The impact of dysgeusia on treatment exposure of adjuvant S-1 therapy after curative gastrectomy

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Background

- Although patients who are treated with chemotherapy sometimes complain dysgeusia, medical staff often regard it as inevitable adverse event and tend to ignore it¹⁾.
- The mechanism of dysgeusia by chemotherapy and its onset are not clear, therefore, adequate supportive care for dysgeusia is not established²⁾.
- There are several reports about the impact of dysgeusia on quality of life (QOL) , however, that on treatment exposure is rarely reported^{1,3,4)}.
- S-1 is an oral anticancer drug and is standard adjuvant treatment for gastric cancer in Japan.
- The continuation of adjuvant S-1 is thought to be improving survival of patients who received curative gastrectomy.
- There are few reports about the impact of dysgeusia on treatment outcome⁵⁾.

Aim

- The aim of this study is to investigate the impact of dysgeusia on treatment outcome.

Methods

The subjects were patients who received S-1 as adjuvant therapy after curative gastrectomy at Shizuoka Cancer Center between January 2007 and September 2013.

Treatment schedule (Adjuvant S-1 treatment)
S-1 was administered twice a day for 28 days followed by a 14-days rest.

- Inclusion criteria were as follows:
- No history of S-1 monotherapy
 - Histologically diagnosed adenocarcinoma
 - Stage: pStage II/III (Japanese Classification of Gastric Cancer 14th Edition)
 - Curative gastrectomy with D2 dissection
 - Age: 20-80 years
 - ECOG PS: 0-1

Results

Patients’ Characteristics

	With dysgeusia N = 60	Without dysgeusia N = 154	<i>P</i> value
Median age (years)	66 (41–77)	67 (38–79)	0.894 [#]
Sex Male/Female	41/19	109/45	0.742 [*]
PS ⁺ 0/1/2/3	42/18/0/0	108/46/0/0	1.000 [*]
Stage II/IIIA/IIIB	33/22/5	59/62/33	0.032[*]
Pathology Undifferentiated/Differentiated	35/25	84/70	0.648 [*]
Surgical procedure Total gastrectomy/ Distal gastrectomy	16/44	75/79	0.004[*]

+, ECOG Performance Status #; Mann-Whiteny *U* test, *, Fisher’s exact test,

Incidences of dysgeusia (N=214)

Grade	N	%
1	46	21.5%
2	14	6.5%

Treatment completion rate (N=214)

With dysgeusia N = 60	Without dysgeusia N = 154	<i>P</i> value
39 (65.0%)	116 (75.3%)	0.173

Fisher’s exact test

Two patients were discontinued due to dysgeusia.

Time to dysgeusia

Incidences of adverse events

	With dysgeusia N = 60		Without dysgeusia N = 154		<i>P</i> value
	Any Grade (%)	Grade 3/4 (%)	Any Grade (%)	Grade 3/4 (%)	
Leukopenia	37 (61.7)	0 (0)	88 (57.1)	4 (2.6)	0.646
Neutropenia	39 (65.0)	7 (11.7)	98 (63.6)	25 (16.2)	0.876
Anemia	58 (96.7)	2 (3.3)	147 (95.4)	9 (5.8)	1.000
Thrombocytopenia	19 (31.7)	1 (1.7)	32 (20.8)	1 (0.6)	0.109
Anorexia	47 (78.3)	7 (11.7)	94 (61.0)	9 (5.8)	0.017
Nausea	21 (35.0)	1 (1.7)	52 (33.7)	1 (0.6)	0.874
Vomiting	8 (13.3)	0 (0)	14 (9.1)	0 (0)	0.452
Mucositis	29 (48.3)	1 (1.7)	51 (33.1)	1 (0.6)	0.042
Diarrhea	30 (50.0)	4 (6.7)	73 (47.4)	7 (4.5)	0.762
Fatigue	41 (68.3)	3 (5.0)	85 (55.2)	4 (2.6)	0.090
Rash	17 (28.3)	0 (0)	35 (22.7)	2 (1.3)	0.382
Pigmentation	24 (40.0)	0 (0)	50 (32.3)	1 (0.6)	0.338
Hand–Foot syndrome	7 (11.7)	1 (1.7)	20 (13.0)	1 (0.6)	1.000
Watery eyes	18 (30.0)	1 (1.7)	46 (30.0)	12 (7.8)	0.167

CTCAE v4.03 Fisher’s exact test

Recurrence-free survival rate (RFS)

Overall survival rate (OS)

Discussion

- The incidence of dysgeusia was 28.0%, which tends to be higher than that previously reported^{5,6)}. In addition, 2 patients were discontinued from the treatment due to dysgeusia.
- Treatment completion rate of patients without dysgeusia tended to be higher than those with dysgeusia. On the other hand, RFS and OS of patients without dysgeusia is worse than those with dysgeusia. The reason for this is thought that it might be the insufficient evaluation of dysgeusia. Besides there might be many latent cases were mixed.
- There is a large difference in time to onset of dysgeusia.

Conclusions

- The completion rate of planned adjuvant S-1 therapy is lower in dysgeusia group than non-dysgeusia group.
- This study suggests the management of dysgeusia may contribute for the continuation of S-1 as adjuvant therapy.

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