
- Facial Palsy or Trigeminal Neuralgia Red Flags for spreading cSCC
- Consider Extent of resection, Allow for Skip Lesions
- Reconstruction considerations
- Adjuvant Radiotherapy

What are the Risk Factors for Neck Metastases from cSCC?

Tumour Factors:

Size: Tumors >2 cm

Depth of Invasion Tumors that invade beyond the subcutaneous fat

Poor Differentiation a higher risk

Perineural Invasion

Location:

Critical sites Tumours located on the ear lip or temple

Patient Factors:

Immunosuppression: Increase tumour burden

Age: Older patients are at higher risk.

Histopathology: PNI LVI

ECS Spread beyond the lymph node capsule

Previous Treatments:

SCC in scar

Prior RT to head and neck area

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NCCN Guidelines Version 1.2024
Squamous Cell Skin Cancer

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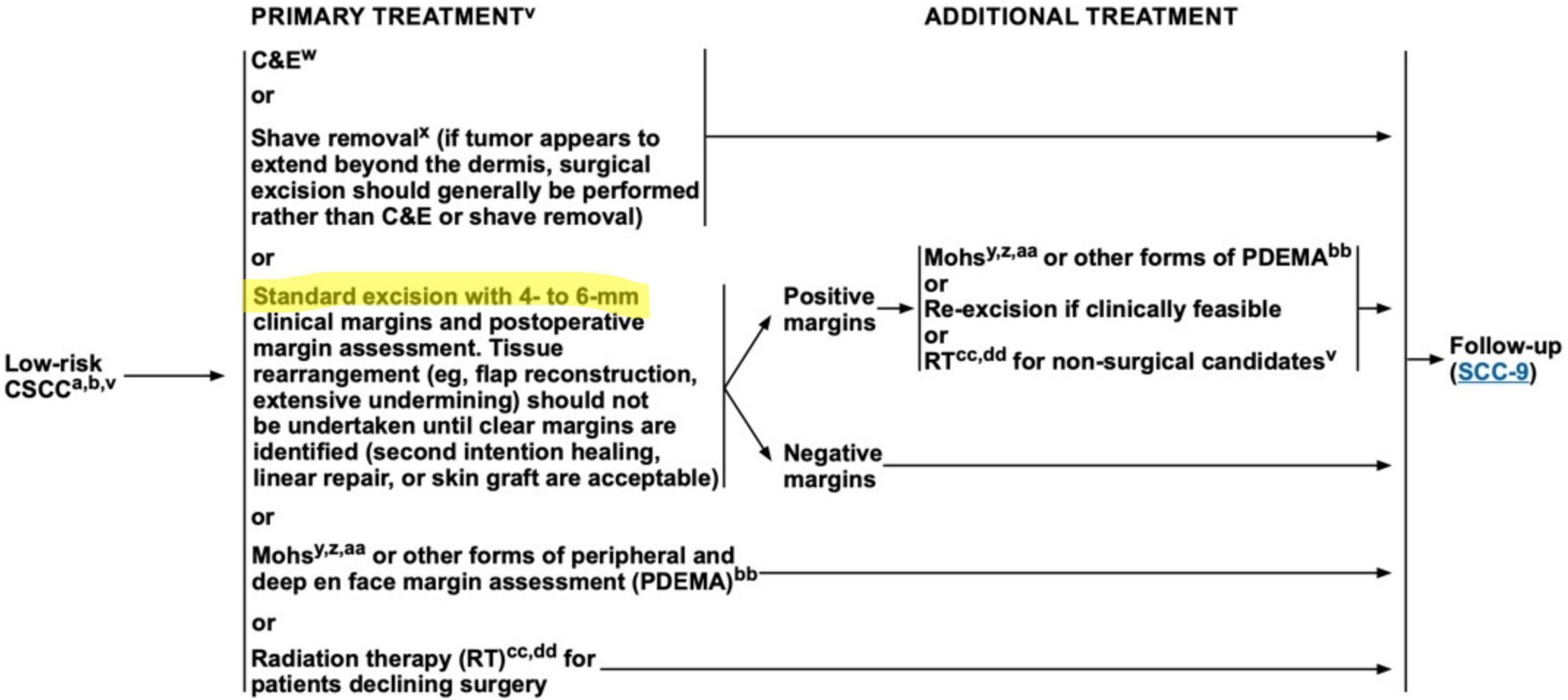

