

Materials and Methods: All patients with oral tongue squamous cell carcinoma (SCC) treated with definitive or adjuvant radiotherapy (RT) in our department between January 1998 and December 2006 were included. They were categorized into 2 groups (Group A: ≤ 40 years old and Group B: > 40 years old). Overall survival (OS), locoregional relapse-free survival (LRF) and metastasis-free survival (MFS) were calculated. Survival was estimated using Kaplan-Meier method. Qualitative variables were analyzed with Fisher exact test. $p < 0.05$ was deemed significant.

Results: Eighty-nine patients were included with 11 (12%) patients in Group A and 78 (88%) patients in Group B. There were 55% females in Group A compared to 21% in Group B ($p = 0.024$). Median age for all patients was 54 years (range 18–87), 30 years for Group A and 56 years for Group B. More patients in Group B had history of smoking and alcohol intake (41% vs. 18% and 31% vs. 18% respectively). Most patients (80%) had primary surgery. Two (2%) patients in Group B had definitive RT. Three (27%) patients in Group A and 12 (15%) patients in Group B were given definitive chemoRT. In Group A, 27% had T3/4 and 36% had N0 disease. In Group B, 49% had T3/4 and 15% had N0 disease. Group B tend to present with Stage 3/4 disease (94% vs. 73%, $p = 0.176$) but Group A had more poorly differentiated SCC (27% vs. 9%, $p = 0.484$). Margin status, lymphovascular/perineural invasion and extranodal extension were similar in both groups. Median follow-up were 13.9 months (3.4–83.9) for Group A and 13.7 months (2.3–117.0) for Group B. Four (36%) patients in Group A and 37 (47%) patients in Group B died of cancer. Two (18%) Group A and 2 (3%) Group B patients had persistent disease. Locoregional relapses were found in 18/36% and distant metastasis occurred in 9/15% in Group A and B respectively. Median OS for all patients was 96.9 months but this was not reached in Group A. The 2/5-year OS were 64/64% (Group A) and 59/52% (Group B). The 2/5-year LRF were 58/58% (Group A) and 56/53% (Group B). The 2/5-year MFS were 86/86% (Group A) and 84/81% (Group B). These survival differences were not statistically significant, even after stratifying for tumor stage (1/2 vs. 3/4).

Conclusions: Young oral tongue patients in our local population had similar pathological features and clinical outcomes compared to the older patients. However, locoregional failure was substantial in both groups and aggressive treatment is needed to improve outcome.

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POSTER

Hyperbaric oxygen concurrent with superselective intra-arterial carboplatin chemoradiotherapy enhances survival of patients with oral cancer

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Background: A hypoxic cell fraction within a tumor tissue decreases the effect of radiotherapy and chemotherapy and gives a poor prognosis. Because the oxygen tension of tumor tissues remains higher than that of normal tissue after hyperbaric oxygen (HBO) exposure, recent study suggests that irradiation within 15 min after HBO exposure enhances the antitumor effect of radiotherapy in malignant tumors. We retrospectively evaluated the effect of HBO given concurrently with intra-arterial carboplatin chemoradiotherapy in patients with oral cancer.

Patients and Methods: At our institution, 101 patients with oral cancer, including those with recurrent lesions or cervical lymph node metastasis, were treated with superselective intra-arterial carboplatin infusion, external beam radiotherapy, UFT (tegafur-uracil) and/or surgery between April 1995 and November 2008. Treatment was combined with HBO for 51 patients and 50 were treated without HBO exposure. HBO was administered in a multiplace hyperbaric chamber according to the following schedule: 13 min of compression with air, 60 min of oxygen inhalation using an oxygen mask with a reservoir at 2.5 atmospheres absolute, and 10 min of decompression with oxygen inhalation. Radiotherapy was performed five times weekly immediately after HBO exposure.

Results: See the table.

