

p53 expression, proliferation rate (Ki-67) and angiogenesis (CD34) were evaluated by immunohistochemistry. DFS was estimated by the Kaplan-Meier method and comparisons by the log-rank test.

Results: After a median follow-up of 17.2 months (mo), 6 pts relapsed and there were 6 deaths (2 in relapsed pts). Two distant relapses were observed. The median DFS (mDFS) of the 32 pts was not reached. The 2-year DFS rate was 54%. In the group of 29 pts without ECS (mDFS not reached), 8 relapsed, as compared to the 3 pts with ECS, in which 2 relapsed (mDFS 12.8 mo, HR 4.46; 95%CI 1.26–362.34, $p=0.034$). Due to the acute toxicity of CRT, only 20 pts received the 3 planned cycles of chemotherapy (CT), and 2 relapses occurred among these 20 pts (mDFS not reached). On the contrary, among the 12 pts that received 1 or 2 cycles, 8 relapsed (mDFS 14.3 mo, HR 7.75; 95%CI 2.11–29.06, $p=0.002$). Unexpectedly, considering the tumor grade, 6 pts relapsed among the 24 with grade 2/3 tumors (mDFS not reached), as compared to 4 pts among the 8 with grade 1 tumor (mDFS 20.8 mo, HR 2.76; 95%CI 0.78–18.36, $p=0.098$). No differences in DFS were observed according to primary site, tumor size, number of involved nodes, margin status, LVI, NI, duration of RT, p53-status, proliferation rate or angiogenesis.

Conclusions: Less than 3 cycles of CT and ECS could be identified as risk factors for relapsing after adjuvant CRT. Our data support the essential role of CT in this setting, but local and distant failures remain a problem in high-risk HNSCC pts submitted to adjuvant CRT.

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PUBLICATION

Concomitant radiochemotherapy with Mitomycin C and Cisplatin in inoperable carcinoma of the head and neck: preliminary results of phase II study

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Background: Phase II study on concomitant radiotherapy (RT) and chemotherapy with Mitomycin C (MMC) and Cisplatin (CP) in inoperable squamous cell carcinoma of the head and neck.

Material and methods: Treatment consisted of: (1) conventional RT (35X2 Gy/day in 7 weeks); (2) MMC 15 mg/m² IV, applied after delivery of 10 Gy (bioreductive agent, selectively toxic for hypoxic cells); (3) CP 14 mg/m²/day IV, applied during the last 10 fractions of RT (to counteract the effect of accelerated repopulation of surviving clonogens in tumor). Daily dose of CP was chosen after determination of dose limiting toxicity and maximum-tolerated dose in escalation part of the protocol [*Radiother Oncol* 2004; 73 (Suppl 1): S302]. Side-effects of the therapy were graded according to NCI and RTOG toxicity scales.

Results: Between 3/02 and 10/04, 24 male pts, 39–69 yrs old (median 57), entered the study. Sites of origin were oropharynx 12; hypopharynx 8; larynx 2; oral cavity 1; unknown 1. All tumors were UICC TNM stage IV (T4 19 [79%]; N3 7 [29%]).

Twenty pts (83%) were treated according to the protocol: all pts were irradiated to 70 Gy and received MMC. Four pts had <10 applications of CP.

The incidence of grade 3 acute systemic toxicity was 14 events that occurred in 10 pts (42%): leukopenia 5; hypokalemia 3; thrombocytopenia 2; hypocalcemia 2; increased creatinine and GGT in 1 pt each. Weight loss during therapy was 0–19% (median 9%); nasogastric-feeding tube was inserted in 7 pts (29%). Grade ≥3 radiomucositis was recorded in 21 pts (86%) and dermatitis in 8 pts (33%). In 10 out of 16 complete responders (63%), 16 severe (grade ≥3) late adverse events were recorded: skin fibrosis 5; xerostomia 3; impaired function of the larynx 3; hypothyroidism 2; pain, ototoxicity, and neurotoxicity in 1 pt each.

