

# HYPERSELECTIVE INTRA-ARTERIAL PREOPERATIVE CHEMOTHERAPY IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY: PRELIMINARY RESULTS<sup>1</sup>

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## SUMMARY

**Objectives:** To investigate radiological response and findings after Intra Arterial Chemotherapy (IAC) for patients with Squamous Cell Carcinoma (SCC) of the oral cavity.

**Materials and methods:** Patients received 1-2 cycles of IAC. Radiological assessment was performed on day 7 and day 21 after each cycle using CT scan and MRI.

**Results:** Six patients (median age: 52, ranging 46-60; male/female: 5/1) received 10 cycles (4 patients received 2 cycles). Primary tumors were floor of the mouth (4 patients) and oral tongue (2 patients). TNM classification was T2N0-2b in 3 patients and T4N0-1 in 3 patients. All patients had good locoregional/systemic tolerance and 3 showed clinical objective response (OR). Four patients were evaluable on both CT and MRI, 1 patient on MRI only and 1 patient did not tolerate imaging. Three patients showed OR both on CT and MRI, 1 patient showed stable disease (SD) on CT and OR on MRI and 1 patient showed SD on MRI. Contrast-enhancement of hemiperfused tongue was reported in all evaluable patients. Two patients presented intratumoral necrosis and 5 patients displayed local edema (MRI). One patient had modification of the sternocleidomastoid muscle after IAC.

**Conclusion:** Radiological modifications were observed in the infused area and correlated well with clinical response. This study is ongoing.

*Key words:* targeted chemotherapy, head and neck cancer, induction chemotherapy.

## RÉSUMÉ

**Chimiothérapie hypersélective intra-artérielle pré-opératoire des carcinomes de la cavité orale : résultats préliminaires**

**But :** évaluer la réponse en imagerie après chimiothérapie intra-artérielle en cas de carcinoma de la cavité orale.

**Matériels et méthodes :** 1 à 2 cycles de chimiothérapie ont été administrés. L'évaluation en scanner et en IRM a été faite aux 7<sup>e</sup> et 21<sup>e</sup> jours.

**Résultats :** 10 cycles ont été administrés chez six patients (âge moyen : 52 ans, extrêmes : 46-60 ; M/F : 5/1 ; chez 4 patients : 2 cycles). La localisation tumorale était le plancher buccal (n = 4) et la langue (n = 2). La classification TNM était T2N0-2b chez 3 patients et T4N0-1 chez 3 patients. La tolérance locorégionale et systémique était bonne chez tous les patients et une réponse clinique objective était observée chez 3 patients. Quatre patients étaient évaluable à la fois par scanner et IRM, un patient par IRM seulement ; le bilan d'imagerie complet n'a pu être effectué chez un patient. Une réponse objective était observée en scanner et en IRM chez 3 patients ; chez un patient notées une stabilité en scanner et une réponse objective en IRM ; chez un patient était notée une stabilité en IRM. Un rehaussement de l'hémilangue perfusée était observé chez tous les patients évaluable. Une nécrose intratumorale était notée chez deux patients et un œdème local en IRM chez 5 patients. Chez un patient, une modification du muscle sternocleidomastoidien était observée.

**Conclusion :** des modifications radiologiques sont observées dans la région perfusée, corrélées à la réponse clinique. Cette étude est en cours.

*Mots-clés :* chimiothérapie ciblée, cancers de la tête et du cou, chimiothérapie induite.

## INTRODUCTION

Squamous cell carcinoma of the oral cavity has a high rate of locoregional relapse that warrants improvement of locoregional control [4]. Intra-arterial chemotherapy delivery improves primary tumor targeting [1, 3]. New therapeutic agents such as taxanes have proven their high efficacy in head and neck squamous cell carcinoma [2]. This prompted us to combine docetaxel and cisplatin as

a preoperative intra-arterial chemotherapy as part of multimodality approach for patients with squamous cell carcinoma of the oral cavity.

The objectives were to investigate the radiological response and findings after treatment with hyperselective intra-arterial chemotherapy delivery.

## METHODS AND MATERIAL

The main patient selection criteria were: untreated T2 to T4, N0 to 2, M0 squamous cell carcinoma of the oral cavity; good Performance Status (OMS 0-1); adequate renal, hepatic and hematological functions.

