Results: For all patients, neck recurrence was found in 22 patients, and 3 of them accompanied with local recurrence. Local recurrence was only found in 6 patients. One patient developed distant metastasis but no local regional failure. Neck recurrence was found 6.6% (7/125) in those who received neck OP, but 18.3% (15/67) in those who did not receive neck OP. The difference was significant (p = 0.004). Among tongue cancer patients, neck recurrence was 36% (8/22) in neck OP patients, but 4.5% (3/66) in those without neck OP. The difference was significant (p = 0.003). Among buccal cancer patients, neck recurrence was 13.6% (3/22) in neck OP patients, and 3.1% (1/32) in those without neck OP. Primary tumor stage, tumor invasion depth and tumor margins were not related to neck recurrence.

Conclusion: We will suggest prophylactic supraomhyoid neck dissection as part of treatment to staged T1-2N0M0 of tongue cancer patients to improve the tumor control. However, longer follow-up and larger sample size are needed in order to understand the role of prophylactic neck dissection on the other subsite of oral cancers.

663 PUBLICATION

Tumor perfusion studies using fast magnetic resonance imaging in head and neck cancer treated with radiotherapy

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Purpose: This study investigated sequential changes in tumor perfusion and assessed significance in the prediction of outcome of patients with head and neck cancer treated with radiotherapy.

Methods: MRI perfusion studies were performed in 14 patients with head and neck cancer. Three sequential studies were obtained in each patient; immediately before radiotherapy, after a dose of 20 Gy (early therapy), and after completion of radiotherapy. Perfusion imagings of tumors were obtained using T1-weighted gradient-echo (Fast SPGR) imaging. During bolus injection of Gd-DTPA, dynamic MRI images were recorded from the same slice. Tumor perfusin was evaluated by a maximum signal intensity of tumor (SImax; maximum value of SI in tumor/SI of background).

Results: Tumor with SImax increments (SImax (20 Gy)/SImax (pretherapy) $\geq$ 1.3) in the early therapy had a good radiosensitivity.

Conclusion: High tumor perfusion early during the course of therapy demonstrates good radiosensitivity. This phenomenon may be reflected to reoxygenation of the tumor during early radiation therapy (before 20 Gy).

664 PUBLICATION

Long-term follow up of larynx leukoplakia under treatment with retinyl palmitate and prospective impact of proteolytic enzyms

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Purpose: Retinoic acid derivatives have gained interest because of their efficiency in suppressing carcinogenesis and because of some promising results of chemoprevention in clinical trials. In our study for the first time patients with larynx leukoplakia were treated with high dose retinyl palmitate.

Methods: This study had two phases. In the first phase, all patients underwent induction therapy with a high dose of retinyl palmitate (A-Mulsin Hochkonzentrat™, Mucos Pharma, Geretsried, GERMANY) 300,000 IU/day for the first week up to 1,500,000 IU/day, in patients with resistent lesions, in the fifth week. Patients whose lesions progressed during this period were withdrawn from the study. In the second phase, patients whose lesions responded to the treatment or remained stable were then assigned to a maintenance therapy of 150.000 IU/day.

Results: We observed a remission rate of 75% (15 out of 20 patients). Among the 5 patients with partial response, 3 relapsed. The median duration of treatment and follow up was 18 months (range 12–24 months).

Conclusion: Because of the positive results we observed with retinyl palmitate in larynx leukoplakia we started four years ago a double blind study using retinyl palmitate and proteolytic enzyms in head and neck cancer, in order to diminish local recurrences and metastases.

665 PUBLICATION

'Tomudex' (raltitrexed) and cisplatin in the treatment of patients with locally advanced or metastatic head and neck cancer (HNSCC): A Phase I/II study

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Objectives: A combination of infusional 5-fluorouracil and cisplatin is the standard treatment for patients (pts) with advanced or metastatic HNSCC. However, 'Tomudex' (raltitrexed) in combination with cisplatin has a more favourable infusion regimen and may be less toxic. To assess the toxicity, maximum tolerated dose (MTD), and activity of different doses of 'Tomudex' in combination with a fixed dose of cisplatin, an open, dose-escalation Phase I/II study has been initiated.

Methods: Pts with advanced or metastatic HNSCC were treated with a 3-weekly cycle of 'Tomudex' (15-min infusion) followed by cisplatin 100 mg/m[2] (4-h infusion). Dose escalation with 4 doses of 'Tomudex' (2.0, 2.5, 3.0, 3.5 mg/m[2]) was planned for sequential groups of at least 3 pts and dose-limiting toxicity (DLT) was assessed after the first 2 cycles. The recommended dose level will be expanded to include 6 pts to further evaluate efficacy and toxicity.

Results: 6/9 treated pts were evaluable for toxicity and efficacy. The mean age was 57 years (51–71 years), mean Karnofsky score was 90 (80–100), and mean number of cycles per patient was 3.2 (range 1–5). The first two dose levels have not been associated with any DLT. Mild nausea, vomiting, nephrotoxicity, and WHO grade II–III leucopenia were each observed in 3 pts and grade II thrombocytopenia in 1 pt. In 3 of the first 5 pts treated, creatinine clearance decreased by 40–70% with partial recovery (not expressed in WHO criteria). 1 pt with persisting serious renal failure was withdrawn from the study. The cisplatin dose has now been reduced to 80 mg/m[2] due to the observed cisplatin-induced nephrotoxicity. To date, 2 pts have entered the third dose level ('Tomudex' 3.0 mg/m[2] and cisplatin 80 mg/m[2]). At the first two dose levels partial response was observed in 3/6 pts and stable disease in 3/6 pts.

Conclusion: Preliminary results suggest that this combination of 'Tomudex' and cisplatin has promising therapeutic activity in pts with HNSCC. Pts are currently being recruited and the MTD has not yet been reached. Final results will be presented at this meeting. 'Tomudex' is a trade mark, the property of Zeneca Ltd.

666 PUBLICATION

A randomised trial of opioid versus tricyclic antidepressants for radiation induced mucositis pain in patients with head and neck cancer

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Purpose: Patients who receive radiotherapy for head and neck malignancies develop painful mucositis. The pain is characterised as burning or stinging sensations much like neuropathic pain sensations. The purpose of the study was to compare the analgetic effect of a tricyclic antidepressant (TC), commonly used in the treatment of neuropathic pain, and opioid on radiation induced mucositis pain.

Materials and Methods: Fourty-two patients receiving 66–68 Gy external radiation according to guidelines in the Danish Head and Neck Cancer Association underwent randomisation to either morphine 5 mg × 6/day or TC 25 mg × 2/day when their pain was insufficiently managed with weak analgetics. Patients with insufficient pain management, received supplementary medicine from the opposite treatment arm. The pain was evaluated weekly using a VAS-scale and related to the degree of mucositis.

Results: Twenty-one patients entered each treatment arm. Two patients in each arm were non-evaluable. Eight patients in the TC arm managed with TC alone, but for 11 patients it was necessary to add morphine. The 19 evaluable patients in the morphine arm required no additional treatment.

Conclusion: Some of head and neck cancer patients with radiation induced mucositis pain, seem to have sufficient pain control on TC alone, which might be an advantage in patients with relative contraindications to opioid-treatment.