

Editorial

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Head and neck squamous cell carcinomas (HNSCCs) are of particular interest because of their good level of curability after multidisciplinary treatment. HNSCCs represent about 550 000 new cases each year around the world. In the US, there were 49 260 new cases in 2010 with 11 480 deaths. In Western countries, the incidence decreases with the efficient fight against tobacco, but in other countries the incidence increases nevertheless. Tobacco and alcohol intake are well-known risk factors. But in Sweden and other Western countries, the increase of incidence of oropharyngeal cancer and most tonsil cancers in young adults who never smoke or drink led to the discovery of a new etiologic factor: infection by human papillomavirus (HPV). Dr Psyrri describes this new etiology. Importantly, the prognosis of HPV⁺ HNSCCs is better with better response to treatments and all future clinical trials will need to be stratified on HPV positivity.

The challenge of the treatment of HNSCC is two-fold: to cure and to preserve function. To preserve function, new surgical techniques have emerged and transoral minimal-invasive robotic surgery could represent a new hope. It seems today that recovery of patients is faster, but one has to wait for long-term results (Dr Ceruse). Following the same idea, to decrease long-term complications of the radiotherapy, new techniques are developed. A randomized phase III study showed that intensity-modulated radiation therapy could decrease toxicity without affecting carcinologic results, a definitive publication is planned soon. Implementation of other new techniques such as cyberknife, proton therapy, or hadron therapy is awaited (Dr Thariat *et al.*). Mucositis is the major acute complication of radiotherapy; Dr Sonis details its mechanism and the proposed treatments and future researches. Chemoradiation showed its role for organ preservation mostly in laryngeal cancer in randomized trials, but cancer statistics showed that mortality of laryngeal cancer increased these last years since the development of larynx preservation.

Recently, the widespread use of induction chemotherapy (Pointreau *et al.*) could reverse this unwanted tendency and future statistical analyses are important. With regard to induction chemotherapy, the following questions arise: which potentialization for radiotherapy after induction is best and is induction followed by radiotherapy (chemotherapy) better than chemoradiation? After relapse,

chemotherapy is indicated if no salvage surgery is possible. Methotrexate (Fayette *et al.*) remains a standard, but combination of chemotherapies allows higher response rates without increase of survival. However, as the majority of patients are symptomatic at the time of recurrence, a higher response rate allows a better quality of life. The addition of targeted therapies against epidermal growth factor (EGFR) gives longer survival for selected patients. On the basis of these results, a new generation of EGFR inhibitors was developed and they were explored in the induction treatment (Machiels *et al.*). After relapse for localized disease, reirradiation is explored and could become a new standard in the future (Janot *et al.*); despite its toxicity, small studies seem to show that patients could benefit from it. Patients with HNSCC often have swallowing difficulties and the nutrition status is very important during treatment. Dr Ravasco focuses on this aspect, which is not secondary as nutritional support can increase the survival of patients. As treatments are aggressive, elderly patients are often undertreated. Recent data showed that if selected elderly patients can support treatments they can achieve similar survival as younger ones.

Despite all this progress, new and more efficient treatment strategies are urgently needed. The solution will probably come from novel discoveries in molecular biology that will allow a better understanding of the cancer, and secondly, the design of new treatments that target the discovered pathways. Dr Grandis *et al.* discuss the discovery of new targets and also focus on the cMET/HGF pathway whose activation can partially explain the failure of EGFR inhibition. Furthermore, new developments in immunology can be relevant in HNSCC, as it was shown that these tumors express a lot of tumor antigen and that immunostimulation through cytokines before surgery can increase overall survival; Dr Young reviews immunotherapy in HNSCC.

A specific issue in HNSCC is the difficulty when comparing different trials as types of tumors and objectives are different. A challenge is to design solid trials and Dr Fortpied *et al.* reviewed issues in clinical trials and proposed some pathways to overcome them.

Finally, Dr De la Fouchardière reviews new advances in thyroid cancers whose treatment was recently radically modified with the introduction of targeted therapies.