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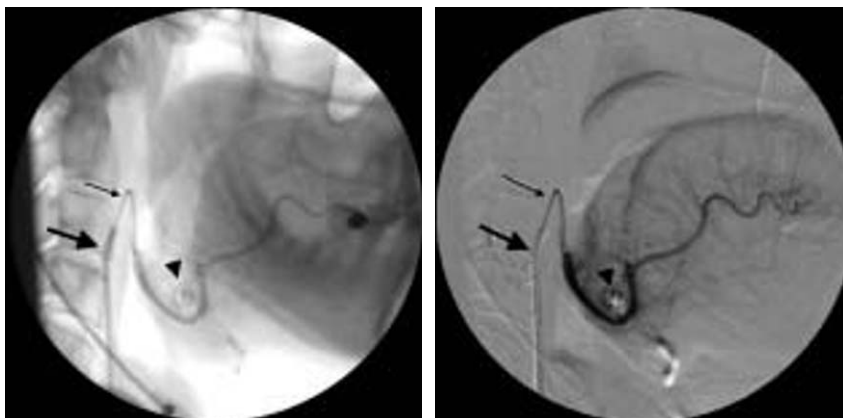


FIG. 1. – a and b) hyper-selective angiography of left tongue artery with macro catheter (large arrow) and 2.6 F micro catheter (slim arrow). Steel coils can be seen in right lingual artery (head of arrow).

FIG. 1. – a et b) arteriographie hyper-selective de l'artère linguale gauche avec un macro-catheter (flèche large) et un micro-catheter 2.6 F (flèche mince). Coils d'embolisation de l'artère linguale droite (tête de flèche).

The choice of chemotherapy was a combination of active, non vasotoxic, antitumor agents for which metabolism is not necessary, with high distribution volume and tissue penetration. So the intra-arterial treatment was: docetaxel ( $75\text{mg}/\text{m}^2$  over 60min) followed by cisplatin ( $75\text{mg}/\text{m}^2$  over 30min) on day 1, eventually repeated once between day 21-28, before surgery.

All catheterizations were performed via a transfemoral approach by the Seldinger technique. Procedure was a selective catheterization of the lingual artery ipsilateral to the tumor using a 2.6F micro-catheter inserted through a 5F guiding catheter placed in the external carotid artery to allow free flow perfusion of chemotherapy without occlusion of the lingual artery (*figure 1*). In case of medial tumor one lingual artery was occluded with steel coils and perfusion of chemotherapy was performed by the other lingual artery. Intra-arterial procedure was monitored with digital subtraction angiography.

Toxicity was evaluated weekly according to NCI-CTC criteria and antitumor activity was based on OMS criteria (bidimensional measurements).

CT scan and MRI were performed initially (within 2 weeks before treatment), and repeated between day 5-10 and day 14-28 after each cycle. Contrast-enhanced CT was performed using Hi speed CT General Electric Medical Systems (120 KV; 240 mA; 1.5 pitch; 3 mm thickness). MRI was performed with Signa Horizon LX General Electric Medical Systems (1.5 Tesla). Sequences were: T1-W, T2-W and fatsat contrast-enhanced T1-W (24cm FOV; 4mm thickness;  $384 \times 224$  matrix for T2-W and  $512 \times 256$  matrix for T1-W images).

## RESULTS

### Population

Six patients (median age: 52 years, ranging 46-60; sex-ratio male/female: 5/1) received 10 cycles (4 patients received 2 cycles and 2 patients 1 cycle). Primary tumors were located in the floor of the mouth (4 patients) and oral tongue (2 patients). TNM classification was T2N0-2b in 3 patients and T4N0-1 in 3 patients.

### Clinical toxicity and response

Locoregional tolerance was good except for 3 episodes of local pain (grade 3 in 1 patient and grade 2 in 2 patients), one episode of grade 2 local edema and 2 episodes of superficial grade 1 tongue mucosal necrosis. All patients presented expected grade 3 alopecia and only one patient showed asymptomatic grade 2 neutropenia. Among 6 treated patients, 4 patients presented clinical objective response (partial response), and 2 patients displayed stable disease.

### Radiological findings and response to the treatment

One patient was not evaluable according to radiological procedure: imaging modality was not similar before and after intra-arterial chemotherapy (MRI/CT). Moderate to important contrast-enhancement of hemiperfused tongue and local edema were reported in all evaluable patients (5 patients) (*figure 2*). Those modifications were more visible on MRI compared to CT scan. Two patients presented intratumoral necrosis (*figure 3*). One patient had probable chemotherapy-induced alteration of sternocleidomastoid muscle after IAC (*figure 4*). Four patients were evaluable on both CT and MRI. One patient was evaluable on MRI only. Three patients showed objective response both on CT and MRI, one patient showed stable disease on CT and objective response on MRI and one patient showed stable disease on MRI (*figure 5*).

## DISCUSSION – CONCLUSION

Overall, intra-arterial chemotherapy was well tolerated and radiological modifications were observed in the infused area. Despite a limited number of treated patients, early radiological evaluation correlated well with clinical response.

Preoperative intra-arterial chemotherapy (vincristine, bleomycin) has already proven his efficacy (medial survival) for floor of mouth tumors [3], however chemotherapy in this study was administrated for several days through temporal surgical catheterism. Pre-operative punctual chemotherapy by

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