We analysed a retrospective series of patients (pts) treated with a multimodal approach including induction chemotherapy (CT).
Material and Methods: Between 2000 and 2008, 29 pts with stage III-IV malignant epithelial tumours of ethmoid and nasal cavity were treated. Adenocarcinoma and salivary gland-type carcinomas were excluded. Treatment consisted of induction CT platinum-based (with docetaxel, 5 fluorouracil or etoposide or vinorelbine) followed by concomitant chemo-radiotherapy (group A, 18 pts) or craniofacial resection (CFR) and postoperative radiotherapy (RT), with or without concomitant cisplatin (group B, 11 pts). Follow up ranged from 7 to 87 months (median 37 months).
Results: See the table.

Characteristics	Group A: CT+CT/RT n (%)	Group B: CT+CFR+RT(CT) n (%)
Stage III	4 (22)	3 (27)
Stage IV	14 (78)	8 (73)
T3	5 (28)	3 (28)
T4a	6 (33)	4 (36)
T4b	7 (39)	4 (36)
Squamous cell carcinoma	7 (39)	6 (54)
SNUC	9 (50)	1 (9)
SNEC	1 (5.5)	1 (9)
Small cell carcinoma	1 (5.5)	3 (28)
Neuroendocrine YES	4 (22)	4 (36)
Differentiation NO	14 (78)	7 (64)

SNUC = Sinonasal undifferentiated carcinoma; SNEC= Sinonasal neuroendocrine carcinoma

Only 3 pts showed neck nodal disease at diagnosis (1 N1, 2 N2), all in group A. Radiological response to induction CT showed partial response in all but 4 pts (1 complete remission and 3 stable disease). Globally, 3- and 5-year (yr) overall survival is 68% and 42%. Fifteen pts showed a local recurrence: 11 in group A (9 pts underwent a salvage CFR) and 4 in group B. Only one pt treated with salvage surgery at local site reached ultimate local control. Two pts with isolate node recurrence were treated with surgery. Distant metastasis developed in 4 pts (1 in group A and 3 in group B). Treatment strategy did not impact on DFS. Neurendocrine differentiation in tumours was associated with reduced disease free survival (DFS) ($p = 0.01$). All small cell carcinomas and SNECs recurred in 2 yrs time, while 3 yr DFS of squamous cell carcinoma and SNUC is about 65%.
Conclusions: Survival of advanced stage nasal cavity and ethmoid carcinomas is not satisfactory. Induction CT followed by concurrent CT/RT is able to reach disease control similar to multimodality treatments including CFR, at least in some histotypes. Efforts should be spent to improve treatment of bad prognosis histologies, in particular with neuroendocrine differentiation.

8536 POSTER

Immunohistochemical study to identify prognostic biomolecular markers for nasopharyngeal carcinoma

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Background: We performed immunohistochemical study with pre-treatment biopsy specimens to identify prognostic biomolecular markers for nasopharyngeal carcinoma (NPC).
Material and Methods: From January 1998 through December 2006, 68 patients were histologically diagnosed as non-metastatic NPC and treated with radiotherapy at Seoul National University Hospital. Only 38 patients had the paraffin block for the immunohistochemical study. Thirty-one patients had undifferentiated carcinoma and 7 patients had squamous cell carcinoma. Thirty-two patients (84%) had advanced stage NPC (2002 AJCC Stage III-IV). All patients, except for 6, were treated with induction chemotherapy with two or three cycles of cisplatin based regimen followed by either radiotherapy alone (19 patients) or concurrent chemoradiotherapy with cisplatin (13 patients). Immunohistochemical staining was done for Met, COX-2, EGFR, $nm^2$3-H1, p63, Cathepsin-D, p53, *C-erb*B2, CD138, STAT5, Egr1, CSE1L, STAT3 and LIN28 with the usual methods.
Results: The median follow-up time was 30 months (range, 11−83 months) for all patients and 39 months (range, 19−83 months) for surviving patients. Thirty-five patients were Met positive and 22 patients showed high expression (58%). Twenty-seven patients exhibited CD138 and 17 patients showed high grade (45%). Twenty-two patients showed Egr1 expression (58%). High Met and CD138 expression were statistically significant negative prognostic factors on survival. The expression of Egr1 had a positive prognostic effect on survival. The combined score (CS) of these three prognostic factors, Met (0, low; 1, high) plus CD138 (0, negative; 1, low; 2, high) minus Egr1 (0, negative; 1, positive), was a strong prognostic factor. The median survival curve was distinctly separated according to this combined score (median survival: CS −1 or 0, 76 mo; CS 1, 71 mo; CS 2, 42 mo; CS 3, 24 mo, $P = 0.001$). The patients with Egr1 expression also showed better progression-free survival (PFS) than those without Egr1 expression. No prognostic value was revealed in COX-2, EGFR, $nm^2$3-H1, p63, Cathepsin-D, p53, *C-erb*B2, STAT5, CSE1L, STAT3 and LIN28.
Conclusions: High Met and CD138 expression were evaluated as negative prognostic factors on OS in NPC. The expression of Egr1 was a positive predictive value for PFS as well as OS. The combined score of these markers could be used to stratify biomolecular risk groups.