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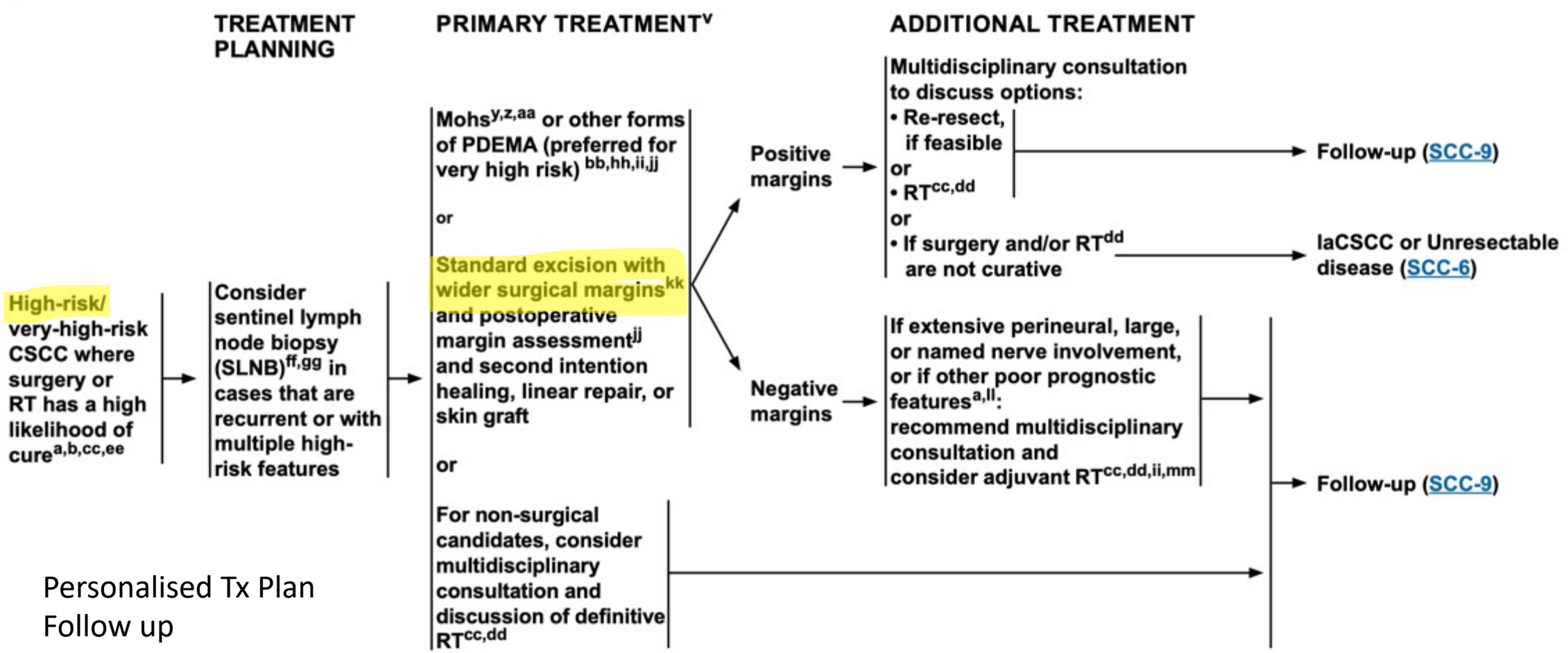

