

재발성 두경부암종의 항암화학요법

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1. Introduction

1) Prognosis of advanced squamous cell carcinoma of the head and neck(HNSCC)

- (1) 5-year survival $\leq 30\%$
- (2) failure pattern
 - a. local recurrences : most common(60-70%)
 - b. distant metastases : 20-30%
 - c. second primary tumors : 10 to 20%
- (3) poor prognosis with locally recurrent or metastatic disease : median survival of 5mos

2) Approach to recurrent HNSCC : multidisciplinary

- (1) Prognostic factors of recurrent HNSCC
 - a. Performance status and extent of disease recurrence
 - b. Previous treatment
- (2) Role of chemotherapy in recurrent and/or met-

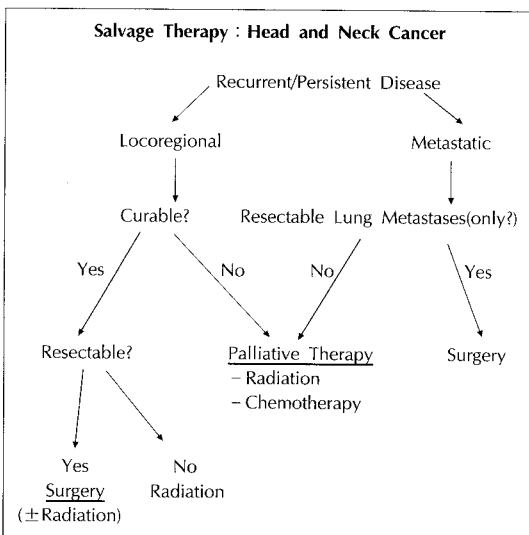


Fig. 1. Algorithm for salvage therapy of advanced head and neck cancer.

Table 1. Influence of previous treatment and site of disease on chemotherapy outcome

Site of disease and Previous therapy	No.	CR(%)	RR(%)
Locoregional after RT+/- Surgery	36	0	3(8)
Locoregional+metastases after RT+/- Surgery	17	0	2(12)
Metastasis after RT+/- Surgery	26	2(8)	12(46)
Previously untreated(all metastatic)	11	3(27)	8(73)
Total	90	5(5.6)	25(28)

astatic HNSCC

a. palliative i.e., improvement of disease-related symptoms(pain, dysphagia, speech function, etc.) cf. QL (Quality of life) issues

b. curative ; 20% longterm survival with concomitant chemoradiotherapy

2. Chemotherapy in the treatment of recurrent and/or metastatic head and neck cancer

1) Single-agent chemotherapy

- (1) Methotrexate
- (2) Cisplatin

Table 2. Single-agent activity in recurrent or metastatic head and neck cancer

Agent	Average response rate(range) [%]
Anthracyclines	13(0-44)
Bleomycin	21(6-45)
Carboplatin	21(14-27)
Cisplatin	28(8-41)
Cyclophosphamide	36
Fluorouracil	15(0-33)
Ifosfamide	37(6-52)
Methotrexate	30(8-57)
Vinblastine	29
Vinorelbine	22

*Single agent chemotherapy rarely results in clinical complete responses(CRs) and is used exclusively for palliation in recurrent or metastatic HNSCC.

- 2) **Combination chemotherapy**
- (1) Principles
- a. different mechanisms of action
- b. different toxicity profiles
- (2) Combinations without Cisplatin
- (3) Cisplatin-based combinations
- a. Before the 1980s
- b. Kish et al(1984) : 70% RR(27% CR) in 30 patients treated with cisplatin and 96-hour infusion of fluorouracil every 3 weeks
- 3) **Randomized studies comparing single-agent and multiple-drug chemotherapy**

- 4) **New agents**
- 5) **New combinations**
- (1) Biomodulation of 5-FU with calcium folinate (Leucovorin) ; FL, PFL
- (2) Cisplatin and Carboplatin
3. **Concomitant chemoradiotherapy for previously irradiated HNSCC**
- 1) Haraf et al., Univ. of Chicago(1996)
: 45 patients with unresectable locally or regionally recurrent disease
-5-FU+hydroxyurea + / - cisplatin and concomitant

Table 3. Activity of non-cisplatin-containing regimens in recurrent or metastatic HNSCC