8537 POSTER

Hemophagocytosis-related keratinization in squamous cell carcinoma and carcinoma in-situ of the oral mucosa

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Background: Round-shaped dyskeratosis (RSK), a kind of keratin pearl, is one of the histological features of carcinoma in-situ (CIS) of the oral mucosa. Our hypothesis for the histopathogenesis of this peculiar structure is that RSK foci are generated by keratinization of basal cells which are exposed to oxidative stress by hemoglobin derived from erythrocytes which are extravasated due to the collapse of blood vascular channels in the stroma.
Material and Methods: To stage the RSK formation process in oral CIS, a total of 50 surgical specimens of oral CIS and squamous cell carcinoma (SCC) containing RSK or keratin pearl foci were investigated by immunohistochemistry for various cytokeratin (CK) subtypes and vascular endothelium- and erythrocyte-related antigens. ZK-1, a human oral SCC-derived cell system, was exposed to erythrocytes or hemoglobin and examined for its CK phenotypes and heme oxygenase-1 (HO-1) expression levels by immunofluorescence and RT-PCR. In addition, the dynamics of protease activated receptor-2 (PAR-2), a candidate for regulating hemophagocytosis, were determined to confirm the molecular mechanisms underlying this phenomenon.
Results: RSK specifically immunopositive for CK10 and CK17, and CK10/CK17/HO-1 expressions were also confirmed in the basal cells facing collapsed blood vessels, around which erythrocytes were disseminated. ZK-1cells showed erythro-/hemo-phagocytosis when incubated with erythrocytes or hemoglobin, and phagocytotic ZK-1 cells showed enhanced immunofluorescence intensities for CK10, CK17, and HO-1. At the same time, mRNA expression levels were elevated for the three molecules. Those expression levels were also enhanced when ZK1 cells were stimulated with PAR-2 agonist peptides.
Conclusions: RSK and some of the keratin pearls in oral CIS and SCC, characterized by their particular expressions of CK17 and CK10, are obviously induced by hemophagocytosis-related oxidative stress. PAR-2 may be involved in the hemophagocytosis by CIS or SCC cells, which seems to be induced by hemolysis due to rupture of intraepithelial blood vessels, which are also characteristic of oral CIS. Based on the results, we propose a new concept of abnormal keratinization caused by hemophagocytosis. This 'hemophagocytosis-related dyskeratosis' starts from the basal end of the epithelial layer, which is in a reverse direction to that of normal keratinization.

8538 POSTER

Xerostomia and dysphagia related quality of life in patients treated with interstitial brachytherapy boost for head neck cancer

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Background: To study patients' perspective of xerostomia and dysphagia after treatment for head and neck cancer with external beam radiation (EBRT) and interstitial brachytherapy (BRT)
Methods: Patients with head and neck cancer previously treated with BRT either alone or in combination with EBRT who were controlled and attended the follow up clinic were considered suitable for the study. Xerostomia questionnaire (XQ) and dysphagia questionnaire (DQ) were served to consecutive eligible patients from Jan 2008 to Jan 2009 at a single head neck unit. XQ (Meirovitz 2006) consisting of 8 questions with scores from 0−10 and higher score indicating more xerostomia was selected. Each item score was added and the sum score transformed linearly to a final score ranging between 0−100. DQ (Murry 1998) was used in which each item was scored on 3 point scale and the final score for each patient was the mean score of the 10 items with higher score suggesting better outcome.