Personalised Tx Plan
Follow up

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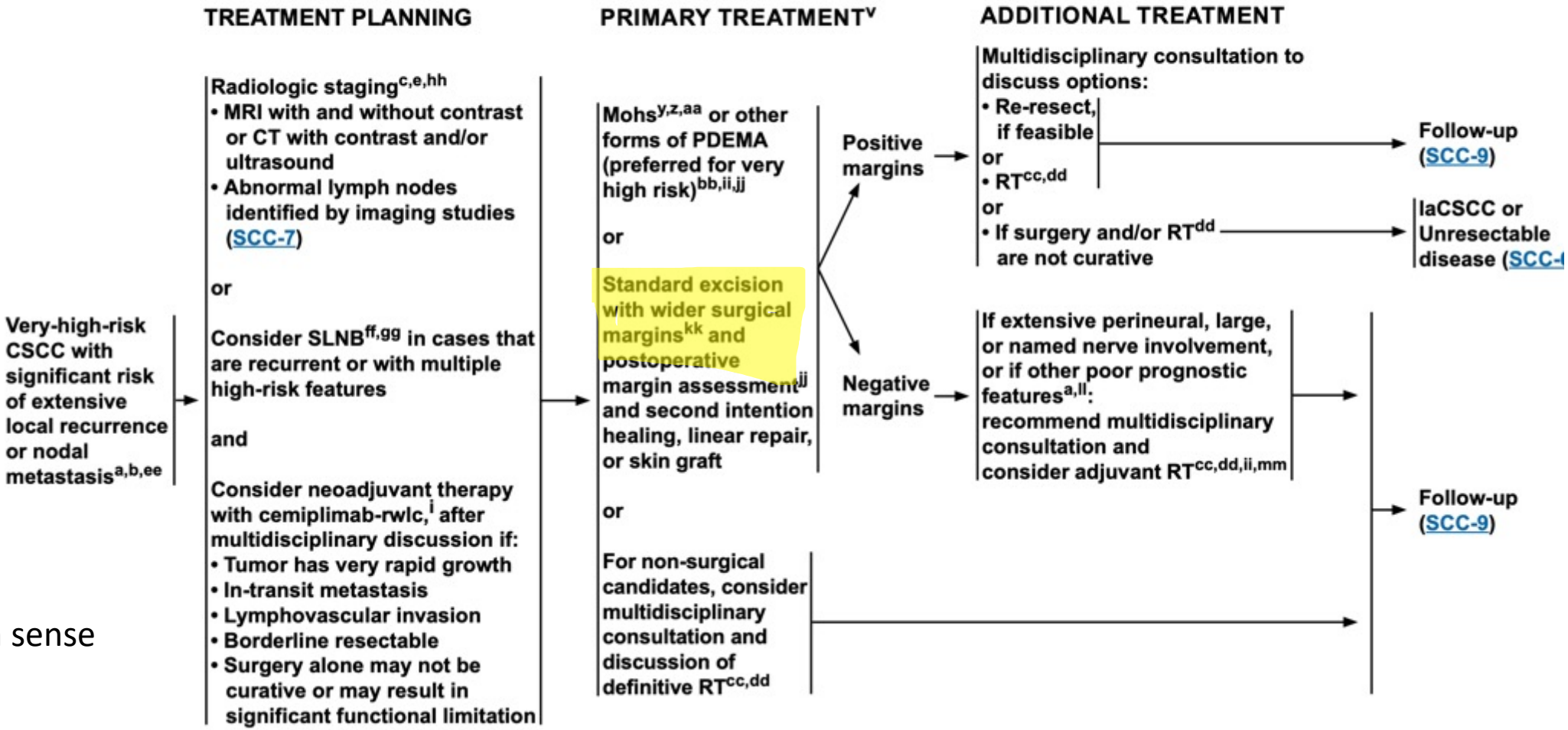

Common sense

Follow up plans
3yrs to Life
Dedicated resource
Data
Audit
Quality Improvement
Peer Review
Collaborative Trials

FOLLOW-UP

Local disease:

- H&P[xx,yy,zz]
  - For patients who are low risk:
    Every 3–12 mo for 2 y, then every 6–12 mo for 3 y, then annually for life[b]
  - For patients who are high risk:
    Every 3–6 mo for 2 y, then every 6–12 mo for 3 y, then annually for life[b]
  - For patients who are very high risk:
    Every 3–6 mo for 2 y, then every 6 mo for 3 y, then every 6–12 mo for life[b]
- Consider imaging:
  - If clinical exam is insufficient for following disease
  - If there is appreciable risk of subclinical local or nodal recurrence[e]
- Patient education
  - Sun protection
  - Self examination of skin

Regional disease:

- H&P[xx,yy,zz,]
  - Every 2–3 mo for 1 y,
    then every 2–4 mo for 1 y,
    then every 4–6 mo for 3 y,
    then every 6–12 mo for life
- Consider imaging:
  - If clinical exam is insufficient for following disease
  - If there is appreciable risk of subclinical local or nodal recurrence[e,aaa]
- Patient education
  - Sun protection
  - Self examination of skin
    and lymph nodes

Stratification to Determine Treatment Options and Follow-up for Local CSCC Based

Merkel Cell Carcinoma

A rare type of skin cancer that starts in Merkel cells, which are found in the epidermis and near nerve endings Neuroendocrine carcinoma of the skin

