

Influence of Pathologic Complete Response to Induction Chemotherapy on Long-Term Survival of Patients Advanced Squamous Cell Carcinoma of the Oral Cavity Tongue

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Abstract

Objective: To discuss long-term efficacy of preoperative induction chemotherapy(IC) plus surgery± radiotherapy in patients with resectable stage III or IV squamous cell carcinoma of the oral cavity tongue (SCCOT).

Methods: From June 1996 to December 2005, 73 patients with advanced SCCOT were treated with IC followed by surgery ± radiotherapy, at the Cancer Center of Sun Yat-sen University. The 5-year overall survival (OS), local control and reasons of treatment failure were analyzed retrospectively.

Results: 73 patients aged from 22 to 77 years with untreated, clinical T1–4 N0-2M0 SCCOT underwent IC followed by surgery ± radiotherapy. After IC, 17 patients (23.3%) achieved clinical complete response; 44 patients (60.3%) clinical partial response; 12 patients (16.4%) no response or progression, and overall response rate was 89.0% (65/77). On final surgical pathology, 14 patients (19.2%) achieved histological complete response; 59 patients (80.8%) histological incomplete response. The 5-year OS was 59.8%, local control was 69.9% (51/73). No treatment-associated deaths occurred, and toxicity was modest.

Conclusion: IC plus surgery ± radiotherapy was a treatment modality that was tolerated with encouraging survival outcome in advanced resectable SCCOT patients. Response rate with this regimen was limited, but the responders were associated with excellent prognosis.

Keywords: Advanced oral tongue cancer; Induction chemotherapy; Squamous cell carcinoma

Introduction

Recently, local-regional control of oral cavity cancers had been enhanced in most part because of more aggressive surgical resections facilitated by modern reconstructive methods and advances in radiotherapy. Additionally, concomitant chemotherapy added to postoperative radiotherapy may improve local-regional control in patients with oral cavity cancers possessing high-risk features [1-3]. Two published meta-analyses [4-6] concluded that chemotherapy was associated with a small advantage in survival (4% to 6%) in advanced head and neck cancer. While, Licitra et al. [7] reported a randomized controlled trial of IC (3 cycles of cisplatin and fluorouracil) for resectable oral cavity cancer (98 patients in the treatment group and 97 patients in the control group), and there was no evidence of improved survival for both arm (5-year overall survival 55%). In short, tumor control and survival were unsatisfactory in advanced resectable SCCOT. Attempting to improve disease control and ultimately OS, clinical trials involving multimodality treatment regimens combining surgery, radiotherapy, and chemotherapy had been under investigated. Although the use of IC improved local-regional control, and survival rates for oral cavity cancer [8,9], it had failed to demonstrate a

consistent improvement in survival [9], and distant metastasis remained a problem [8]. We reviewed the medical records of 73 patients with advanced SCCOT treated at our cancer center from June 1996 to December 2005, and analyzed the 5-year OS, local control and reasons of treatment failure, retrospectively. Our goal was to discuss the long-term efficacy of preoperative IC plus surgery ± radiotherapy in patients with resectable advanced SCCOT.

Methods

Patients

Eligibility criteria included the following: newly diagnosed, previously untreated, pathologically confirmed squamous cell carcinoma of the anterior two thirds of tongue (anterior activities tongue), resectable stage III (T1-3N0-1M0) or IV (T1-4aN0-2M0) (Union for International Cancer Control, UICC 2002) disease without distant metastases (T4b, T4c or N3 tumors were excluded because there was lack of consensus of whether they were resectable for cure by surgery).

Pretreatment evaluation included a complete history, physical examination, performance status, serum chemistry profile, complete blood cell count, chest radiography, computed tomography (CT) or

magnetic resonance imaging (MRI), bilateral cervical and supraclavicular ultrasonography, and abdominal ultrasonography. The medical records of these patients were reviewed to assess the patients' characteristics, including age, sex, primary site, clinical stage, clinical response to chemotherapy, subsequent local modalities, date of disease progression, and final status on the last follow-up examination. Follow-up data obtained included the date and type of any recurrences (local, regional, distant) and the date of last contact and disease status at that time.

