

8568

POSTER

# **Protection of Oral Mucosa in Patients With Oral Tongue Squamous Cell Carcinoma Treated Postoperatively With Intensity Modulated Radiotherapy**

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**Purpose:** To present initial results of protection of oral mucosa aiming to reduce the severity of acute oral mucositis in postoperative intensity modulated radiotherapy (IMRT) patients with oral tongue squamous cell carcinoma compared to IMRT without oral mucosa sparing.

**Methods and Materials:** A total of 48 patients with oral tongue squamous cell carcinoma who received postoperative IMRT in our institution were randomized to two groups: the oral sparing group and oral unsparing group. For the oral sparing group (24 patients), the patients had distinctive sparing of the oral mucosa outside the planning target volume (PTV). The main spared site that with a dose of <32 Gy as far as possible was the portion of the mucosa including bilateral cheeks, upper lip and lower lip mucosa that was defined as the united site. For the oral unsparing group (24 patients), the protection of the oral mucosa was not intended. The severity of clinical acute mucositis of each patient in the united site and the 3 other oral sites (contralateral oral tongue, hard palate and soft palate) was assessed weekly during IMRT until complete healing. Oral mucositis grading was performed based on the National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0 (CTCAE). Dosimetry in each oral site and some therapeutic measures related to acute mucositis between the two groups were compared.

**Results:** During IMRT, there no grade 4 and more acute mucositis in all oral sites in this study. As compared with oral unsparing group, the incidences of grade 3 and 2 mucositis in the united site were significantly lower in the oral sparing group (0% and 25%, respectively, vs. 45.8% and 54.2%, respectively,  $p=0.000$ ). Dosimetric analysis revealed that the mean dose to the united site was significant reduce with oral sparing than without oral sparing ( $41.8\pm7.4$  Gy vs.  $58.8\pm2.2$  Gy,  $p=0.000$ ). The oral sparing IMRT was associated with significant reduce in using of analgesics ( $p=0.043$ ) and intravenous antibiotics ( $p=0.039$ ), those related to severity of acute mucositis, including mouth pain and infections.

**Conclusions:** Use of oral sparing IMRT for postoperative patients with oral tongue carcinoma resulted in significant decrease in severity of acute mucositis in the oral sparing site and led to less symptoms and benefits in terms of quality of life preservation.

8569

POSTER

# **Radiotherapy After Hyperbaric Oxygen Concurrent With Superselective Intra-arterial Carboplatin Chemotherapy Enhances Survival of Patients With Oral Cancer**

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**Background:** A hypoxic cell fraction within a tumour tissue decreases the effect of radiotherapy and chemotherapy and gives a poor prognosis. Because the oxygen tension of tumour 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 antitumour effect of radiotherapy in malignant tumours. 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, 125 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 January 2011. Treatment was combined with HBO for 62 patients and 63 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:** Details of patient characteristics and treatment outcomes are summarized in Table 1. Of the 56 patients whose tumours were treated with chemoradiotherapy without surgery, 32 also received HBO (CR-wHBO group) and 24 were treated without HBO (CR-woHBO group). Of the 63 patients whose tumours were resected after preoperative chemoradiotherapy, 29 received HBO (S-wHBO group) and 34 were treated

without HBO (S-woHBO group). The disease-specific survival rate of patients treated with HBO (66%) was significantly higher than that of patients treated without HBO (42%) ( $p=0.009$ ). In addition, the five-year disease-specific survival rates were: S-wHBO group, 80%; S-woHBO group, 65%; CR-wHBO group, 57%; and CR-woHBO group, 27%. A log-rank test showed that the differences between the survival rate of each group were significant ( $p=0.007$ ).

**Conclusion:** These results suggest that radiotherapy after hyperbaric oxygen concurrent with intra-arterial carboplatin chemotherapy 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.

Table 1. Characteristics of the 125 patients and treatment result

	without HBO (63 tumours)	with HBO (62 tumours)	p value
Gender			0.707
male	40	42	
female	23	20	
Age	66.7±10.1	67.6±9.8	0.611
T classification			0.022
T0	0	5	
T1	1	2	
T2	16	26	
T3	6	3	
T4	32	24	
rT2	1	1	
rT3	60	1	
rT4	5	0	
Tx	2	0	
N classification			0.258
N0	30	35	
N1	12	9	
N2	19	18	
N3	1	0	
rN1	1	0	
Carboplatin dosage (mg)	476±120	455±109	0.338
Pretreatment hemoglobin level (g/dl)	12.90±1.97	13.04±1.76	0.886
Irradiated dose (Gy)	43.8±18	48.7±18.6	0.145
Surgery of primary tumour			0.284
Yes	34	29	
No	26	33	
Prognosis			0.001
No evidence of disease	23	41	
Alive with disease	0	1	
Died of their disease	34	15	
Died of another disease	6	5	

8570

POSTER

# **Phase II Study of Cetuximab With Concomitant-boost Radiotherapy (RT) in Japanese Patients With Locally Advanced Squamous Cell Carcinoma of the Head and Neck (LA-SCCHN)**

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**Background:** The multinational randomized phase III study demonstrated the significantly improvement of OS, response rate in cetuximab + RT group compared to RT alone for LA-SCCHN (Bonner et al. 2006). We conducted a phase II, open-labeled, multicenter study in Japanese patients with locally advanced SCCHN in order to assess feasibility, safety and efficacy of cetuximab treatment in combination with concomitant-boost RT regimen.

**Material and Methods:** Patients with stage III or IV SCCHN arising in the oropharynx, hypopharynx, or larynx, which is expressing EGFR, were enrolled. The treatment period was 7 weeks (Week 1 to 7). Cetuximab was initiated with 400 mg/m<sup>2</sup> from Week 1, followed by weekly infusions of 250 mg/m<sup>2</sup> from Week 2 to 7. RT was initiated from Week 2 to 7 (i.e.