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.

1093 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/m^2 IV, applied after delivery of 10 Gy (bioreductive agent, selectively toxic for hypoxic cells); (3) CP 14 mg/m^2/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 pats, presented results justify additional recruitment of pts.

1094 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.

1095 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/m^2 (day 1), cisplatin 75 mg/m^2 (day 1) and 5-FU 750 mg/m^2 (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

with chemotherapy. Each patient received 3 cycles of treatment before continuing to radiotherapy of 70 Gy (fractionated) as local treatment.
Results: Between January 2000 and December 2003, a total of 69 patients were enrolled and assessable for response and toxicity analysis. The median age was 55 years (age range 45–70 years). The anatomical sites were oral cavity (45%), nasopharynx (35%) and larynx (20%). Overall response rate was 96% with complete response seen in 42 patients (61%) and partial response in 24 patients (35%). The remaining patients (4%) showed stable disease. The median time for follow-up was 45 months. The most common hematological side effects were neutropenia (35 patients; 51%) out of which G3/4 was found in 10 patients. The non-hematological events were vomiting (28 patients; 41%) and stomatitis (10 patients; 14%). There were no treatment related deaths.
Conclusion: For treatment of locally advanced SCCHN, docetaxel in combination with cisplatin and 5-FU may be an effective regimen with a manageable toxicity profile.

1096 PUBLICATION

Tamoxifen as a novel chemotherapeutic agent treating anaplastic thyroid cancer.

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Introduction: Anaplastic Thyroid Cancer (ATC) is a highly aggressive rare neoplasm with a dismal prognosis. It represents 2% of all thyroid cancers with a mean survival of 3–7 months. The majority of ATC patients develop metastases during their illness hence there is an essential role for systemic chemotherapy. Doxorubicin, cisplatin and paxlitaxel to date offer poor chemotherapeutic response.
Method: We have investigated the anti-proliferative effects using colorometric dimethyl-thiazol-diphenyltetrazolium bromide (MTT), pro-apoptotic effects was investigated using flow cytometry and annexin V and anti-invasive properties using Matrigel invasion assays at varying concentrations of tamoxifen on anaplastic thyroid carcinoma cell line Cal-62.

Results:

Tamoxifen	Control	1 μg/ml	2 μg/ml	5 μg/ml	10 μg/ml
Proliferation	100	97±1.07*	93±0.75*	64±1.07 **	23±1.07**
Apoptosis	4.7±0.46	11.2±2.39	26.4±14*	24.8±2.19	22.9±6.89
	Control	**Tamoxifen**	**Vegf**	**Tamx + Vegf**	
Migration	95.8±3.1	0*	124±3.15**	45.6±3.14**	

P < 0.05 vs control Anova Scheffe post hoc analysis

Conclusion: These data suggest tamoxifen warrants further investigation as a novel therapeutic agent in the treatment of Anaplastic Thyroid Cancer

1097 PUBLICATION

Lovastatin and X-irradiation induced redistribution in cell cycle and growth inhibition of FaDu cells in vitro