- **Causes and Risk Factors**
- Not entirely clear, but often linked to the Merkel Cell Polyomavirus
  - 80% MCC cases;
- **Risk Factors:**
  - Long-term sun exposure UV-B p-53 mutation
  - Weakened immune system UV-A and Methoxsalen use in Psoriasis; T cell Immunodeficiency
  - Older age (average diagnosis around 70 years old)
  - History of other skin cancers
- **Appearance:** Fast-growing, painless nodules that can be flesh-coloured, bluish-red, or purple.
- **30% Occult Neck disease**
- Face, head, neck, but can appear anywhere on the body

- **Diagnosis**
- Biopsy of the affected area
  - Ultrasound, CT scan,
  - PET-CT scan

Staging

- **TNM System:**
  - **Tumour (T):** (T1 to T4)
  - **Node (N):** Spread to nodes
  - **Metastasis (M)**

Table 1
Important features of Merkel cell carcinoma.[7]

Acronym	Meaning
A	Asymptomatic/lack of tenderness
E	Expanding rapidly
I	Immunosuppression
O	Over 50 years of age
U	Site exposed to ultraviolet light on a person with fair skin

Clinical staging guidelines for Merkel cell carcinoma by the American Joint Committee on Cancer (AJCC) 2010.

Stage	Local disease	Lymph nodes	Metastasis	5-year disease-free survival
I (T1)	Yes	No	No	79% with –ve SNB 60% with no SNB
II (T 2, 3, 4)	Yes	No	No	58%, 49%, 47%
III (N+, any T)	No	Yes	No	Micro 42% Macro 26%
IV (Any T or N)	No	Yes	Yes	18%

- **Surgery:** Wide Excision margins 1cm if Tumour <2cm
- Neck management 30% micro-metastases in Nodes
- Mohs Not recommended in UK
- **Radiotherapy:**
- **Chemotherapy:** For advanced cases
- **Immunotherapy:**
- **Prognosis**
- **Factors Affecting Prognosis:**
  - Stage at diagnosis
  - Patient’s overall health
  - Response to treatment

NCCN Guidelines Merkel Cell

Note excision margins
No Moh's in UK
No SLNB in UK

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Merkel Cell Carcinoma

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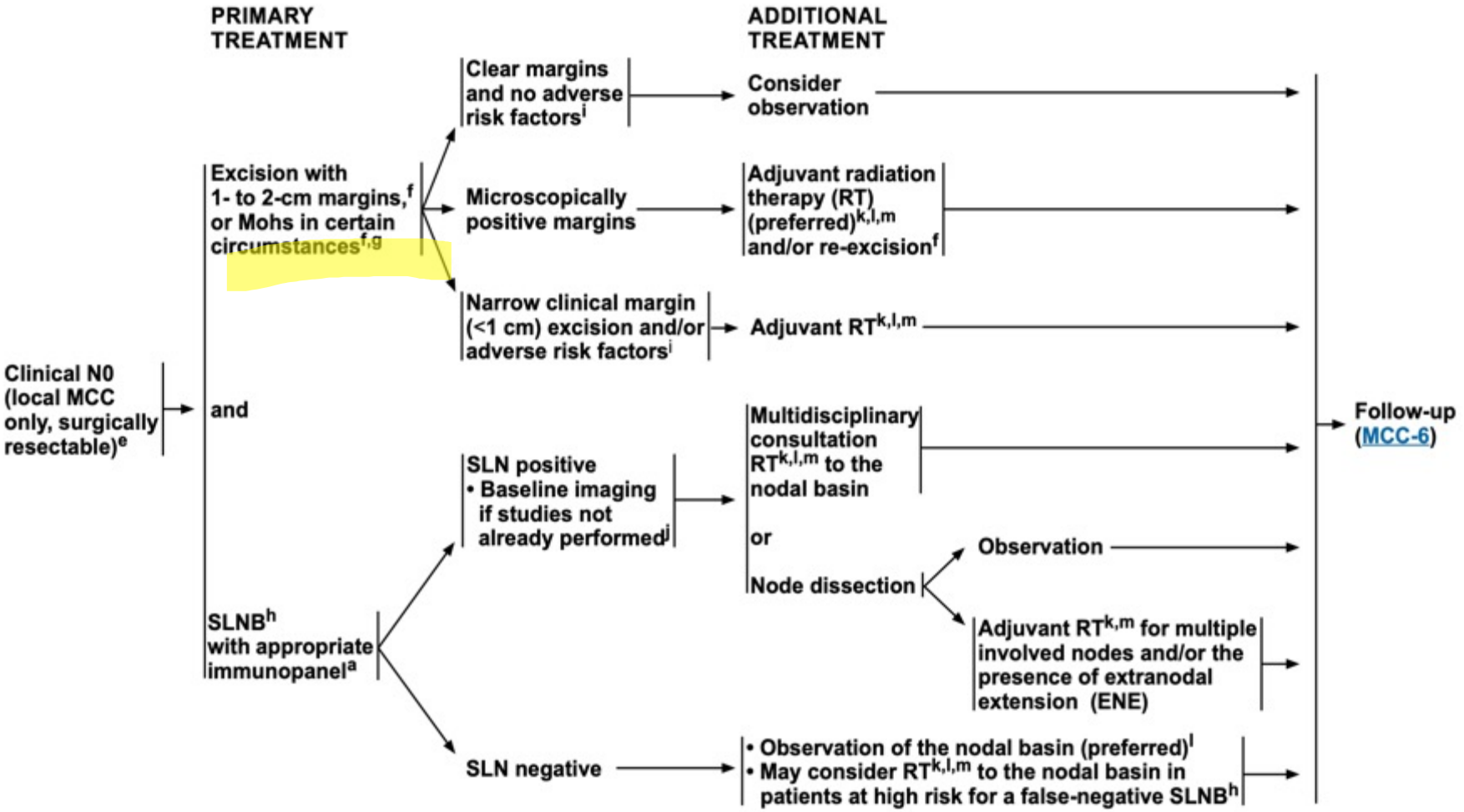
CLINICAL N0 DISEASE, LOCAL MCC ONLY, SURGICALLY RESECTABLE