Treatment

All patients were evaluated by surgeons, radiation oncologists, and medical oncologists before the time of receiving an initial 3 cycles of IC, and the responses to IC were evaluated by appropriate radiological studies. Patients' clinical responses were categorized in accordance with RECIST (Response Evaluation Criteria In Solid Tumors) (2000). Pathologic responses to IC were evaluated on the basis of the final surgical pathology review. Toxic effects associated with IC were categorized and graded according to the Common Toxicity Criteria scale (Version 2.0).

Sometimes, despite a clinical complete response, surgical was chosen, basically in tumors with infiltration of bone or cartilage. The extent of eventual surgical resection was not altered by subsequent response to IC. Surgery was performed 3 weeks after completion of IC and recovery of white blood cell count, and usually followed by postoperative radiotherapy. Surgical resection was designed to encompass residual disease to ensure a clear margin and consisted of glossectomy at the primary tumor site and neck dissection. Glossectomies were classified as hemiglossectomy (removal of approximately half of the tongue), or subtotal glossectomy (removal of more than half of the tongue). All patients underwent, at minimum, ipsilateral selective (levels I, II, and III) neck dissection. When patients had lymph nodes involved at presentation, functional neck dissection was performed in N1 to N2a and modified radical neck dissection or radical neck dissection was in N2b. Different reconstruction techniques were used: pectoralis major myocutaneous flap, free shares anterolateral flap, and free forearm skin flap.

Upon review of surgical pathology, patients with clear histologic margins at the primary tumor site without lymph node involvement or perineural invasion received no additional treatment, when patients not meeting these criterions received standard postoperative adjuvant radiotherapy (4 weeks after completion surgery). Those with extracapsular nodal extension or multiple other adverse pathologic features (poorly differentiated tumor, perineural invasion, multiple positive nodes, or close margins) received postoperative radiotherapy, and doses depending on pathologic results (positive margins, number of positive neck nodes, or extracapsular spread).

Statistical analysis

Survival time was assessed from the first day of hospitalized until death or until last contact. Patients who developed a second primary tumor were not considered to have progressive primary disease. Actuarial survival rates were calculated according to Kaplan–Meier method, comparisons were performed using log-rank test and $p < 0.05$ was set as the level of statistical significance. Calculations were completed using SPSS software (version 16.0).

Follow-up

Patients were followed up regularly, every month for first three months, every three to six months for two years and with decreasing frequency in the subsequent period. Median follow-up period was 70.86 months (range from 1.9 to 188.0 months). Follow-up evaluations were carried out with physical examination and/or imaging studies, including computed tomography scan, or magnetic resonance imaging.

Result

Pretreatment demographic and clinical variables

From June 1996 to December 2005, 73 patients with locally advanced SCCOT were treated preoperatively with IC (3 cycles of cisplatin and 5-fluorouracil) followed by surgery (resection of the primary tumor and neck) \pm radiotherapy, at the Cancer Center of Sun Yat-sen University. The retrospective analysis showed that the mean age was 48 years (median, 47 years; range, 22–77 years), and 43 patients (58.9%) were men, and 30 (41.1%) were women. The staging evaluation was showed in Table 1, 39 patients (53.4%) were clinical III stage (T3N0M0 10 patients; T2N1M0 10 patients; and T3N1M0 19 patient), and 34 patients (46.6%) were IV disease (T4aN0M0 17 patients; T4aN1M0 9 patients; T4aN2bM0 2 patients; T2N2aM0 4 patients; and T3N2aM0 2 patients). Regional neck lymph node involvement was present in 46 patients and 27 other patients had no cervical node disease.