Radiologically, locoregional complete response rate at 3 mos was 54% (local, 74%; regional 67%). After successful surgery of residual neck disease in 3 pts, it was 87% regionally and 67% locoregionally. Two pts developed systemic mets. For pts alive on April 30, 2005, a median follow-up time was 19 mos (range 7–25 mos). The disease-free, disease-specific and overall survival rates at 18 mos were 53% (95% CI, 32–74%), 74% (95% CI, 56–92%), and 68% (95% CI, 49–87%), respectively.

Conclusions: Tested regimen was not associated with unacceptable toxicity. Considering prognostically extremely unfavorable profile of our pts, presented results justify additional recruitment of pts.

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PUBLICATION

In vivo optical coherence tomography monitoring of radiation mucositis in patients with head and neck cancer

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There are several systems for mucosal toxicity scoring in and after radio- and chemotherapy (WHO 1979, RTOG/EORTC 1984, LENT/SOMA 1995, CTCAE 2003). All of them are based on the visual estimation of mucosal changes (oral erythema, oedema, patches, ulceration) and on the patient's complaints (pain, xerostomia, swallowing and chewing dysfunction). There are no methods in the current practice to assess microscopic changes of mucosal structure during and after irradiation in various tissue components. Optical coherence tomography (OCT) has been actively developed since 1991. It creates real time cross-sectional images of subsurface tissues at a depth of up to 2 mm with spatial resolution close to that of the cellular level (10 to 15 µm). Clinical OCT applications include detection of early cancer and precancer, biopsy guidance, assessment of the lateral extent of neoplastic processes, differential diagnosis of diseases with similar clinical manifestation, and treatment follow up.

This study objective was to estimate changes of oral mucosa during and after radio- and chemotherapy using OCT imaging.

Materials and methods: From June 2004 to March 2005, 11 patients with stage II-IV of oropharyngeal squamous cell cancer were included into a prospective study. Patients were performed conventional radiation or chemoradiation (5FU+cisplatin) therapy up to total doses 66–70 Gy. OCT imaging was performed daily starting from the first day of irradiation in four points of oral mucosa: right and left cheek, right and left anterior pillar. After treatment, patients were monitored in 1.5, 3, 6, 9 and 12 months. Mucosal toxicity was scored according to CTCAE 2003.

Results: OCT imaging visualized mucosal changes, corresponding to different stages of acute mucositis development (Sonis, 1998). Normal mucosa has a high-contrast stratified structure. Its OCT images began to lose contrast after a total dose 2–6 Gy when no clinical manifestations were observed. Inflammatory phase appears in OCT images as reduced contrast between epithelium and connective tissue. Further reduction of epithelial thickness and contrast were observed in epithelial phase. Ulceration phase had completely unstructured OCT images. The recovery of normal mucosal structure lasted more than 100 days after end of the treatment, when no visual changes of mucosa were observed.

Conclusion: Mucosal changes, associated with acute reaction, can be visualized by OCT before any visual signs of mucositis development and can be seen when visual signs already disappeared. Further studies, combined with image processing, can lead to quantification of mucositis development in OCT images.

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PUBLICATION

Clinical experience of using docetaxel, cisplatin and 5-fluorouracil as induction chemotherapy in Bangladeshi patients with non-resectable head and neck cancer

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Background: Significant activity has been shown with the combination of docetaxel, cisplatin and 5-fluorouracil (TPF) in the treatment of squamous cell carcinoma of the head and neck. We conducted a phase study to examine the response rate and toxicity of the TPF regimen in Bangladeshi patients.

Materials and Methods: Patients with non-resectable locally advanced cancers in head and neck region were treated with docetaxel 75 mg/m² (day 1), cisplatin 75 mg/m² (day 1) and 5-FU 750 mg/m² (day 1 to day 4) for every 21 days. Eligibility criteria of patients were over 35 years age, histologically confirmed squamous cell carcinoma (SCCHN), adequate hematological, renal and hepatic functions and no prior treatment