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## Recent findings on the impact of ErbB receptors status on prognosis and therapy of head and neck squamous cell carcinoma

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Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer type. has often an aggressive course and is poorly responsive to current therapeutic approaches, so that 5-year survival rates for patients diagnosed with advanced disease is lower than 50%. The Epidermal Growth Factor Receptor (EGFR) has emerged as an established oncogene in HNSCC. Indeed, although HNSCCs are a heterogeneous group of cancers which differ for histological, molecular and clinical features, EGFR is overexpressed or mutated in a percentage of cases up to about 90%. Moreover, aberrant expression of the other members of the ErbB receptor family, ErbB2, ErbB3 and Erb84, has also been reported in variable proportions of HINSCCs. Therefore, an increased expression/activity of one or multiple ErbB receptors is found in the vast majority of patients with HNSCC. While aberrant Erb8 signaling has long been known to play a critical role in tumor growth, angiogenesis, invasion, metastatization and resistance to therapy, more recent evidence has revealed its impact on other features of cancer cells' biology, such as the ability to evade antitumor immunity. In this paper we will review recent findings on how ErbB receptors expression and activity, including that associated with non-canonical signaling mechanisms, impacts on prognosis and therapy of HNSCC.

head and neck squamous cell carcinoma, EGFR, ErbB receptors, Cetuximab, immune checkpoint inhibitors

#### 1. Introduction

Head and neck (HN) cancers include a heterogeneous group of cancers which differ for histological, molecular and clinical features (1-3). More than 90% of HN cancers are squamous cell carcinomas (HNSCCs) arising from the mucosal epithelium of the oral cavity, pharynx and larynx, while much less common HN subtypes originate from the salivary glands, sinuses, muscles or nerves in the head and neck! (2-4).

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