Effect of various patient and treatment related factors on the outcome with respect to xerostomia and dysphagia were analyzed.
Results: Fifty one consecutive eligible patients participated in this prospective study. There were 48 males and 3 females (median age 54 years). Median treatment to evaluation time (follow up) for the entire group was 50 months (2−201months). Forty seven patients had received combined EBRT and BRT while 4 patients received BRT alone. EBRT was delivered using standard portals with a median dose of 44 Gy/22 fractions over 4 weeks. BRT was low dose rate in 23 patients and high dose rate in 28 patients. Median dose of BRT was 30 Gy with LDR and 20 Gy with HDR BRT. The median xerostomia score was only 16 (Range: 0−73) suggestive of recovery of the salivary glands. There was no difference in the xerostomia while eating (stimulated) vs at rest (basal) for the entire population. Xerostomia scores in patients treated with LDR BRT vs HDR BRT were comparable. XQ scores compared favorably with published results using the same questionnaire after intensity modulated radiation therapy (IMRT) (Meirovitz 2006). Median dysphagia score was 2.4 (Range 1.4−3) for the entire population indicating good swallowing status post BRT. There was significant correlation between the xerostomia and the dysphagia scores (<0.001).
Conclusion: Patient reported xerostomia was consistently low with usage of brachytherapy both at rest (basal) and while eating (stimulated) signifying organ and function preservation. Significant correlation of dysphagia and xerostomia scores suggests that xerostomia and dysphagia are closely interrelated.

8539 POSTER

Induction chemotherapy with docetaxel, cisplatin and S-1 (TPS) followed by proton therapy concurrent with cisplatin in the patients with T4 nasal cavity cancer

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Background: In the treatment of the patients (pts) with T4 nasal cavity cancer, definitive chemoradiotherapy was contraindicated due to the risk of brain damage or blindness. The chemotherapy combination with docetaxel, cisplatin and S-1 (TPS) has shown to be well tolerated and active (Tahara M, ASCO2007, 2009). We conducted a retrospective analysis to evaluate the efficacy and feasibility of induction chemotherapy of TPS followed by proton therapy (PBT) concurrent with cisplatin in pts with T4 nasal cavity cancer.
Methods: Fourteen pts with T4 nasal cavity cancer treated with induction chemotherapy of TPS were analyzed. TPS consisted of 1-hour infusion of docetaxel at 60 to 70 mg/m^2, 2-hour infusions of cisplatin at 70 mg/m^2/day on day 1 and S-1 twice daily on days 1−14 at 60 to 80 mg/m^2/day. The treatment was repeated every 3 or 4-weeks with maximum number of treatment cycle of 3 cycles. According to the response of TPS, pts received either PBT concurrent with cisplatin or PBT alone.
Results: Nine males and 5 females; median age of 45.7 years (22−60); 7 olfactory neuroblastoma, 3 SCC and 4 others; 14 intracranial invasion and 5 optic nerve invasion. Median cycle of TPS was 2.6. Most common grade 3 or 4 hematological toxicities were neutropenia (59.4%). Most common grade3 or 4 non-hematological toxicities were nausea (13.5%). After the completion of TPS, 1 achieved complete response and 5 achieved partial response with an overall response rate of 42.8%. Of the 14 pts after receiving TPS, 11 received PBT concurrent with cisplatin, 2 received PBT alone and one received palliative radiation. No severe toxicity was observed during PBT. After the completion of PBT, 11 pts achieved complete response and 1 pts have not yet confirmed response. No brain damage or blindness was seen.
Conclusion: Induction chemotherapy of TPS followed by PBT concurrent with cisplatin was well tolerated. The antitumor activity is very promising, and this warrants further investigation.