Table 1 Treatment result of the 101 patients/CAPTION>

Prognosis*	without HBO (50 tumors)	with HBO (51 tumors)
No evidence of disease	16	33
Alive with disease	0	3
Died of their disease	2811	
Died of another disease	6	4

*p-value = 0.001

Of the 51 patients whose tumors were treated with chemoradiotherapy without surgery, 30 also received HBO (CR-wHBO group) and 21 were

treated without HBO (CR-woHBO group). Of the 50 patients whose tumors were resected after preoperative chemoradiotherapy, 20 received HBO (S-wHBO group) and 30 were treated without HBO (S-woHBO group). The disease-specific survival rate of patients treated with HBO (70%) was significantly higher than that of patients treated without HBO (40%) ($p = 0.012$). In addition, the five-year disease-specific survival rates were: S-wHBO group, 86%; S-woHBO group, 60%; CR-wHBO group, 53%; and CR-woHBO group, 27%. A logrank test showed that the differences between the survival rate of each group were significant ($p = 0.003$).

Conclusion: These results suggest that adding HBO to intra-arterial carboplatin chemoradiotherapy enhances the survival of patients with oral cancer, and that HBO is a useful adjunct to chemoradiotherapy for squamous cell cancer of the oral cavity.

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POSTER

A prospective, open-label, randomized phase II trial to evaluate the changes of bone resorption marker after administration of zoledronic acid (ZOL) in nasopharyngeal cancer (NPC) patients with bone metastases (BM)

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Background: ZOL is the only bisphosphonate that has demonstrated efficacy for the prevention of skeletal-related events (SREs) in patients with BM in a wide range of tumor types. Recent retrospective analyses also show that normalization of N-telopeptide of type I collagen (NTX) over 3 months by the treatment of ZOL provided a continuum of SRE risk reduction and survival benefit in patients with BM. Therefore, we conducted the prospective open-label randomized phase II trial to evaluate the changes of NTX after administration of ZOL in NPC patients with BM.

Methods: Newly diagnoses NPC patients with BM were randomized to receive chemotherapy of Cisplatin (20 mg/m² IV, D1–5) plus FU(500 mg/m² IV, D1–5) (CF regimen, q3wks) and intravenous ZOL (4 mg, q4wks, for 3months, CF+ZOL Group) or same chemotherapy alone (CF Group). Urinary NTX was measured by ELISA method at baseline and 1, 2, 3 months after administration of ZOL in all patients.

Results: Sixty patients were enrolled into the study, 30 patients in each group. The median chemotherapy numbers was same (4 and 4, respectively) in two groups. The median baseline NTX level was no difference between two groups (75.4 and 95.6 nM BCE/mM creatinine, respectively $P > 0.05$). The NTX decreased 65.9% within 1 month in CF+ZOL group, whereas NTX increased 2.61% in CF group ($P < 0.01$). The median NTX decrease percentage in 2, 3 months after treatment were 70.8%, 86.5% in CF+ZOL Group and 15.9%, 34.5% in CF Group respectively ($P < 0.01$, $P < 0.01$).

Conclusion: ZOL administered with chemotherapy (CF) consistently reduced NTX levels in NPC patients with BM, indicating potential benefit of ZOL may exist in this group of patients. The value of NTX reduction in NPC patients with BM will need to further study in larger prospective randomized trials.

The median change from baseline values for NTX (%)

Time (m)	1	2	3
Group 1(CF+ ZOL)	-65.9	-70.8	-86.5
Group 2 (CF)	2.61	-15.9	-34.5
P value	$P < 0.01$	$P < 0.01$	$P < 0.01$

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POSTER

Prognostic value of ERCC1 T19007C polymorphism in head and neck squamous cell carcinoma (HNSCC) patients presenting with high- or intermediate-risk features treated with adjuvant chemoradiation (CRT)

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Background: Adjuvant cisplatin (CDDP)-based CRT can increase progression-free survival (PFS) and overall survival (OS) in patients (pts) with high- or intermediate-risk HNSCC. ERCC1 is a DNA repair protein

related to resistance to chemo- and RT, and the T19007C polymorphism at codon 118 may be associated to reduced ERCC1 mRNA expression and protein levels. We retrospectively studied the prognostic value of the T19007C polymorphism in high- or intermediate-risk HNSCC pts treated with adjuvant CRT.

