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Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline

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Abstract Cutaneous squamous cell carcinoma (cSCC) is one of the most common cancers in Caucasian populations, accounting for 20% of all cutaneous malignancies. A unique collaboration of multi-disciplinary experts from the European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO) and the European Organization of Research and Treatment of Cancer (EORTC) was formed to make recommendations on

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Prognosis
Management
Surgical excision
Radiation therapy
Systemic treatment
Follow up

cSCC diagnosis and management, based on a critical review of the literature, existing guidelines and the expert's experience. The diagnosis of cSCC is primarily based on clinical features. A biopsy or excision and histologic confirmation should be performed in all clinically suspicious lesions in order to facilitate the prognostic classification and correct management of cSCC. The first line treatment of cutaneous SCC is complete surgical excision with histopathological control of excision margins. The EDF–EADO–EORTC consensus group recommends a standardised minimal margin of 5 mm even for low-risk tumours. For tumours, with histological thickness of >6 mm or in tumours with high risk pathological features, e.g. high histological grade, subcutaneous invasion, perineural invasion, recurrent tumours and/or tumours at high risk locations an extended margin of 10 mm is recommended. As lymph node involvement by cSCC increases the risk of recurrence and mortality, a lymph node ultrasound is highly recommended, particularly in tumours with high-risk characteristics. In the case of clinical suspicion or positive findings upon imaging, a histologic confirmation should be sought either by fine needle aspiration or by open lymph node biopsy. In large infiltrating tumours with signs of involvement of underlying structures, additional imaging tests, such as CT or MRI imaging may be required to accurately assess the extent of the tumour and the presence of metastatic spread. Current staging systems for cSCC are not optimal, as they have been developed for head and neck tumours and lack extensive validation or adequate prognostic discrimination in certain stages with heterogeneous outcome measures. Sentinel lymph node biopsy has been used in patients with cSCC, but there is no conclusive evidence of its prognostic or therapeutic value. In the case of lymph node involvement by cSCC, the preferred treatment is a regional lymph node dissection. Radiation therapy represents a fair alternative to surgery in the non-surgical treatment of small cSCCs in low risk areas. It generally should be discussed either as a primary treatment for inoperable cSCC or in the adjuvant setting. Stage IV cSCC can be responsive to various chemotherapeutic agents; however, there is no standard regimen. EGFR inhibitors such as cetuximab or erlotinib, should be discussed as second line treatments after mono- or polychemotherapy failure and disease progression or within the framework of clinical trials. There is no standardised follow-up schedule for patients with cSCC. A close follow-up plan is recommended based on risk assessment of locoregional recurrences, metastatic spread or development of new lesions.

1. Introduction

These guidelines have been written under the auspices of the European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO) and the European Organization of Research and Treatment of Cancer (EORTC) in order to assist clinicians in treating patients with cutaneous squamous cell carcinoma (cSCC) in Europe. The paper was initiated due to advances in the histological diagnosis and the prognostic classification of cSCC with implications for treatment. The guidelines address in detail all aspects of cSCC management, from the clinical and histological diagnosis of primary tumour to the systemic treatment of advanced or metastatic disease. We focus on invasive cSCC, excluding the early intraepidermal SCC-like AK, and Bowen's disease, and mucosal tumours, such as those located in the genital area, or those in the labial-buccal-nasal area, which are often mixed with cSCC under the label of 'head and neck' tumours. Prevention issues are also briefly addressed. It is hoped that this set of guidelines will assist healthcare providers in managing their patients according to the current standards of care and evidence-based medicine. It is not intended to replace national guidelines accepted in their original country. These guidelines reflect the best published data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may modify the conclusions or recommendations in this report. In addition, it may be necessary to deviate from these guidelines for individual patients or under special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, deviation from them should not necessarily be deemed negligent.

2. Methods

To construct this EDF–EADO–EORTC guideline, an extensive search with terms 'cutaneous squamous cell carcinoma' using the PubMed, EMBASE and Cochrane Library was conducted (until 31st October). Articles included systematic reviews, pooled analyses and meta-analyses. We excluded case reports and studies on specific localisations, particularly oral and anogenital

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