The 3rd International Conference on Innovative Approaches in Head and Neck Oncology (ICHNO)

Highlights from the 3rd International Conference on Innovative Approaches in Head and Neck Oncology (ICHNO, Barcelona, February 24-26, 2011)

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From February 24th - February 26th the 3rd International Conference on Innovative Approaches in Head and Neck Oncology (ICHNO) was hosted in Barcelona, Spain. This meeting was a collaborative effort of the European Society for Therapeutic Radiology and Oncology (ESTRO), the European Head and Neck Society (EHNS), and the European Society for Medical Oncology (ESMO) in collaboration with other European partners. The major topics addressed at the meeting were biological patient profiling and risk factors, emerging diagnostic and therapeutic tools, functional outcome of treatments, the management of elderly patients, recurrent and metastatic disease and other clinical controversies such as sequential versus concomitant chemotherapy versus concomitant targeted agents, post-chemo-radiotherapy neck dissection, etcetera.
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Introduction

This report offers a brief overview of the most important data presented during the 3rd International Conference on Innovative Approaches in Head and Neck Oncology (ICHNO).

Update on clinical trials

The ARCON-trial combined accelerated radiotherapy to counteract tumour repopulation with carbogen breathing and nicotinamide to reduce chronic and acute hypoxia. Kaanders et al reported the updated results (median follow-up: 44 months) of a randomised phase III trial comparing accelerated radiotherapy (68 Gy within 36-38 days) versus accelerated radiotherapy plus nicotinamide (60mg/kg, 1-1.5 h before the first fraction every day) and carbogen (breathing during radiotherapy).[1] The toxicity levels were equal between the treatment arms. Overall local control and survival were similar between the 2 arms. A significant gain in regional control was observed in favour of ARCON for advanced laryngeal cancer. Based on the pimidazole study, the hypoxic status of the primary tumour could select the patients most likely to benefit from ARCON.

Boeje et al described the comorbidities in 13,651 squamous cell head and neck cancer (SCCHN)

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from the DAHANCA-database.[2] The most frequent pre-treatment comordities were cerebrovascular (10.8%), chronic pulmonary (10.8%) and cardiovascular diseases (10%). One third had comorbidity according to Charlson Comorbidity Index (CCI): 16%, 9%, and 9% for score 1, 2, and 3, respectively. Comorbidity was statistically associated with overall survival (HR: 1.12 for CCI score 1, HR: 1.26 for CCI score 2, HR: 1.46 for CCI score 3 compared to HR: 1 for CCI score 0).

An individual patient data meta-analysis of the MACH-NC group was presented by Blanchard and colleagues.[3] The aim of this meta-analysis was to study the efficacy and toxicity of cisplatin/5-Fluorouracil/docetaxel or paclitaxel (TPF) versus cisplatin/5-Fluorouracil (PF) induction regimen. Six randomised trials were identified (2044 patients). Median follow-up was 4.9 years. The HR of death was 0.79 (IC 95%: 0.7-0.89), the HR of progression or death was 0.73 (IC 95%: 0.64-0.83) and the absolute benefit for distant failure at 5 years was 5%, all in favour of TPF.

Imaging and diagnosis

Hermans et al reviewed the recent imaging developments in Magnetic Resonance Imaging (MRI). Among the different imaging techniques available, diffusion-weighted MRI (DWI) seems to be promising for (i) the staging of neck lymph nodes and (ii) for the differential diagnosis between persistent disease/recurrence and treatment-induced changes after (chemo)radiation.[4]

FDG PET/scan should be performed in case of clinically unknown primary, if CT or MRI fail to reveal the primary tumour, and to diagnose distant metastases. PET has been proved effective for detecting residual tumour. The role of PET is also investigated in treatment plan for radiotherapy and treatment response evaluation (i.e. to identify early the patients who benefit from therapy).[5] New PET tracers with novel radiopharmaceuticals are under investigation (i.e. hypoxia tracer: (18F)EF5,….) with the aims of predicting the response to specific treatment or to be used as a prognosis tool.[5,6]

Narrow band imaging is an optical technique in which a filtered light selectively absorbed by hemoglobin enhances the mucosal neoangiogenetic pattern of superficial neoplasms. Its accuracy is implemented by a high definition television camera (HDTV).[7] Among a population of 551 SCCHN, this biological endoscopy allowed a better definition of tumour extension (upstage of 59 neoplasms), detection of 5 synchronous lesions, evaluation of incomplete response to radiotherapy in 2 cases, and identification of 2 unknown primaries. Specificity and sensibility were 84% and 97%, respectively.

Gene expression profiles and molecular prognosis parameters

Takes et al validated a gene expression signature for distinguishing metastatic from non-metastatic lymph node(s) in SCCHN.[8] In this study, combining the results of clinical and radiological examination with the gene signature performed on the primary tumour, the rate of undetected nodal metastasis decreases to 11% in the relevant group of early stage cancers of the oral cavity (cT1-2N0). Toustrup et al identified 15 genes allowing to classify the tumour as hypoxic.[9] In the DAHANCA 5 trial, the locoregional tumour control at 5 years was significantly improved with a HR of 0.42 in those classified as more hypoxic and receiving nimorazole compared to those categorised as" more" hypoxic treated with placebo: 49% versus 18%, p=0.002. This difference in locoregional control was not seen in the less hypoxic group, where the locoregional control was similar between placebo and nimorazole group.

