



Induction chemotherapy prior to surgery with or without postoperative radiotherapy for oral cavity cancer patients: Systematic review and meta-analysis



Gustavo N. Marta^{a,*}, Rachel Riera^b, Paolo Bossi^c, Lai-ping Zhong^d, Lisa Licitra^c,
Cristiane R. Macedo^e, Gilberto de Castro Junior^f, André L. Carvalho^g,
William N. William Jr.^h, Luis Paulo Kowalskiⁱ

^a Department of Radiation Oncology, Hospital Sírio-Libanês and Instituto do Câncer do Estado de São Paulo – Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

^b Brazilian Cochrane Center and Discipline of Emergency Medicine and Evidence-Based Medicine
Universidade Federal de São Paulo – Escola Paulista de Medicina (UNIFESP-PM), São Paulo, Brazil

^c Head and Neck Cancer Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

^d Department of Oral & Maxillofacial-Head & Neck Oncology, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, China

^e Brazilian Cochrane Center and Post Graduation Program of Internal Medicine Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil

^f Department of Clinical Oncology, Hospital Sírio-Libanês and Instituto do Câncer do Estado de São Paulo – Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

^g Department of Head and Neck Cancer, Hospital do Câncer de Barretos – Fundação Pio XII, São Paulo, Brazil

^h Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, USA

ⁱ Department of Head and Neck Surgery and Otorhinolaryngology, A.C. Camargo Cancer Center, São Paulo, Brazil

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Abstract Background: Locoregionally advanced oral cavity cancers are aggressive tumours with high risk of relapse after definitive treatment. This study was performed to assess the effectiveness and safety of induction chemotherapy prior to surgery for untreated oral cavity cancer patients.

Material and methods: Only prospective phase III randomised studies comparing induction chemotherapy followed by surgery with or without postoperative radiotherapy (Chemo

* Corresponding author at: Hospital Sírio-Libanês – Department of Radiation Oncology, Rua Dona Adma Jafet 91, Sao Paulo-SP 01308-050, Brazil. Tel.: +55 11 31550558; fax: +55 11 31550983.

E-mail addresses: gnmarta@uol.com.br (G.N. Marta), rachelriera@hotmail.com (R. Riera), paolo.Bossi@istitutotumori.mi.it (P. Bossi), zhonglp@hotmail.com (L.-p. Zhong), lisa.licitra@istitutotumori.mi.it (L. Licitra), vcrisrufa@uol.com.br (C.R. Macedo), gilberto.castro@usp.br (G. de Castro Junior), alopesscarvalho@uol.com.br (A.L. Carvalho), wnwillia@mdanderson.org (W.N. William Jr.), lp_kowalski@uol.com.br (L.P. Kowalski).

Prognosis
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Group) compared with surgery with or without postoperative radiotherapy (Control Group) were eligible. Two of the authors independently selected and assessed the studies regarding eligibility criteria and risk of bias.

Results: Two studies were selected. A total of 451 patients were randomly assigned to Chemo Group ($n = 226$) versus Control Group ($n = 225$). Most patients had tumours at clinical stages III/IV (89.1%). Both trials were classified as having low risk of bias. No significant overall benefit in favour of induction chemotherapy was found regarding loco-regional recurrence, disease-free survival and overall survival. A subgroup analysis of individual data from cN2 patients showed statistically significant overall survival benefit in favour of induction chemotherapy. The included studies did not directly compare toxicity between the groups and no statistical analysis was performed regarding safety outcomes.

Conclusions: Based on the available studies, induction chemotherapy when administered before surgery with curative intent did not improve clinical outcomes in locoregionally advanced oral cavity cancer patients. Clinically assessed N2 patients might benefit from induction chemotherapy.

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1. Introduction

Squamous cell carcinoma is the most common cancer that occurs in the oral cavity, with an estimated 300,000 new cases worldwide each year [1–3]. Locoregionally advanced oral cavity cancers are aggressive tumours with elevated probabilities of relapse after definitive treatment with surgery or radiotherapy (RT). Therefore, a multimodal approach combining surgery and postoperative radiotherapy or chemoradiotherapy has been proposed [4].

There are insufficient reports from phase III prospective randomised clinical studies to show an ideal approach for patients with locally advanced oral cavity malignancies. Guidelines and treatment options are based upon studies that included a majority of patients with primary cancers at other head and neck sites and also retrospective data.

In general, the primary therapy for locally advanced oral cavity squamous cell carcinoma (SCC) usually involves surgery followed by radiotherapy and chemotherapy (in the setting of high-risk pathological features such as positive resection margins, and extracapsular nodal spread). Upfront chemoradiation is an option for patients who decline surgery, have unresectable tumour and/or are medically inoperable [5]. Nevertheless, overall survival and tumour control are disappointing, because approximately 50% of the patients will die after 5 years from diagnosis, due to local and/or systemic recurrences [6]. Although improvement in surgical techniques and use of adjuvant treatments have been observed, the 5-year survival rate has not improved considerably in recent years, persisting at 55% [7,8].

New treatment strategies for locally advanced oral cavity SCC have been tested, including preoperative chemotherapy. Induction chemotherapy might reduce tumour burden, ameliorate tumour-related symptoms

and improve surgical results. Moreover, induction chemotherapy could treat micrometastatic disease early on, potentially leading to improved overall clinical outcomes [9].

This study was performed to assess the effectiveness and safety of induction chemotherapy prior to surgery for untreated oral cavity SCC patients.

2. Materials and methods

2.1. Study design

This was a systematic review carried out in accordance with The Cochrane Collaboration Handbook of Interventions Systematic Reviews [10]. The manuscript was arranged using the PRISMA Statement as reporting guidance [11].

2.2. Criteria for considering studies for this review

We included trials that assessed any induction chemotherapy strategy followed by surgery with or without postoperative radiotherapy compared with surgery with or without postoperative radiotherapy. Only randomised controlled trials were considered. Cluster or crossover designs were excluded. Oral cavity SCC patients (any age) who had not received prior treatment were eligible.

The main outcome measures were overall survival (OS), local control (LC) and toxicity as assessed at any time point after the interventions. At least one of these three outcomes should have been assessed and reported in the trial to be included in the present analysis.

2.3. Search methods for identifying studies

The electronic search was conducted with no language, publication year or publication status

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