22 INVITED

Planned neck dissection after chemoradiation for advanced head and neck cancer. Is it always indicated?

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Patients with advanced head and neck squamous cell carcinoma (HNSCC) may benefit from organ preservation treatments based on chemotherapy and radiotherapy (CRT) without compromising survival. This strategy has led to controversial issues concerning the role of neck dissection (ND) following chemoradiation for patients with N2−3 disease. Residual neck disease may be still present in as much as 30 to 50% of patients after completion of CRT. Should ND be proposed to all patients with advanced regional disease at diagnosis regardless whether the response in the neck is partial or complete or only to those with clinical and or radiological evidence of residual lymph node disease, remains controversial. Proponents of planned ND argue that the procedure reduces the regional failure rate and possibly improves the cause-specific survival and that a salvage ND in the event of neck recurrence is unlikely to succeed. Proponents of abstention of ND in case of clinical complete response (CCR) argue that the probability of an isolated recurrence in the neck is low, that no survival benefit has been demonstrated in complete responders and that a systematic planned ND strategy results in overtreatment in more than 70% of patients who have no residual tumor in the neck with increased morbidity.

Today, there are no ongoing prospective trials addressing these specific issues: (1) how often is a CCR achieved after CRT; (2) how accurately does a CCR predict a pathologic complete response (PCR) at neck dissection or the absence of regional relapse if observation is decided; (3) in patients with CCR, does neck dissection yield any additional survival benefit?

The controversy is fuelled by the difficulty to accurately predict a PCR in the neck after CRT because clinical examination, CT and MRI lack sensitivity and specificity. In this respect, the use of PET has gained increasing interest. Recent retrospective studies reported that negative post CRT PET was highly correlated with negative pathologic findings after ND or with the absence of neck relapse (NPV of 97–100%, cut off SUV $\geqslant$3.0). However, these results contrast strongly with those reported elsewhere with NPV varying from 14% to 73%. The differences between these studies can be attributed to many factors like timing of PET after radiation, treatment outcome of the patients (complete response rate assessed by CT and/or MRI), timing of ND, pathology evaluation and quality of PET imaging. A critical point is the timing of PET after radiation. Previous PET studies have demonstrated that best results are obtained when PET is performed 10−12 weeks after radiotherapy. However, some surgeons are still reluctant to perform ND at 12 weeks, fearing a higher rate of postoperative complications. Recently, some authors reported that selective ND was suitable in most post CRT situations and was associated with a low rate of complications.

Since the begin this year, a prospective multicenter registration study is getting under way, sponsored by the GETTEC (French head and neck cooperator study group), to validate the use of PET as a tool able to accurately predict a post CRT complete response and therefore, to select which patients should benefit from post CRT ND. The primary objective should be to assess the NPV of PET in correctly predicting the absence of remaining invaded lymph nodes after CRT. The secondary objectives should assess (1) the suitability of a “no ND” approach in patients considered as complete responders, (2) the ability of PET to correctly predict remaining pathologically invade lymph nodes (PPV) after CRT in patients with a positive PET and who will undergo ND. The results of this prospective study should be of utmost importance to better define whic patients really need post CRT ND.

Special session (Mon, 24 Sep, 13:30−14:30)
What is the optimal treatment of glioblastoma in elderly patients?

23 INVITED

Improving treatment for elderly patients with glioblastoma – is there a role for chemotherapy only?

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The standard treatment of malignant gliomas (WHO grades III and IV) includes tumor resection, involved-field radiotherapy and possibly nitrosourea-based chemotherapy. A modest benefit of adjuvant nitrosourea-based chemotherapy has been confirmed across all age and risk groups. Yet, young age and good Karnofsky performance score are the most potent therapy-independent favorable prognostic factors, and nitrosourea-based chemotherapy is less well tolerated in elderly patients (>65 years). Therefore, the role, if any, of chemotherapy in this patient population has remained controversial. Temozolomide is an alkylating agent which has shown activity in recurrent malignant glioma. The safety profile of temozolomide is superior to that of nitrosoureas, both in terms of cumulative myelotoxicity and pulmonary toxicity. The drug has also been explored in the first-line treatment of glioblastoma, with favorable results, which gave rise to the EORTC 26981 NCIC CE3 trial, which demonstrated a benefit for radiotherapy plus temozolomide chemotherapy compared to radiotherapy alone in the first-line treatment of glioblastoma. Whether elderly patients gained a benefit from that combined modality treatment is at least questionable. The median survival time for elderly malignant glioma patients is in the range of a few months. Radiotherapy is the standard treatment and superior to best supportive care both with respect to progression-free and overall survival. The benefit derived from surgery and radiotherapy is modest, and both treatments are less well tolerated in elderly patients than in the young. The availability of a potentially effective pharmacological agent for malignant glioma, which exhibits a rather favorable safety profile, necessitates a reconsideration of the widespread therapeutic nihilism in the face of malignant glioma in the elderly. However, most elder glioblastoma patients are probably not candidates for combined modality treatment. Therefore, the present studies seek to compare the standard postsurgical treatment of malignant glioma in elderly patients with a Karnofsky performance score >60, involved-field radiotherapy to a dose of 54−60 Gy, with temozolomide alone. In the German Methusalem/NOA-08 trial temozolomide shall be used in a novel one week on/one week off schedule, which allows a dose intensification of up to 2 compared with the standard regime of 150–200 mg/m^2 $\times$ 5 days and which has shown efficacy in recurrent glioblastoma in phase II studies. An EORTC/NCIC approach for an international study initiative looks at radiochemotherapy (with a shortened course of radiotherapy) with temozolomide versus radiotherapy alone in this population.

24 INVITED

Best palliative care or radiotherapy in patients over 70 years of age: what is the difference? An ANOCEF trial

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BACKGROUND: There is no community standard for the treatment of glioblastoma in patients 70 years of age or older. We conducted a randomized trial that compared radiotherapy and supportive care with supportive care alone in such patients. METHODS: Patients 70 years of age or older with a newly diagnosed anaplastic astrocytoma or glioblastoma and a Karnofsky performance score of 70 or higher were randomly assigned to receive supportive care only or supportive care plus radiotherapy (focal radiation in daily fractions of 1.8 Gy given 5 days per week, for a total dose of 50 Gy). The primary end point was overall survival; secondary end points were progression-free survival, tolerance of radiotherapy, health-related quality of life, and cognition. RESULTS: We randomly assigned 85 patients from 10 centers to receive either radiotherapy and supportive care or supportive care alone. The trial was discontinued at the first interim analysis, which showed that with a preset boundary of efficacy, radiotherapy and supportive care were superior to supportive care alone. A final analysis was carried out for the 81 patients with glioblastoma (median age, 73 years; range, 70 to 85). At a median follow-up of 21 weeks, the median survival for the 39 patients who received radiotherapy plus supportive care was 29.1 weeks, as compared with 16.9 weeks for the 42 patients who received supportive care alone. The hazard ratio for death in the radiotherapy group was 0.47 (95% confidence interval, 0.29 to 0.76; P = 0.002). There were no severe adverse events related to radiotherapy. The results of quality-of-life and cognitive evaluations over time did not differ significantly between the treatment