Reference	Regimen	No. of patients	Response rate(%)
Clavel et al.	Mtx-Bleo-Vcr	92	28
Jacobs	Mtx-FU	30	16
Pitman et al.	Mtx-FU	11	100
Price et al.	Vcr-Bleo-Mtx-FU-Dox	85	67
Tannock et al.	Bleo-Vcr-Mtx-FU-Hu-Mp	57	11
Thatcher et al.	Dox-FU-Bleo-Mtx	25	40
Turner & Waed	Bleo-Vcr-Mtx	46	67
Wittes et al.	Cyclo-Dox-Mtx-Bleo	26	35
Woods et al.	Mtx-Vcr-Bleo	33	24

Table 4. Activity of cisplatin-containing regimens in recurrent or metastatic HNSCC

Author	Regimen	No. of patients	Response rate(%)
Caradonna et al.	CDDP-Bleo-Mtx	19	74
Creagan et al.	CDDP-Dox-Cyclo	25	64
Ervin et al.	CDDP-Bleo-Mtx	11	100
Jacobs	CDDP-Mtx	12	24
Perry et al.	Vb-Bleo-CDDP	42	45
Rozenzweig et al.	CDDP-Mtx-Bleo-Vcr	72	50
Vogl & Kaplan	CDDP-Mtx-Bleo	31	61

Table 5. Activity of cisplatin-fluorouracil(CDDP-FU) combination in recurrent or metastatic HNSCC

Reference	Treatment	No. of patients	Response rate(%)		
			PR	CR	Overall
Kish et al.	CDDP 100mg/m ² d1 FU 1g/m ² /24h d1-4	30	43	27	70
Amrein & Weitzam	CDDP 80mg/m ² d1 FU 800mg/m ² /24h d2-6	39	28	18	46
Creagan et al.	CDDP 100mg/m ² d1 FU 1g/m ² /24h d1-4	20	25	0	25
Dasmahaparta et al.	CDDP 100mg/m ² d1 FU 1g/m ² /24h d1-5	18	11	0	11
Rowiand et al.	CDDP 100mg/m ² d1 FU 1g/m ² /24h d1-5	21	47	24	71

Abbreviations : CR=complete response ; d=day(s) ; PR=partial response.

Table 6. Randomized trials of single-agent versus multiple agent chemotherapy in recurrent or metastatic HNSCC

Reference	Treatment	No. of patients	Response rate(%)(percentage CR)	Median survival(mo.)
Clavel et al.	CDDP	113	15(2.5)	6.5
	CDDP-FU	108	31a(1.7)	6.5
	CABO	126	34a(9.5)	6.5
Forastiere et al.	Mtx	88	10(2)	5.6
	CDDP-FU	87	32a(6)	5
	Carbo-JU	86	21a(2)	6.6
Jacobs et al.	CDDP	83	17(4)	6
	FU	83	13(2)	6
	CDDP-FU	79	32a(6)	6
Stell	Mtx	50	12(0)	6
	CDDP	50	26(2)	7
	Mtx-CDDP	50	22(0)	6
	CDDP-FU	50	24(6)	7
Vogl et al.	Mtx	83	35(8)	5.6
	CDDP-Mtx-Bleo	80	48a(16)	5.6
Williams et al.	Mtx	98	16(0)	6
	CDDP-Vb-Bleo	92	24(1)	6

A p < 0.05 versus single agent therapy.

*higher response rates, but no influence on survival!

Table 7. New agents in HNSCC

Chemotherapy	CR+PR(%)
Paclitaxel	40
Docetaxel	31
Ifosfamide	26
Topotecan	22
Vinorelbine	22
Gemcitabine	13

cf. ECOG : Phase III trial of High dose vs Low dose Paclitaxel with Cisplatin

– no advantage for high dose Paclitaxel(Forastiere et al. Proc Am Soc Clin Oncol 1997 [abstract])

cf. Phase II evaluation of 96 hour paclitaxel infusion (Feb. 1997 by ECOG)

cf. A randomized phase III evaluation of Paclitaxel+Cisplatin versus Cisplatin+5-FU(March 1997 by ECOG)

radiotherapy

at 5 years, Overall survival 14.6%

Progression-free survival 13.5%

Local/regional control 20%

2) higher response rate with approx. 20% of longterm survival-cure of some patients!

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