Stage	No	P value
T stage		
T2	14	0.002
T3	31	
T4	28	
N stage		
N0	27	0.037
N1	38	
N2	8	
N3	0	
Clinical stage		
III stage	39	0.036
IV stage	34	

Table 1: The clinical stage of 73 patients with advanced squamous cell carcinoma of the oral cavity tongue

Chemotherapy regimen and response to induction chemotherapy

All patients were treated with PF (DDP and 5-fluorouracil infusion). PF regimen: Cisplatin 20 mg/m²/day ivd days 1 to 5, and 5-FU 1,000 mg/m²/day in continuous infusion days 1 to 5 every 21 days during 3 cycles. When patients suffering grade 3 or 4 toxicity, we reduced by 25% of the chemotherapy dose. After completion of three

cycles of IC, 17 cases of CR, 44 cases of PR and 12 cases of SR in the primary site and neck lymph node were confirmed, giving an overall response rate of 83.6% (61/73). On the basis of pathologic review of the surgical specimen, 15 patients (20.5%) had a histologic complete response at the tongue and neck.

Toxic effects of induction chemotherapy

Toxic effects associated with IC were presented in Table 2. There were no treatment-associated deaths. Eleven episodes of grade 4 toxic effects were recorded, and ten of which reflected expected bone marrow suppression; similarly, of the 23 episodes of grade 3 toxic effects, 20 were cytopenias. Of the grade 1 and 2 toxic effects, the most common effect was gastrointestinal-related symptoms.

Toxicity	Number of patients			
	Grade1	Grade2	Grade3	Grade4
Alopecia	10	4	1	0
Anemia	0	2	0	0
Anorexia	11	4	1	0
Constipation	6	0	0	0
Febrile neutropenia	2	0	0	0
Granulocytopenia	0	0	11	5
Infection	0	0	0	0
Leukopenia	2		9	5
Nausea	12	6	0	0
Rash	3	0	0	0
Stomatitis	2	1	0	0
Thrombocytopenia	0	0		0
Thrombophlebitis	2	0	0	0
Vomiting	7	1	0	1

Table 2: Selected toxic effects of induction chemotherapy

Local Therapies

Extent of surgery in this series was considerable: 23 patients underwent subtotal glossectomies, 29 patients underwent hemiglossectomies, 21 patients underwent subtotal glossectomies and flap-based reconstructions; 4 patients had bilateral neck dissections, and all the other patients received unilateral neck dissections (1 patient had radical neck dissections, 20 patients had modified radical neck dissections, 25 patients had functional neck dissections, 23 patients had selective neck dissections); 4 patients had tracheotomy. No patient had a positive margin on final pathology. Adjuvant postoperative radiotherapy was recommended for these patients who had at least one of adverse pathologic features. Radiation therapy was given postoperatively to a total dose of primary: ≥ 60 Gy (2.0 Gy/day); involved neck nodal stations: ≥ 60 Gy (2.0 Gy/day), uninvolved neck nodal stations: ≥ 50 Gy (2.0 Gy/day). Postoperative radiation was used in 52 patients, four patients received less than 60Gy, and one patient did not finish radiotherapy (due to skin toxicity).

Recurrence

With a median follow-up of 70 months (range 2–188 months; 11 patients had <12 months of follow-up). The main causes of death were the recurrence of the primary sites or regional recurrence. Overall, 22 patients died from tumor or regional node recurrence, 5 died from other cancers (3 from secondary esophageal carcinoma, 1 from secondary gingival carcinoma, 1 from secondary breast cancer), 1 died of a cerebral hemorrhage and the death of the remaining 6 patients was unclear. There was no death due to combined treatments. After undergoing surgery, the local control rate was 69.9% (51/73). No case was noted in terms of distant metastasis at the following time. The most common type of recurrence was local or regional recurrence. The recurrence patterns showed 5 patients with primary recurrence, 7 patients with regional neck lymph node relapse, and 10 patients with relapse in both sites.