- PDEMA peripheral and deep en face margin assessment
- Mohs

NCCN Guidelines BCC Low Risk

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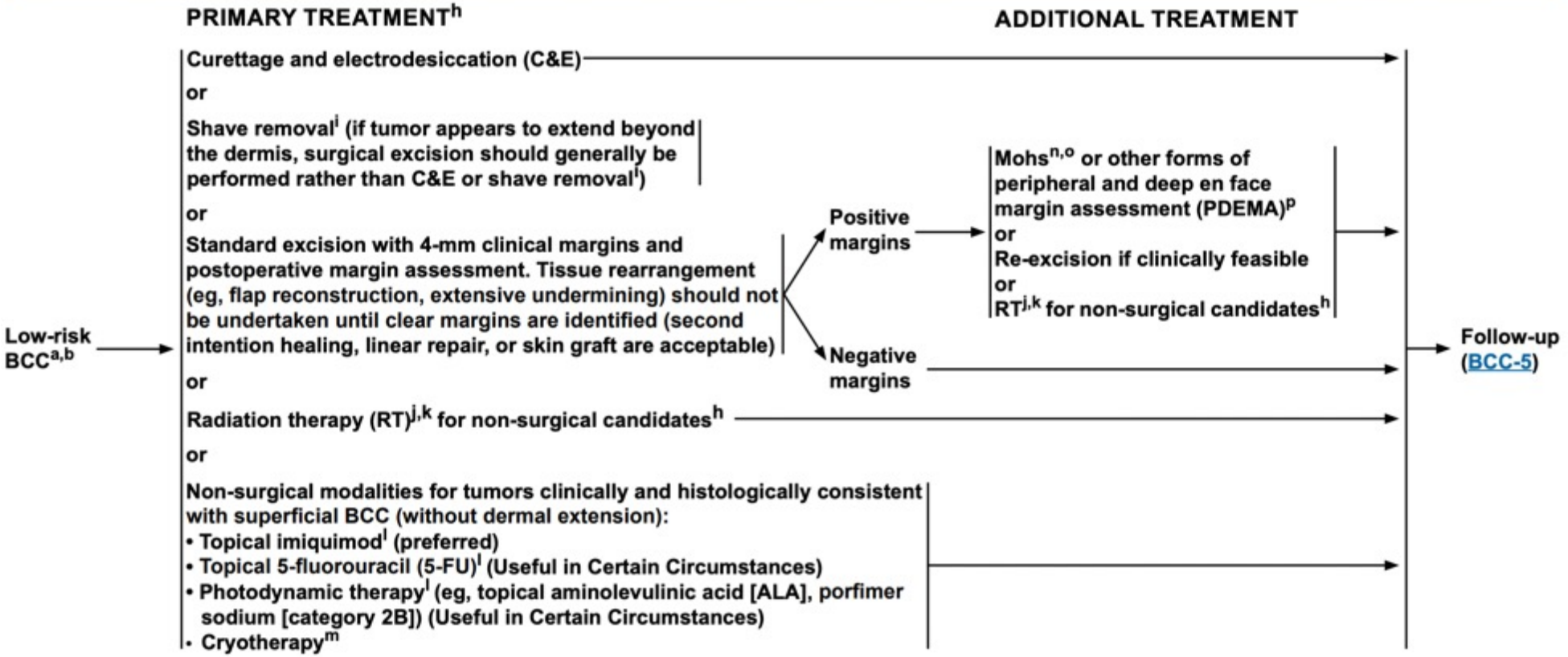

