

# New induction chemotherapy using intra-arterial infusion for tongue squamous cell carcinoma to avoid reconstructive surgery: A 6 case reports

### ABSTRACT

Most tongue squamous cell carcinoma (TSCC) classified as T3 require reconstructive surgery, which inevitably causes problems with oral functions. We propose new induction chemotherapy using intra-arterial infusion for TSCC classified as T3 to avoid reconstructive surgery. This chemotherapy regimen consists of intra-arterial infusion of docetaxel and cisplatin and systemic administration of 5-fluorouracil. As a result of this treatment, the therapeutic effect was a complete response in five patients and a partial response in one patient, and the overall response rate was 100%. All six patients underwent partial resection because their tumors shrank with this induction chemotherapy. In addition, adverse events of grade 3 or more did not occur in all six patients. The median follow-up duration for all patients was 34 months, and they are alive. This intra-arterial chemotherapy regimen was shown to be highly efficacious and safe.

**Keywords:** Induction chemotherapy, intra-arterial infusion, squamous cell carcinoma, tongue

### INTRODUCTION

The tongue is an extremely important tissue for swallowing, mastication, and articulation, but its function is impaired by reconstructive surgery in many cases of tongue squamous cell carcinoma (TSCC) classified as T3. We believe that achieving both functional preservation and prognosis improvement will become an important challenge for oral surgeons in the future. Therefore, induction chemotherapy should be considered as one of the treatment options to preserve function and improve prognosis.

We focused on the route of drug administration and proposed more effective induction chemotherapy for TSCC. The treatment regimen included conventional anticancer drugs. Docetaxel (DOC) and cisplatin (CDDP) were administered continuously via the artery, and 5-fluorouracil (5-FU) was administered systemically (intra-arterial DCF therapy). Then, the surgical excision range was reduced as much as possible according to the therapeutic effect to preserve the tongue functions. Here, we report six cases with TSCC classified as T3 who received intra-arterial DCF therapy, avoided reconstructive surgery, and achieved a favorable prognosis.

### CASE REPORT

We have performed intra-arterial DCF therapy for six cases of TSCC classified as T3 (five males and one female) with a median age of 71 years. As described in our previous report,<sup>[1]</sup> an intra-arterial catheter was inserted under local anesthesia via the superficial temporal artery. We performed intra-arterial DCF therapy as follows; on days one and two, 20 mg/body of DOC was continuously administered for 24 h via the artery, and on days three and four, 20 mg/body

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CDDP was also administered for three hours via the artery. In addition, from days one to five, 500 mg/day of 5-FU was continuously administered intravenously [Figure 1]. The second course of treatment was administered four weeks after the first course and was essentially completed in two cycles. Table 1 shows the clinical features of the six patients. The overall response rate (ORR) was 100%, and all six patients underwent partial glossectomy with functional preservation. The median follow-up period for six patients was 34 months (range: 19–47 months). All six patients are alive. Adverse events of grade 3 or more did not occur in all six patients [Table 2].

Day	1	2	3	4	5
	DOC	DOC	CDDP	CDDP	
	20 mg/body	20 mg/body	20 mg/body	20 mg/body	
	Continuous intra-venous infusion				
	5-FU 500 mg/body/day →				

Figure 1: The regimen of intra-arterial infusion of docetaxel and cisplatin and intravenous 5-fluorouracil

### CASE 1

A 70-year-old man presented with a lesion measuring 27 × 22 mm on the right tongue margin. Based on the MR images, the depth of invasion was diagnosed as 13 mm [Figure 2a]. Before intra-arterial DCF therapy, the markings were performed approximately 5 mm from the indurated tumor border [Figure 2b]. After two cycles of intra-arterial DCF therapy, the treatment effect achieved CR [Figure 3a]. The excisional margin was inside the marking points and included the muscle layer [Figure 3b]. It has been 42 months since the surgery, but no recurrence has been observed at the primary site.

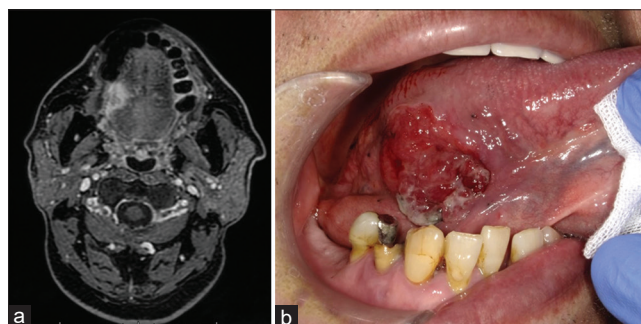


Figure 2: (a) MR image at the initial examination in case 1. (b) The markings before intra-arterial DCF therapy