Survival analysis

24 patients were alive (32.9%) at the time of analysis, and 23 patients (31.5%) had a long-term survival (more than 10 years). The univariate analysis showed statistically significant differences in tumor size (T stage) ($p=0.038$) (Figure 1A), initial cervical nodal status at diagnosis negative over positive ($p=0.037$) (Figure 1B), stage III over stage IV patients ($p=0.036$) (Figure 1C), different clinical response to chemotherapy ($p=0.025$) (Figure 1D), and negative pathology response over positive ($p=0.002$) (Figure 2). The 5-year OS for negative cervical nodal status over positive cervical nodal at diagnosis were 80.8% and 47.4%. No statistical differences were observed between the age of patients of 55 years or less and older patients ($p=0.102$), and between male and female ($p=0.261$). Multivariate analysis of the major prognostic factors identified in the univariate analysis (different T stage, clinical positive vs. negative nodes, stage III vs. IV, different clinical responders to chemotherapy, and negative pathology response vs. positive) showed that clinical nodes (relative risk 2.633; 95% confidence interval 1.173–5.909; $p=0.019$), different clinical responders to chemotherapy (relative risk 2.634; 95% confidence interval 1.329–5.221; $p=0.006$) and negative pathology response over positive (relative risk 4.529; 95% confidence interval 1.027–19.967; $p=0.046$) had statistical significance but there was no statistical significance between different T stage and clinical stage, which was showed in Table 3.

Variables in the Equation								
							95% confidence interval for RR	
	B	SE	Wald	df	sig	RR	lower	upper
clinical state node	0.968	0.413	5.507	1	0.019	2.633	1.173	5.909
clinical response to chemotherapy	0.969	0.349	7.699	1	0.006	2.634	1.329	5.221
histology specimen of	1.511	0.757	3.983	1	0.046	4.529	1.027	19.969

Table 3: Multivariate analysis of the major prognostic factors.

Discussion

Patients with carcinoma of the oral tongue frequently had advanced stages (III and IV) at the time of presentation, and required a multimodality approach to obtain satisfactory results. IC was one of the commonly adopted induction methods to treat head and neck carcinoma. It was used to improve local control rate, decrease distant metastasis rate, and thus improved the OS rate. PF (Cisplatin and continuous infusion of 5-fluorouracil (5-FU)) had been established as the standard induction regimen for advanced cases [4-7]. Previous studies of preoperative chemotherapy with PF combination regime showed encouraging results in patients with advanced head and neck carcinoma: even though the overall survival was not improved [7,10-12], IC achieved high major response (clinical complete or partial response) rate (approximately 48%, range 15%–82%) [7,10,11], with no significant increase in postoperative morbidity and mortality. While other reports [4,12-14] revealed the results with regard to the effect favored IC and the improvement in OS ranged from 4% to 21%.

The results of our study indicated that responders (clinical complete or partial response patients) obtained a long-term survival of approx 62.5% (5-year OS), which was significantly better than that in nonresponders (41.7%) according to the univariate analysis. This survival improvement had been maintained when the response to chemotherapy was combined with other prognostic factors in the multivariate analysis, suggesting that response was a powerful, individualized prognostic factor [15]. The reports by the Department of Veteran Affairs Laryngeal Study Group [16] and the European Organization [17] for Research and Treatment of Cancer demonstrated IC with PF followed by radiation therapy in responders with advanced laryngeal, and hypopharyngeal cancer, respectively, resulted in two thirds of the patients retaining their larynx without a survival disadvantage compared with non-responders who received surgery and post-operative radiation therapy.