Patients and Methods: Pts diagnosed with non-metastatic SCC of oral cavity (OC), oropharynx (OP), hypopharynx (HP) or larynx (L), presenting high- or intermediate-risk features (EORTC), submitted to surgery with curative intent and adjuvant CRT were included. CRT consisted of 60–70 Gy (2 Gy/d, 5 times/wk) and CDDP 100 mg/m² on days 1, 22 and 43. ERCC1 genotyping was analyzed by PCR-RFLP. Results: 69 pts were included, median age 56 y, 81% male.

Primary sites: OC 41%, OP 12%, HP 16%, L 32%. Stage III 14%, IV 86%, being T3-T4 78%, N2-N3 58%; 27 pts had nodal extracapsular spread (ECS) and 18 pts had positive margins. Overall, high-risk features were present in 40 pts (58%) and intermediate-risk features in 29 pts (42%). During the median follow-up of 47 mo, 18 pts relapsed (11 loco-regional and 7 distant), and 29 deaths were observed (20 disease-related). The median PFS was 36.6 mo, and the median OS was 52.5 mo. Neither positive margins nor ECS were found to be prognostic in terms of OS, but negative margins were associated to a non-significant higher median OS (53.8 vs. 42.0 mo; HR 0.67, 95% CI 0.27–1.51; $p = 0.308$). 29/46 pts (63%) presented the T19007 polymorphism. This polymorphism was related to a non-significant higher median OS (50.3 vs. 43.2 mo; HR 1.35, 95% CI 0.56–3.34; $p = 0.494$). Second primary tumors were diagnosed in 10 pts and their incidence was not related to the T19007C polymorphism ($p = 0.40$, Fisher).

Conclusion: Non-significant higher OS was detected in HNSCC pts presenting the T19007 ERCC1 genotype and treated with adjuvant cisplatin-based chemoradiation. ERCC1 polymorphisms must be further explored in HNSCC pts in order to improve their risk stratification.

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POSTER

The prognostic value of p16 status in advanced stage oropharyngeal carcinoma according to treatment regimen

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Background: The overexpression of p16 in tumors has been proposed as a surrogate marker for clinically relevant human papilloma virus (HPV) infection. There is prospective evidence that HPV positive/p16 positive head and neck squamous cell carcinomas have an improved prognosis when compared to HPV negative tumors. In-vitro studies suggest that chemotherapy and altered fractionation may enhance the tumorocidal effects of radiotherapy in HPV positive tumors. The purpose of this retrospective study is to examine the prognostic effect of p16 status in two separate cohorts of loco-regionally advanced oropharyngeal carcinomas treated with chemoradiotherapy (CIRT) or accelerated fractionation (AF) radiotherapy alone in the province of British Columbia.

Methods: Eligibility criteria were stage 3 or 4, biopsy proven squamous cell carcinoma of the oropharynx, treated with curative intent CIRT or AF. From January 1, 2000 to July 1, 2007, our provincial database yielded 78 eligible cases: 45 in the CIRT cohort and 33 cases in the AF cohort. Formalin-fixed paraffin-embedded tissue biopsies were stained using the commercially available mouse monoclonal antibody p16 (CINtec p16-INKa histology kit, MTM Laboratory AG). The expression of p16 was scored by an independent pathologist blinded to the outcomes of cases.

Results: The CIRT cohort of 45 cases were treated with 70 Gy in 35 fractions with concurrent cisplatin (100 mg/m²) every 3 weeks. The median age was 57 (30–73) years and median follow up was 42 (5–62) months. At two and three years, disease-free survival (DFS) was 79% (68–90) and 74% (62–86), and overall survival (OS) was 88% (81–94) and 81% (70–91), respectively. The AF cohort of 33 cases were treated with 66 Gy in 33 fractions over 38 days or 33 days. The median age was 58 (36–77) years and median follow up was 39 (4–77) months. At two and three years, DFS was 65% (48–82) and 58% (40–75) and OS was 74% (58–89) and 71% (54–87), respectively. p16 status will be tested in univariate and multivariate analyses to examine the prognostic value for DFS and OS, in each of the cohorts. The results will be presented.