Dysphagia and Quality of Life

Mortensen et al established a multivariate predictive model for predicting acute and late dysphagia after radiotherapy in the DAHANCA 6 & 7 trials.[10] The following factors were significant independent prognosis factors for acute dysphagia: T3-T4 tumours, N-positive, non-glottic cancer, age >62, baseline dysphagia >0, and accelerated radiotherapy. The following factors were predictive for late dysphagia: non-glottic cancer, T3-T4, and baseline dysphagia >0. These factors may be useful to identify patients who could benefit from prophylactic measures against swallowing dysfunction. Christianen et al showed that grade 2-4 dysphagia at 12 and 18 months after curative (chemo)radiation was best predicted by a model consisting of the mean dose administered to the pharyngeal constrictor

muscle (PMC) superior and the PMC medius. For 24 months, a model with the PMC superior was most predictive.[11] Langendijk et al showed after multivariate analysis that the only 2 independent prognosis factors for feeding tube dependency at 6 months were the mean dose in the PMC superior and concomitant chemoradiation.[12]

Human papillomavirus (HPV)

Tumour HPV status detected by hybridisation in situ is a strong and independent prognostic factor for survival among patients with oropharyngeal cancer. Weynand et al investigated HPV infection and p16 immunochemistry in SCCHN (all sites). One third of patients showed at least panHPV positivity by PCR but only one third of these patients were p16 positive supporting an absence of correlation between these 2 techniques.[13] These data suggested that other mechanisms than HPV could lead to p16 expression and that the presence of HPV detected by PCR could be too sensitive and does not necessarily imply oncogenicity. Nuyts et al found that 30% of oropharyngeal cancer in Leuven (Belgium) were HPV positive.[14] They showed that the p16 staining was correlated with locoregional control after radiotherapy ($p=0.01$) and that tumours with p16 positive have a better locoregional control after radiotherapy even if they were HPV negative.
O'Sullivan et al confirmed that HPV positive oropharynx cancer have superior survival compared to HPV negative.[15] Interestingly, they observed that radiation therapy alone gave >85% survival for HPV positive minimal smoking patients which was identical to HPV positive patients treated with chemoradiation, suggesting that HPV positive patients with minimal smoking (excepting N3) may be suitable for radiotherapy alone.

Thyroid cancer

Miccoli et al reported his experience with minimally invasive video-assisted thyroidectomy.[16] They performed more than 2000 thyroidectomies with this technique and the main indications were: undetermined thyroid nodules less than 3 cm and papillary thyroid cancer less than 2 cm. In their hands, this approach was well-tolerated.
Schlumberger et al reviewed the targeted therapies for thyroid cancer.[17] Drugs used now are mainly anti-angiogenic and some are targeting the RET tyrosine kinase. Benefits demonstrated with vandetanib on both objective response (OR) rate and progression-free survival (PFS) justify its use in medullary thyroid cancer. In refractory differentiated thyroid carcinoma, these agents give OR in 8-32%. Phase III trials are ongoing. Outside clinical trials, sorafenib or sunitinib are frequently used for those patients.

Image guided treatments

The role of robotic surgery was discussed by Holsinger et al.[18] Robotic surgery is 'a surgical procedure or technology that adds a computer technology-enhanced device to the interaction between a surgeon and a patient during a surgical operation and assumes some degree of control heretofore completely reserved for the surgeon'. The daVinci Surgical System is currently the most popular commercial platform for robotic surgery. Some surgeons claim that this technique may decrease treatment toxicity. However, prospective investigations and randomised trials are needed before its routine implementation in SCCHN surgery.

Metastatic/recurrent disease

Re-irradiation has been generally associated with important toxicities (bleeding,…) precluding its large utilization. However, re-irradiation has been recently demonstrated to be improved by new technologies (IMRT&SBRT,…).[19] In the experience of Centre Oscar Lambret, 80 patients have been re-irradiated with a total dose of 36 Gy in 6 fractions of 6 Gy. Local control rate was >70% at 18 months with very mild toxicity. Leemans reported his experience in salvage surgery. In his series, five year overall survival was 31%.[20] He concluded that "provided that careful selection of patients is performed, salvage surgery post chemoradiation is feasible in a minority of patients with satisfactory results". For patients non-eligible for re-irradiation or salvage surgery, the treatment relies on chemotherapy (primary platinum-based chemotherapy in fit patient, secondary taxanes or methotrexate) and anti-EGFR monoclonal antibodies. However, the prognosis remains poor with a median overall survival of

approximately 10 months. The next challenge is to better understand the mechanisms of anti-EGFR resistance in SCCHN.[21]

Sinonasal and base of skull tumours

Sinonasal malignancies remain a challenge due to its rarity, the variety of histologies (>20) and the difficulty to give "a state of the art" treatment due to the retrospective nature of the published series. Pooling all together several histologies, multimodal treatment including surgery and radiotherapy seems to be associated with better survival than single modality.[22] *Sherrer* discussed the potential role of hadrontherapy in this indication that may be an option in selected patients.[23] Unresectable tumour, should be treated with a combination of chemotherapy and radiation therapy. Besides, standard external surgical approaches, *Nicolai et al.* reported its expertise acquired in the endoscopic management of naso-ethmoidal malignancies with or without involvement of the adjacent skull base.[24] His data shows that endoscopic surgery plays a relevant role in the management of sinonasal malignancies in expert hands with favourable outcome. Contraindications for a pure endoscopic approach are: extensive lacrimal pathway involvement, involvement of the frontal sinus, infiltration of the bony walls of the maxillary sinus except the medial bone, invasion of hard palate, nasal bones and orbital content, and extensive dural invasion.

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