For head and neck cancers, cisplatin-based regimen had produced clinical overall response rates of 15%–82% and complete response (CR) rates of 20%-50% [7,10,11,16,17]. The clinical overall response rate in our study was 83.6% and similar to above literature. No matter of which pattern of response to chemotherapy, the extent of eventual surgical resection was not altered and surgery was performed 4 weeks after completion of IC. Kiritani et al. reported that residual tumor cells after preoperative therapy were found by microscopy in the deep tissue where there had been no clinical preoperative evidence of tumor invasion [18,19]. Their finding warns us to excise more carefully at the deep margins of tumors. With regard to the time interval between IC and surgery, the operation should not be delayed more than 5 weeks after the termination of chemotherapy, since in Shibuya et al. [20] study the tumor size decreased greatly during the first 3 weeks but tended to increase thereafter.

After 3 cycles of IC followed by surgery in our study, the 5-year OS for negative pathology responders reached 92.9% and 47.9% for those positive pathology responders. This was close to Xavier Leon et al. report [10]. In their report, the 5-year OS for advanced head and neck patients with negative specimens was 96% significantly better than 62% survival in patients with residual tumor. These results suggested that obtaining negative pathology response to induction chemotherapy was a significant impact factor of the long-term of survival.

The N stage nowadays seemed more important than in the past, and the presence of cervical lymph node metastases was universally accepted as the main factor influencing survival in patients with OSCC

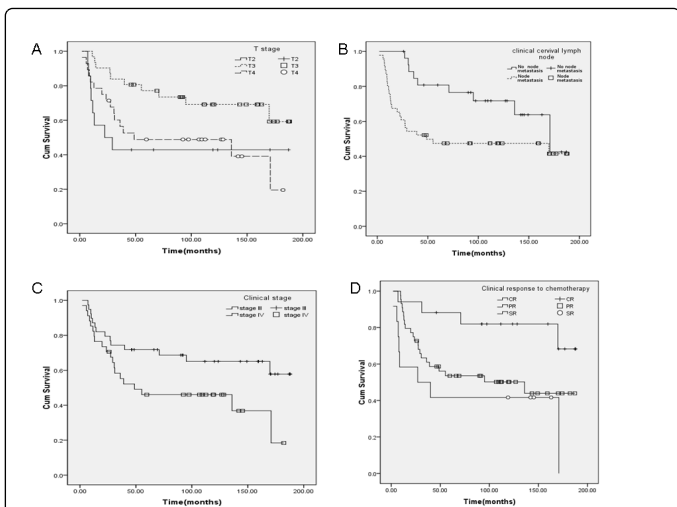


Figure 1 A: Overall survival rate according to different T stage for advanced (stage III or IV) patients with resectable squamous cell carcinoma of the oral cavity tongue. B: Overall survival rate according to clinical cervical lymph node for advanced (stage III or IV) patients with resectable squamous cell carcinoma of the oral cavity tongue. C: Overall survival rate according to clinical stage. D: Overall survival rate according to clinical response to chemotherapy

