

## Special Session (Mon, 21 Sep, 14:00–15:00)

### Metastatic neck nodal carcinoma of unknown primary

34

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#### Diagnostic issues and treatment

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Neck node metastases from unknown origins account for 5–10% of all neck masses. Although metastases at the upper and middle neck can be easily attributed to head and neck cancers, and those to the lower neck may be attributable to a primary origin below the clavicles, this is not a clear rule and, moreover, many different types of cancer can arise from the head and neck region. Diagnostic procedures include complete physical examination, fiberoptic endoscopy of all head and neck regions and upper oesophagus, biopsies of the suspected regions, CT scan Magnetic resonance. PET-scan may be used as additional investigation, although the research of a primary site in the head and neck cancer areas is hampered by some limitations, in particular the its limited resolution. Some molecular assays have been suggested to identify the potential primary site. These include detection of Epstein-Barr virus (EBV) or Human Papilloma virus (HPV). However, at the moment, molecular assays have a limited role and should be regarded as investigational. The most frequent histology is squamous cell carcinoma (in particular in the upper neck). Adenocarcinoma histology and lower neck involvement, suggests origin in the lung, oesophagus, stomach, or pancreas. In these cases, PET scan may help the identification of the primary site. When the primary origin remains unknown, the therapeutic approaches include surgery and radiotherapy. In case of limited neck node involvement (N1), surgery alone and radiotherapy alone show similar efficacy. In N2 or N3 disease, the combined approach is preferred. Surgical neck dissection, with or without postoperative radiotherapy, or the opposite sequence, is suggested in many cases. However, the extent of radiotherapy remains a matter of debate, and should be weighted against acute and late toxicity and, in particular, the risk of a required re-irradiation whether a primary tumour emerges thereafter. Other approaches (hyperthermia or chemotherapy) must be considered investigational. Prognosis depends on histology and extension of neck involvement. Patients with limited neck involvement of squamous cell type may show a long disease free survival and cure may be occasionally achieved. The poorest prognosis is observed in patients with adenocarcinoma from unknown origin.

35

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#### Metastatic neck nodal carcinoma of unknown primary: which radiotherapy is needed?

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Cervical lymph node metastases of squamous cell carcinoma (SCC) of an unknown primary is a rare disease. One thousand eight hundred ninety patients with SCC of unknown primary of the H&N have been reviewed from 21 series reporting patients treated between 1948 to 1992. Overall survival mainly depended on the stage of the neck. For N1 disease (1997 AJCC/TNM classification), the median value of the reported 5 year survival reached 61% (19–90%); for N2a, N2b and N2c-N3 diseases, median values dropped to 45% (15–87%), 40% (15–63%) and 21% (0–62%), respectively. These figures are consistent with survival data of patients with known primary tumors. All series pooled together, the mean incidence of subsequent primaries in the Head & Neck mucosa did not exceed 13%. When split for different treatment modalities, the incidence reached 21% (13–29%) and 12% (0–48%) for patients treated by surgery alone and radiotherapy alone, respectively. Due to the retrospective nature of the analysis, it is likely that the staging procedure was quite different from one study to another. This probably explains the heterogeneity in the incidence of subsequent primary extending from 0 to 48%. When patients treated by radiotherapy are further divided into those irradiated only on the neck (no attempt to cover the head & neck mucosa) and those treated on the neck and the mucosa, the incidence on subsequent primary reached 13% (5–41%) and 11% (0–48%), respectively. Due to the variety of the radiation techniques used, it is likely that patients intended to be treated only on the ipsilateral neck also received some dose on the ipsilateral mucosa. It is not possible to evaluate the influence of the treatment modality on the survival of these patients from the retrospective analysis. In a retrospective Danish series with more than 200 patients, neither the survival nor the disease-free survival was influenced by the extent of the radiation treatment. On the other hand, extensive radiation treatment was associated with a significant morbidity, mainly xerostomia with its subsequent complications (e.g. taste

lost, weight lost, teeth lost, osteoradionecrosis, speech difficulties). The incidence of more than grade 2 xerostomia is estimated in the range of 50 to 60% for extensive H&N irradiation. A reduction by a factor of at least two is expected using a more selective treatment. In conclusion, the review of the literature indicated that the incidence of subsequent primary is rather low and appears to be irrespective of the treatment modality. In particular, no difference could be detected between patients irradiated only on the ipsilateral neck and those irradiated on the neck and the upper aerodigestive tract mucosa.

## Special Session (Mon, 21 Sep, 14:00–15:00)

### Immunotherapy and vaccination for malignant glioma

36

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#### Clinical applications – lessons from pediatrics

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**Background:** The prognosis of patients with high grade glioma (HGG) is poor. We investigate a potential role of active specific immunotherapy to improve the prognosis of these patients.

**Methods:** A cohort comparison trial HGG-IMMUNO-2003 is designed for children and adults to implement immunotherapy with autologous mature dendritic cells loaded with lysate of autologous HGG (DCm-HGG-L) after new resection of the relapsed HGG. By changing per cohort the vaccination schedule and the maturation methodology of the DC, stepwise improvements are aimed.

**Results:** 125 patients with relapsed HGG were treated with new surgery and DC vaccination in 4 consecutive cohorts. Age did not differ in these 4 cohorts nor did the percentage of total resection versus less than total resection. In this group, 28 patients were younger than 20 y. The median PFS and OS in the latter group were 2.5m resp. 16.6m with a 2 y OS of 34.6%. The median PFS and OS for 97 adults with relapsed HGG were 2.6m resp. 8.7m with a 2 y OS of 16.1%. Looking to the subgroup of 88 patients with relapsed GBM who received DC vaccines, about half of the patients got new total resection of their relapsed GBM. Median PFS of 88 patients was 2.5m, median OS was 8.7m, 2 y OS was 16%. The OS of 15 patients <20 y was 14.6m compared to 8.6m in adults, with a 2 y OS of 30.8% versus 13.6%. Extent of resection resulted in significantly improved PFS and OS as well. In adults with relapsed GBM, the median PFS from cohort A to D were 1.94, 1.67, 3.23 and 2.72% with PFS at 2 y of 4% in cohort C and still 15.3% in cohort D. There were no major side effects, and most of the patients were treated in an ambulatory setting. Quality of life measured with the EORTC QoL questionnaire remained stable during vaccination treatment.

**Conclusion:** Our work illustrates feasibility and efficacy of immunotherapy for children and adults with HGG without major toxicity. The younger long-term surviving patients illustrate a level 1c medical evidence of clinical efficacy, while the significant shift in PFS of adults treated with immunotherapy in the consecutive cohorts of patients further illustrate level 2b efficacy. The particular organization of care which we developed to perform DC vaccination, made it possible that patients from several countries had access to the treatment.

## Special Session (Mon, 21 Sep, 14:00–15:00)

### Secondary leukaemia following chemo or radiotherapy

38

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#### Molecular pathogenesis and biology of secondary leukaemias

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**Background:** Chromosomal translocations leading to the generation of chimaeric oncoproteins play an important role in leukaemogenesis, but mechanisms underlying their formation are largely unclear. Substantial