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Background: Identification of drugs which selectively radiosensitise tumours may have important clinical benefits for cancer patients. Such a drug might be lovastatin, a well known antihypercholsterolemic agent which specifically inhibits 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Lovastatin was shown to have the ability to induce growth arrest in the G_0/G_1 phase of the cell cycle in several tumour-derived cell lines. Lovastatin has been evaluated in combination with different chemotherapeutic drugs but little is known about its combination with irradiation. The aim of this project is to investigate the effects of lovastatin and lovastatin combined with X-radiation on the cell cycle distribution and growth of FaDu cells *in vitro*.
Material and methods: The human hypopharyngeal squamous cell carcinoma cell line FaDu was used in all experiments. Lovastatin was dissolved in ethanol. Proliferation was determined by cell counts, cell cycle distribution by flow cytometry. Clonogenic cell survival was determined using colony formation and dilution assays after incubation of cells for 72 hours with lovastatin. For experiments combined with irradiation, cells were irradiated 36 hours after seeding and then treated with lovastatin or cells were irradiated after incubation with lovastatin for 24 – 72 hours.
Results: Lovastatin inhibited cell proliferation in a dose-dependent manner. Combined treatment (4 Gy X-rays and 25 μM lovastatin) showed greater effects on proliferation than both treatments alone. Lovastatin (5 μM – 50 μM) leads to an increased proportion of cells in the G_0/G_1 phase (control 39%, 50 μM lov 69%), a decreased number in S-phase (control 41%, 50 μM lov 17%), and increased apoptosis. Irradiation with 4 Gy X-rays caused an increase in the number in the G_2/M phase. This was not significantly modified by addition of 25 μM of lovastatin. Lovastatin reduced colony formation dose-dependently. Also here the effects of combined treatment were greater than each modality alone.
Conclusion: Lovastatin, in a dose-dependent manner, decreases cell proliferation and clonogenic survival and increases apoptosis. Effects on proliferation are caused by G_0/G_1 arrest. Radiation combined with lovastatin decreases proliferation and clonogenic survival to a greater extent than lovastatin alone.

1098 PUBLICATION

Serum ubiquitin levels and antioxidan system in patients with solid tumors treated with radiotherapy

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Background: The ubiquitin-proteosome system is a major non-lysosomal proteolytic pathway in eukaryotic cells. Ubiquitinated proteins are degraded by an ATP dependent 26S proteosome complex. Ubiquitin, which can conjugate with cellular proteins, is classified into two forms: free ubiquitin and multiubiquitin chains. The multiubiquitin chain acts as a signal to induce degradation of the target proteins by 26S proteasome.
The ubiquitin-proteosome pathway clearly represents an important area of research in cancer biology. On the other hand experimental investigations have showed the relation between ionizing radiation and free oxygen radicals. The aim of this study was to assess the level malondialdehyde (MDA), selenium (Se), ubiquitin (Ub) and activities of superoxide dismutase (SOD) in advanced head-neck cancer patients and compare the results of these parameters which were detected at the beginning, in the middle and at the end of the radiotherapy.
Methods: Sixty patients with advanced epidermoid head and neck carcinoma and sixty healthy cases as the control group were enrolled into the study. Patients were treated with radiotherapy alone. Serum was obtained from venous blood drawn at the beginning of radiotherapy, in the middle of radiotherapy and at the end of the radiotherapy. The MDA, Se, Ub levels and SOD activities in sera were quantified.
Results: Higher serum levels of MDA, lower serum activities of SOD and lower levels of Se and Ub were detected in patients with advanced cancer of head-neck without surgical therapy in comparison to the healthy volunteers. SOD activity slightly decreased during the treatment. Activities of SOD at the end of the treatment significantly decreased as compared to the results of the beginning treatment. The levels of MDA and Se decreased during the treatment but it was not significant. The levels of Ub altered during treatment. Ub markedly decreased in the middle of the treatment compared with the results of the beginning of treatment. The levels of Ub returned the values which were detected at the beginnig of the treatment.
Conclusion: This study demonstrated that serum SOD, MDA, Ub and Se analysis might serve as nonspecific markers in the assessement of oxidative stres response to radiotherapy in advanced head-neck cancer.

1099 PUBLICATION

Immunohistochemical markers PCNA-LI and Ki-67, and DNA index in patients with parathyroid carcinoma

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Background: Parathyroid carcinoma (PC) is an uncommon cancer. Unfortunately, histopathological distinction between PC and parathyroid adenoma is still difficult and, moreover, the clinical outcome of patients varies widely. The aim of this study was to assess the usefulness of antiproliferating cell nuclear antigen labeling index (PCNA-LI), Ki-67 antigen, and tumor nuclear DNA index (DI) in patients with parathyroid carcinoma.
Patients and Methods: Paraffin-embedded archivial tissue sections from 15 patients (11 men, 4 women, median age 65 years, range 30–68 years) with confirmed PC who died of the disease were reviewed. Specimens were stained by using streptavidinbiotin-peroxidase complex standard technique