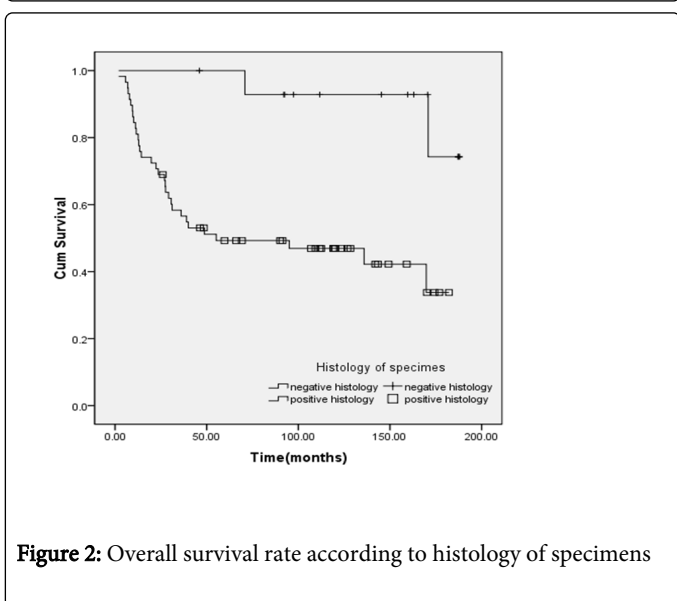


Figure 2: Overall survival rate according to histology of specimens

Response to IC was a main impact factor in long-term survival and the degree of the response also influenced the long-term prognosis. Patients who obtained a clinical complete response reached 5-year OS of 88.2%, those who obtained a clinical partial response reached 53.6% and those with a minor or no clinical response reached 41.7% ($p=0.025$). Patients who obtained negative pathology response reached 5-year OS 92.9%, and those who obtained a partial response reached 47.9%, ($p=0.038$). The responders (clinical complete or partial response patients) obtained 5-year OS 62.5%, which was significantly better than that of nonresponders (41.7%) according to the univariate analysis.

[21]. Without preoperative treatment, Woolgar observed 81% 5-year survival for patients without metastases, 64% for patients with intranodal metastases, and 21% for patients with metastases showing extracapsular spread [22]. Similar results were observed in our study: the 5-year overall survival rate for negative cervical nodal patients was 80.8% and for positive cervical nodal was 47.4%, ($p=0.037$).

Toxicity mainly included allergic reaction, bone marrow inhibition, gastro-intestinal reaction, alopecia, infecting etc. Although 22.6% of our patients presented with Grade 3–4 grade side effects, there was no toxic deaths. The toxicity was significant but tolerable with adequate support. With a median follow-up longer than 3 years, 22 (30.1%) patients died from tumor or regional node recurrence, and the locoregional control was 69.9% (51/73). Moreover, the main cause of death was local or regional recurrence. Even when complete premanagement examinations and careful surgery were performed, however, locoregional recurrence developed in 32% to 73% of patients with various stages [23]. In our material, local-regional control of oral cavity cancers had been slightly enhanced most likely because of preoperative induction chemotherapy, more aggressive surgical resections facilitated by modern reconstructive methods and the use of adjuvant radiotherapy for, close or involved margins, multinodal metastases, and vascular or perineural involvement. No matter whether the cervical lymph node metastases or not at present, neck dissection was performed in all our stage III and IV patients.

Conclusion

IC plus surgery with or without postoperative radiotherapy was a treatment modality that was tolerated with encouraging activity and survival outcome in patients with advanced resectable squamous cell carcinoma of the oral cavity tongue. Response rate with this IC regimen was limited, but the responders were associated with excellent prognosis.

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Conflict of Interest

There are no any commercial associations, current and within the past five years, that might pose a potential, perceived or real conflict of interest.

Note:

Xin-rui Zhang and Di Wu made the same contribution to the paper.

