Squamous cell carcinoma of the head and neck: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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Incidence
In 2002, the crude incidence rates of Squamous cell carcinoma of the head and neck (SCCHN) in Europe were 36/100 000/year in the male population and 7/100 000/year for females, while the corresponding mortality rates were 18 and 3/100 000/year. More than 90% of head and neck malignancies are squamous cell carcinomas.

Diagnosis
Pathologic diagnosis should be made according to the World Health Organization classification from a surgical biopsy sample.

Staging and risk assessment
Routine staging includes physical examination, chest X-ray, head and neck endoscopy, and head and neck computed tomography (CT) scan or magnetic resonance imaging (MRI). A thoracic CT scan may be performed to rule out metastatic disease. The role of 2-[fluorine-18]fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET) at staging is under investigation.

Squamous cell head and neck cancer should be staged according to the TNM system and grouped into categories shown in Table 1.

T4 tumors are subdivided into T4a resectable and T4b unresectable. Stage IV is subdivided into stages IVa and IVb accordingly, and stage IVc for metastatic disease.

Treatment plan
A multidisciplinary treatment schedule should be established in all cases. The patient’s nutritional status must be corrected and maintained. Dental rehabilitation is indicated prior to radiotherapy.

Treatment depends on primary tumor location and extension. Rare squamous head and neck cancer originating from paranasal sinuses and nasopharynx are usually excluded from trial treatment series supporting evidence-based recommendations, so they are excluded from these clinical recommendations.

In early stage (I–II), either conservative surgery or radiotherapy (external radiotherapy or brachytherapy) gives similar loco-regional control. However, this is based only on retrospective studies as there are no randomized trials available for reference. Modern radiotherapy treatment should include 3D conformal radiation therapy and/or intensity modulated radiation therapy (IMRT).

Standard options for locally advanced stage III and IV tumors are: surgery including reconstruction plus post-operative radiotherapy and, for those patients found at surgery to have high risk features (extracapsular extension and/or R1 resection), post-operative chemo–radiotherapy with single agent platinum [I, A]. However in resectable patients, when the anticipated functional outcome with surgery is poor, combined concomitant chemoradiation is preferable. Combined concomitant chemoradiation is the standard treatment in non-resectable patients [I, A]. Radiotherapy given concomitantly with cetuximab has demonstrated a higher response rate, longer disease-free progression and longer overall survival versus radiotherapy alone [I, A].

The role of induction chemotherapy has been reconsidered since the introduction of taxane/platinum-based combinations that have proven to be superior to PF platinum-fluorouracil schedule in loco-regionally advanced disease [I, A]. However, at present, induction chemotherapy is not considered standard treatment in advanced disease.

Induction chemotherapy followed by radiotherapy in responsive patients allows for organ preservation in advanced larynx and hypopharynx cancer in patients otherwise requiring total laryngectomy [I, A]. This treatment option has no negative impact on disease-free or overall survival, although in general those patients undergoing such treatment tend to have a non-significant, slight increase in loco-regional recurrence and a reduction in distant metastatisation [I, A]. In one
randomized trial, concurrent chemo-radiotherapy achieved higher larynx preservation rates. However this was not associated with improved survival over either induction chemotherapy followed by radiation in responsive patients or radiotherapy alone [I, A].

Local, regional and metastatic recurrence
In selected cases of localized recurrence, surgery (if operable) or re-irradiation can be considered. For most patients palliative chemotherapy is the standard option. Weekly methotrexate may be considered as the accepted treatment [I, B]. Although combination chemotherapy (cisplatin, 5-fluorouracil or taxanes) produces higher response rates and may show a better progression-free survival than single agent methotrexate, no overall survival benefit has been demonstrated [II, B]. In a recent study in patients unsuitable for local therapy, the addition of cetuximab to cisplatin or carboplatin plus 5-fluorouracil resulted in longer survival [I, A].

follow-up
Treatment response should be evaluated by clinical examination and CT scan or MRI of head and neck depending on the initial procedure. The aim of follow-up is the early detection of potentially curable loco-regional recurrence and second tumors. Physical examination along with radiologic imaging should be included in the follow-up. FDG-PET scanning may be useful in the presence of doubtful findings, particularly after combined chemoradiation. In such situations its negative predictive value is superior to the positive one. At this time, special attention should be paid to the treatment sequelae that include swallowing and respiratory impairment. Chest X-ray may be included. Evaluation of thyroid function (serum thyroid-stimulating hormone—TSH—levels) in patients with irradiation to the neck is recommended at 1, 2 and 3 years.

note
Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

literature

<table>
<thead>
<tr>
<th>Table 1. TNM categories for squamous cell head and neck cancer</th>
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<tbody>
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<td>Stage I</td>
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<tr>
<td>Stage II</td>
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<tr>
<td>Stage III</td>
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<td>T1, T2, T3, N1, M0</td>
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<td>Stage IV</td>
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