### DISCUSSION

The standard treatment for resectable locally advanced TSCC is radical resection. The five-year overall survival (OS) rates according to the cancer stage of patients who underwent this standard treatment were reported to be 61–77% for stage III and 47–60% for stage IV disease.<sup>[2-5]</sup> Most of these patients also require reconstructive surgery due to extensive tissue defects,<sup>[6]</sup> resulting in functional defects and aesthetic concerns. As such, the current challenge in the treatment of locally advanced TSCC is how to concurrently improve OS and

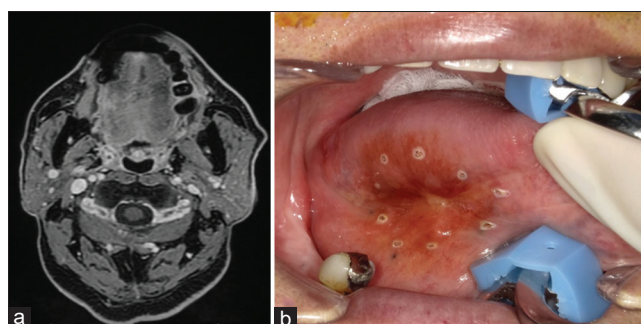


Figure 3: (a) MR image after completion of intra-arterial DCF therapy in case 1. (b) Intraoral photograph at the time of surgery. The excisional margin was inside the marking points

Table 1: Demographics and clinical features of the patients

Patient no.	1	2	3	4	5	6
Sex	M	F	M	M	M	M
Age	70	84	83	69	63	72
TNM	T3N0M0	T3N1M0	T3N0M0	T3N0M0	T3N0M0	T3N0M0
Stage	III	IVA	III	III	III	III
Treatment effects	CR	CR	CR	CR	CR	PR
Histopathological effects	Grade 2	Grade 3	Grade 2	Grade 3	Grade 3	Grade 1
Residual tumor diameter	2 mm	—	1 mm	—	—	23 mm
Surgery	Partial glossectomy	Partial glossectomy and neck dissection	Partial glossectomy	Partial glossectomy	Partial glossectomy	Partial glossectomy
Recurrence	Neck	—	—	—	—	—
Prognosis	Alive	Alive	Alive	Alive	Alive	Alive
Survival period	42 months	27 months	46 months	47 months	21 months	19 months

**Table 2: Toxicity (n=6)**

	Number of patients	
	Grade 1	Grade 2
Anemia	5	0
Neutropenia	0	0
Thrombocytopenia	5	0
Renal dysfunction	0	0
Hyponatremia	3	0
Hyperkalemia	3	0
Hepatic dysfunction	2	1
Anorexia	3	1
Nausea	0	0
Mucositis	4	1
Pain	4	1

preserve oral functions. To solve this problem, we believe that improvement of induction chemotherapy is important, but no chemotherapy has been effective so far. In two randomized studies of chemotherapy for resectable oral SCC, one with CDDP and 5-FU and the other with DOC, CDDP, and 5-FU, CR rates were 33% for T2–T4 and 8.1% for T1–T4, respectively. Although both studies failed to show statistically significant improvement in survival, their results demonstrated that clinical and pathological responses are significant prognostic factors, suggesting that the downstaging of a tumor by induction chemotherapy may lead to less demolition surgery.<sup>[7,8]</sup>

We focused on the route of administration to enhance the synergistic effect of drugs and proposed intra-arterial chemotherapy using DOC, CDDP, and PEP combined with systemic chemotherapy using 5-FU for locally advanced oral SCC.<sup>[1]</sup> The results showed a high therapeutic effect with an ORR of 99.3%. Although this regimen has very little hematotoxicity, Grade 3 mucositis occurred frequently (46.8%), and it was necessary to manage the accompanying pain and anorexia. We removed PEP from the regimen in this study, five out of six patients achieved clinical CR (83.3%), and the ORR for all patients was 100%. This indicates that a sufficient effect can be obtained even without PEP. Under standard treatment, all six cases shown in this report would have required reconstructive surgery. However, with effective intra-arterial DCF therapy, all patients were spared demolition surgery. Moreover, no grade 3 or higher adverse events occurred. There was no mucositis nor difficulty in controlling pain or diet during treatment. The intra-arterial DCF therapy has other benefits besides the combination of drugs. That is, the catheter was placed retrogradely. By indwelling the catheter retrograde via the superficial temporal artery, the catheter can be left in place for a long period, and multiple anticancer drugs can be administered continuously or frequently.<sup>[9]</sup> This is an advantage not seen when using the Seldinger technique via the femoral artery. We believe that intra-arterial DCF therapy is a promising treatment for the functional preservation of TSCC.

## CONCLUSION

We showed higher therapeutic effects by devising the drug combination of three conventional anticancer drugs that have been used for oral cancer. The treatment strategy described here can downgrade the stage of T3 TSCC and could be a promising therapy to achieve both functional preservation and good prognosis.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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