References

- Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefebvre JL, et al. (2004) Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med* 350: 1945-1952.
- Kies MS, Boatright DH, Li G, Blumenschein G, El-Naggar AK, et al. (2012) Phase II trial of induction chemotherapy followed by surgery for squamous cell carcinoma of the oral tongue in young adults. *Head Neck* 34: 1255-1262.
- Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH, et al. (2004) Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *N Engl J Med* 350: 1937-1944.
- Pignon JP, Bourhis J, Domenge C, Designe L (2005) Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-Analysis of Chemotherapy on Head and Neck Cancer. *Lancet* 355:949-955.
- Monnerat C, Faivre S, Temam S, Bourhis J, Raymond E (2002) End points for new agents in induction chemotherapy for locally advanced head and neck cancers. *Ann Oncol* 13: 995-1006.
- Cho YH, Lee SH, Kim DW, Wu HG, Hah JH, et al. (2008) Long-term survival of resectable subset after induction chemotherapy in patients with locally advanced head and neck cancer. *Head Neck* 30: 346-350.
- Licitra L, Grandi C, Guzzo M, Mariani L, Lo Vullo S, et al. (2003) Primary chemotherapy in resectable oral cavity squamous cell cancer: a randomized controlled trial. *J Clin Oncol* 21: 327-333.
- Carvalho AL, Nishimoto IN, Califano JA, Kowalski LP (2005) Trends in incidence and prognosis for head and neck cancer in the United States: a site-specific analysis of the SEER database. *Int J Cancer* 114: 806-816.
- Munro AJ (1995) An overview of randomised controlled trials of adjuvant chemotherapy in head and neck cancer. *Br J Cancer* 71: 83-91.
- León X, Quer M, Orús C, Sancho FJ, de Juan M, et al. (2000) Histologically negative specimens after induction therapy: frequency and impact on survival. *Head Neck* 22: 808-813.
- Hitt R, López-Pousa A, Martínez-Trufero J, Escrig V, Carles J, et al. (2005) Phase III study comparing cisplatin plus fluorouracil to paclitaxel, cisplatin, and fluorouracil induction chemotherapy followed by chemoradiotherapy in locally advanced head and neck cancer. *J Clin Oncol* 23: 8636-8645.
- Zorat PL, Paccagnella A, Cavaniglia G, Loreggian L, Gava A, et al. (2004) Randomized phase III trial of neoadjuvant chemotherapy in head and neck cancer: 10-year follow-up. *J Natl Cancer Inst* 96: 1714-1717.
- Kohno N, Ikari T, Kawaida M, Tanaka K, Kawaura M, et al. (2000) Survival results of neoadjuvant chemotherapy for advanced squamous cell carcinoma of the head and neck. *Jpn J Clin Oncol* 30: 253-258.
- Bourhis J, Amand C, Pignon JP. Update of MACH-NC(Meta-Analysis of Chemotherapy in Head and Neck Cancer) database focused on concomitant chemoradiotherapy. In: ASCO Annual Meeting Proceedings, New Orleans, LA, June 5–8, 2004.
- Grau JJ, Domingo J, Blanch JL, Verger E, Castro V, et al. (2002) Multidisciplinary approach in advanced cancer of the oral cavity: outcome with neoadjuvant chemotherapy according to intention-to-treat local therapy. A phase II study. *Oncology*, 63: 338-345.
- [No authors listed] (1991) Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. The Department of Veterans Affairs Laryngeal Cancer Study Group. *N Engl J Med* 324: 1685-1690.
- Lefebvre JL, Chevalier D, Luboinski B, Kirkpatrick A, Collette L, et al. (1996) Larynx preservation in pyriform sinus cancer: preliminary results of a European Organization for Research and Treatment of Cancer phase III trial. EORTC Head and Neck Cancer Cooperative Group. *J Natl Cancer Inst* 88: 890-899.
- Kirita T, Shimooka H, Yamanaka Y, Tatebayashi S, Yamamoto K, et al. (2001) Prognostic value of response to preoperative chemoradiotherapy and residual tumor grades in tongue carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 91: 293-300.
- Kirita T, Ohgi K, Kawakami M, Miyawaki S, Okamoto M, et al. (2002) Primary tumour resection of tongue carcinoma based on response to preoperative therapy. *Int J Oral Maxillofac Surg* 31: 267-272.
- Shibuya Y, Tanimoto H, Umeda M, Yokoo S, Komori T (2004) Induction chemotherapy with docetaxel, cisplatin and 5-fluorouracil for tongue cancer. *Kobe J Med Sci* 50: 1-7.
- Olasz L, Orsi E, Markó T, Szalma J (2010) Induction chemotherapy response and recurrence rates in correlation with N0 or N+ stage in oral squamous cell cancer (OSCC). *Cancer Metastasis Rev* 29: 607-611.
- Woolgar JA, Rogers S, West CR, Errington RD, Brown JS, et al. (1999) Survival and patterns of recurrence in 200 oral cancer patients treated by radical surgery and neck dissection. *Oral Oncol* 35: 257-265.

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23. Sun LM, Leung SW, Su CY, Wang CJ (1997) The relapse patterns and outcome of postoperative recurrent tongue cancer. *J Oral Maxillofac Surg* 55: 827-831.