High Risk BCC

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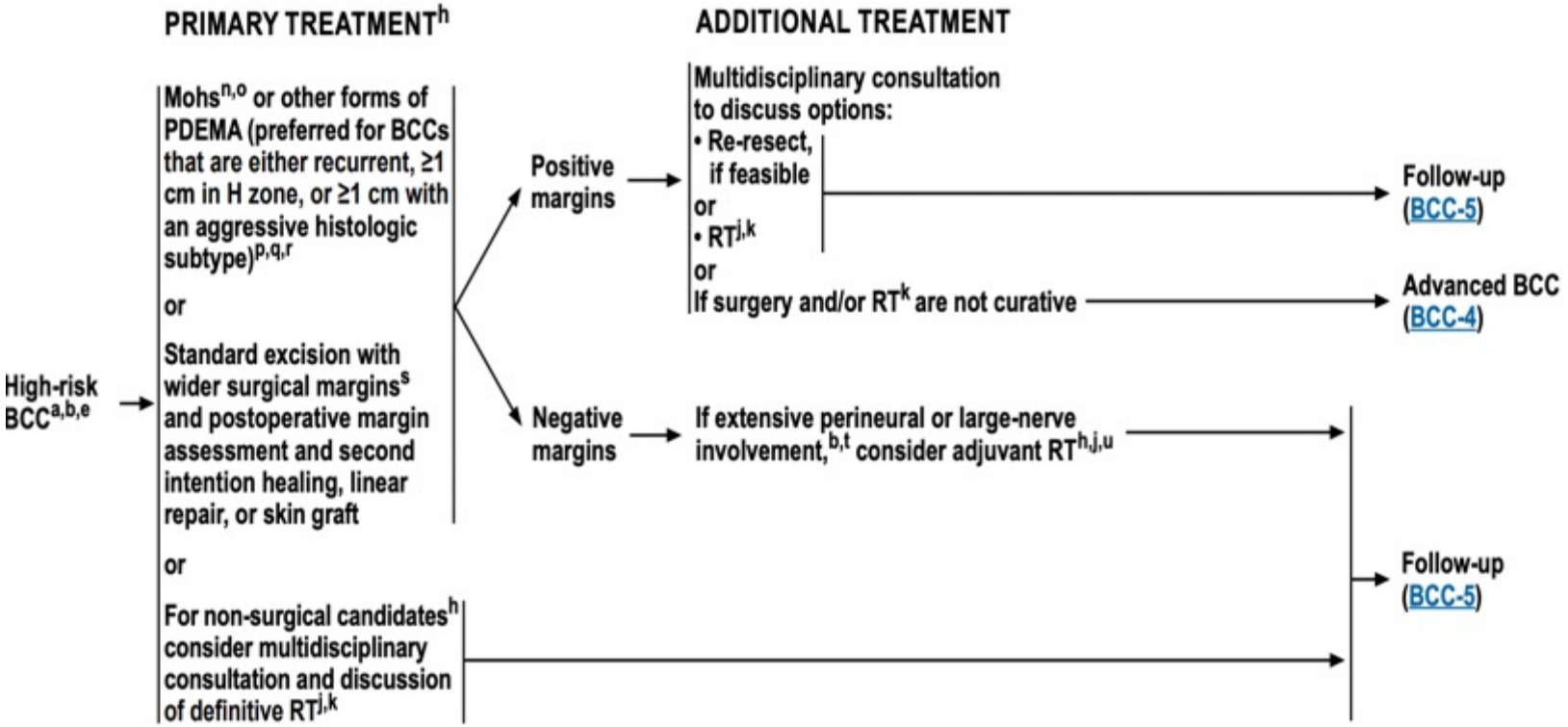

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