Conclusions: This study will provide the first estimate of HPV prevalence, according to p16 status, in loco-regionally advanced oropharyngeal cancer in British Columbia. The relative prognostic effect of p16 status in each therapeutic regime may be hypothesis generating in determining the ideal treatment approach in HPV positive oropharyngeal cancer.

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POSTER

Retrospective study of nasopharyngeal carcinoma managed at a UK tertiary referral centre

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Background: Nasopharyngeal carcinoma is an uncommon cancer in the West. The optimum treatment has evolved over the past 15 years with increasing use of concurrent chemoradiotherapy.

Materials and Methods: Retrospective review of case notes from all patients coded as presenting with nasopharyngeal carcinoma between 1995 and 2005. Of 139 identified patients 126 were treated curatively for nasopharyngeal carcinoma. World Health Organisation (WHO) tumour grade information was available for 80 patients.

Results: Patients treated with chemoradiotherapy showed a significantly better overall survival than those treated with radiotherapy alone ($p = 0.003$). Patients with histological grade 3 tumours showed a better overall and recurrence free survival than those with grade 1 or 2 tumours although chemoradiotherapy showed the greatest benefit in patients with grade 1 tumours. At presentation a bimodal age distribution was noted with 12 (9.5%) patients presenting under the age of 30 compared to the majority of patients who presented between the ages of 50 and 70. The most common mode of presentation was with a neck lump (52%) with 49% of patients presenting for treatment later than 3 months after onset of symptoms.

Conclusions: Chemoradiotherapy confers an advantage over radiotherapy alone in the treatment of nasopharyngeal carcinoma in a UK based population. Grade 1 tumours, less likely to be Epstein Barr Virus related, showed the greatest benefit from chemoradiotherapy. Many patients with nasopharyngeal carcinoma present for treatment late with advanced tumours likely to adversely affect outcome.

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POSTER

Long-term outcome after endoscopic resection in patients with hypopharyngeal carcinoma invading the subepithelium

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Background: Recent developments in endoscopic diagnosis have enabled gastrointestinal endoscopists to detect hypopharyngeal carcinoma in an early stage, especially in Japan. Patients with such early lesions can be treated with endoscopic resection (ER) with minimal invasiveness. However, strict indication for ER in cases of hypopharyngeal carcinoma is unclear. Carcinoma in situ or slightly invaded carcinoma seems to be an indication for ER; however, there is no evidence supporting this hypothesis. In this study, we evaluated long-term outcome after ER in patients with hypopharyngeal carcinoma invading the upper subepithelial layer.

Patients and Methods: From June 2003 through March 2008, 17 patients with squamous cell carcinoma of the hypopharynx underwent ER at Hokkaido University Hospital. The same techniques as those used for gastrointestinal carcinoma such as endoscopic submucosal dissection were used for patients under general anesthesia in the current study. Nine of the patients had histologically confirmed shallow invasion of the subepithelium (the remaining 8 patients having carcinoma in situ). None of those 9 patients wished to undergo open surgery or adjuvant chemoradiotherapy, and they were observed to assess the outcome. Lesion size ranged from 0.9 to 2.5 cm (mean (SD), 2.0±0.5 cm). Depth of tumor invasion in the subepithelium ranged from 300 to 720 µm (mean (SD), 480±150 µm). After treatment, all 9 patients were monitored to detect local or distant recurrence every 3 months during the third year and every 6 months afterward. Follow-up evaluations included gastrointestinal endoscopy, laryngoscopy, CT, and physical examination by an otolaryngologist. Informed consent for all procedures and for participation in observation study was obtained from all subjects.

Results: As of March 2009, none of the 9 patients have died of recurrent hypopharyngeal carcinoma or intercurrent diseases. None of them have had local recurrence or metastasis. No early or late complication due to ER has occurred in the patients. The median follow-up period after treatment in the 9 patients was 43 months (12 months to 66 months). Kaplan-Meier estimates of relapse-free survival rates at 5 years in the 9 patients were 100%.

Conclusion: Although the number of patients in this study was small and further multicenter studies are needed to draw firm conclusions, the results of this study suggest that hypopharyngeal carcinoma with slight invasion to the subepithelium can be successfully treated by ER.