8540 POSTER

Prospective assessment of cutaneous toxicities and treatment interruptions of the association radiotherapy – cetuximab for head and neck cancer patients

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Background: cetuximab is used with radiotherapy for patients with locally advanced head and neck squamous cell carcinomas (Bonner 2006). Toxicity profiles in the radiotherapy alone or the combination in the Bonner's trial were similar, except for acne-like eruptions. Nevertheless, several institutions have since reported increased radiation-dermatitis toxicities. Treatment interruptions have not been clearly reported. The aim of the study was to precise prospectively cutaneous semeiology and to assess the number of unplanned treatment interruptions in an unselected population in a single institution using a standardized assessment of cutaneous toxicities.
Materials and Methods: we conducted an institutionally-approved observational study on 25 consecutive patients treated with combination. Patients all signed an informed consent and underwent weekly anonymized standardized photographs of their neck, face and thorax. Toxicity grades were assessed by a dermatologist, a medical oncologist and radiation oncologist. Expected side effects treatments were standardized.
Results: median follow-up was 7.7 months. There were 20 males/5 females. Performance status was 0 in 52%, 1 in 28% and 2 in 20% of cases. Median age was 63.5 years (41.2−80.0). Primary tumor was in the oral cavity (n = 2), oropharynx (n = 16), nasopharynx (n = 1), larynx (n = 1), hypopharynx (n = 3) or cervical nodes (n = 2). Eight patients (32%) underwent induction chemotherapy using docetaxel-cisplatin-5FU. Sixteen (64%) had $\geqslant$ 7 infusions of cetuximab and 100% the planned dose of radiation. Median treatment time was 53 days (35−77), without any interruption in 14 cases (42%). Treatment interruptions occurred after a median 40 days of treatment (21−52) and lasted for a median 7.5 days (5−15). The maximal acne-like eruptions grade occurred at day 20 (7−55) after the first cetuximab infusion (grade $\geqslant$ 3 n = 2). The maximal in-field radiation-dermatitis grade occurred at day 40 (14−70) (grade $\geqslant$ 3 n = 10). Median weight loss was −2 kg (−10$\pm$4). Antibiotics (mainly tetracyclines) were administered in 19 patients (76%) and morphine in 12 (48%).
Conclusion: the combination of radiotherapy and cetuximab was associated with high rates of in-field radiation-dermatitis. However, all patients received the planned treatment with acceptable treatment breaks thanks to early management of cutaneous toxicities. The data presented at the meeting will include 10 additional patients.

8541 POSTER

Chemoprevention of phytochemicals for head and neck cancers

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Background: Head and neck squamous cell carcinoma (HNSCC) is one of the most common malignancies. Its multi-step and cumulative features strongly support the rationale for prevention or early treatment before invasive lesions grow. Cancer chemoprevention is a very promising strategy for this goal. Unfortunately, its widespread application in clinic has been hampered by several problems, particularly the systemic side effects. It is especially problematic for individuals who are on the medication requiring a prolonged period of time or who are ill due to a secondary cancer. In recent years, there was a significant trend toward the utilization of phytochemicals and other natural supplements as an alternative to traditional practice, to improve the treatment safety.
Materials and Methods: In this review, we explored and discussed the most recent research and clinical progress in chemoprevention of phytochemicals for NMSCs. Our literature search was limited to those reports and articles published within the past 10 years (1998−2008). In addition, references from each of the identified papers were reviewed to find additional related papers for this review.
Results: Based on recognition amongst the literature, four compounds were represented and discussed, which included resveratrol, green tea, perillyl alcohol and Ginger. More than 10 other compounds were also named, with brief introduction. Subsequent research and future study were discussed.
Conclusions: The application of phytochemicals and other natural compounds is an appealing approach for the chemoprevention of HNSCC, in that they are generally nontoxic, less costly and widely available. It would be a promising alternative to current managements, due to reduced side effects without sacrificing clinical advantages. Further studies are warranted to increase the treatment efficacy by improving their bioavailability and combining multiple agents and to validate their benefit in humans by clinical trials.

8542 POSTER

Retrospective analysis of the outcomes of young oral tongue cancer in the National Cancer Centre, Singapore

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Background: A retrospective study to compare the characteristics and outcomes of young oral tongue cancer in our local population.