Biweekly Docetaxel and S-1 Combination Chemotherapy as First-line Treatment for Elderly Patients with Advanced Gastric Cancer

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Abstract. *Background/Aim: This study assessed the toxicity and activity of biweekly docetaxel and S-1 combination therapy in elderly patients with advanced gastric cancer. Patients and Methods: One-hundred and thirteen patients were enrolled: 35 were 75 years old or more. The objective response rate, toxicity, progression-free survival (PFS), and overall survival (OS) were compared. Results: Dose reduction was significantly frequent in the elderly group (24/35 versus 25/78, p<0.001). The overall response rate was 54.9%. Out of these, 18 (15.9%) underwent gastrectomy (13 R0 gastrectomy). The median OS was 17.3 months and the median PFS was 8.0 months. Neutropenia was the most frequently observed hematological toxicity at grade 3 and 4 (34.5%), followed by leukopenia (24.8%). Most non-hematological toxicities were of grade 1 or 2. There were no significant differences in overall response rate, median OS, median PFS, or toxicities between the two groups. Conclusion: This combination offers favourable survival benefits with controllable tolerance for therapy of AGC in the elderly.*

Gastric cancer is one of the most common causes of cancer-related deaths worldwide, although its incidence has recently decreased (1, 2). Although the prognosis of early gastric cancer is satisfactory (3, 4), the one of advanced gastric cancer (AGC) remains poor (5, 6).

Several trials have shown that combination chemotherapy regimens for AGC achieve sufficient response rates and satisfactory survival times with acceptable adverse toxicities (7-10). Out of these, S-1, an oral anticancer drug consisting of a mixture of tegafur and the modulators 5-choloro-2,4-dihydroxypyridine and potassium oxonate in a molar ratio of 1:0.4:1, plays an important role in the treatment of AGC (11). S-1 monotherapy and irinotecan/cisplatin combination therapy achieved a significantly better response rate and progression-free survival (PFS) rate than 5-fluorouracil (5-FU) in the JCOG9912 trial (12), while the SPIRITS trial demonstrated a significant survival benefit of S-1/cisplatin combination therapy compared with S-1 monotherapy (13).

Docetaxel is an anti-microtubule agent that enhances the polymerization of tubulin monomers into stable microtubules and inhibits microtubule de-polymerisation (14). Many studies have reported its clinical activity and acceptable toxicity both with and without other agents in the treatment of AGC (15-17). In our previous study, biweekly docetaxel/S-1 combination therapy showed promising results in patients with AGC (18, 19).

Both agents of docetaxel/S-1 combination therapy have been shown to be efficacious in the treatment of gastric cancer, using different mechanisms of anticancer action that work synergistically. The toxicities of each agent have also been shown to differ, with neutropenia most commonly being caused by docetaxel and gastroenterological toxicities being induced by S-1. However, the feasibility of this combination therapy has not been clarified for elderly patients. In this study, therefore, we compared the efficacy and toxicity of this therapy for AGC in patients aged 75 years or more and in patients less than 75 years of age.

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Patients and Methods

Eligibility. Patients with histologically-proven AGC (curatively unresectable, inoperable or recurrent) were enrolled in this study. Inclusion criteria were as follows: at least one measurable lesion, no prior chemotherapy, age 20 years or more, Eastern Cooperative Oncology Group performance status (PS) <2, estimated life expectancy ≥3 months, adequate liver function (total serum bilirubin <1.5 mg/dl and transaminase no more than twice the normal upper limit for our institution), adequate renal function (serum creatinine within the normal upper limit for our institution, blood urea nitrogen ≤25 mg/dl and 24 h creatinine clearance >50 ml/min), adequate hematopoietic function white blood cell (WBC) count 4,000-12,000/mm^3, absolute neutrophil count >2,000/mm^3, platelet count ≥10×10^4/mm^3 and hemoglobin level ≥9.5 g/dl], and adequate cardiac and pulmonary function. All patients provided written informed consent for participation in this study.

The major exclusion criteria were as follows: brain metastasis, symptomatic infectious disease, past history of drug allergy, symptomatic peripheral neuropathy or edema, other active malignancies, pregnancy or breast feeding, uncontrolled diabetes mellitus, uncontrolled mental illness and gastrointestinal hemorrhage.

This study was approved by the Institutional Review Board of each institution.

Study design and treatment. The primary end point of this study was the objective response rate after two courses of treatment. The secondary end points were toxicity, overall survival (OS) and PFS.

S-1 was administered orally twice daily for one week, according to body surface area (BSA) as follows: BSA <1.25 m^2, 80 mg/day; 1.25 ≤BSA <1.50 m^2, 100 mg/day; 1.50 m^2 ≤BSA, 120 mg/day. This was followed by a drug-free interval of one week. Docetaxel (40 mg/m^2) was administered intravenously on days 1 and 15. Docetaxel was diluted in 100 ml normal saline and infused for 1 h. Dexamethasone (8 mg) was infused 1 h prior to the administration of docetaxel, and a further 4 mg dexamethasone was administered orally for two days to reduce the risk of developing a hypersensitivity reaction. Each course lasted for one month. Treatment was continued until disease progression, patient refusal or unacceptable toxicity occurred.

Dose modification. Toxicity was graded for each cycle according to the National Cancer Institute Common Toxicity Criteria (version 3) (20). Treatment was discontinued if recovery from toxicity did not occur within seven days.

Treatment was continued at the same dose of docetaxel if patients experienced grade 1 toxicities or other non-serious toxicities. For all other treatment-related toxicities of grade 2 intensity or higher, dose modification of docetaxel was implemented as follows: no dose reduction was made after the first appearance of a grade 2 toxicity, but administration was interrupted until the toxicity recovered to grade 0 or 1. Interruption was allowed twice (in two weeks) within a course. Dose reduction of 5 mg/m^2 was necessary after dose-limiting toxicity (DLT) appeared grade 4 hematological toxicity, grade 3 neutropenia with fever, grade 4 thrombocytopenia, and grade 3 or 4 non-hematological toxicities. Moreover, dose reduction was required after the previous interruption. If adverse events did not improve to grade 0 or 1 after three interruptions (in three weeks), the patient was excluded from the study.

The use of granulocyte colony-stimulating factor (G-CSF) was permitted if a patient developed grade 4 neutropenia. Antiemetic treatment was also permitted under the direction of the physician.

The tumor response was assessed according to the Response Evaluation Criteria in Solid Tumours version 1.0 (RECIST) after two courses of treatment (21). The response status of measurable lesions during treatment was evaluated by a barium-meal study, endoscopy, ultrasonography, computed tomography or magnetic-resonance imaging. These evaluations were repeated after one course if there was a partial response (PR). Cytology or diagnostic laparoscopy was additionally employed to assess non-measurable lesions, such as ascites.

Statistical analysis. Data were analyzed using the SPSS statistical software program (SPSS Inc., Chicago, IL, USA). Patients' characteristics were compared using the two-tailed Fisher's exact test or the Chi-square test with Yates correction. The Student's *t*-test was used to evaluate continuous variables and data are presented as the mean±standard deviation (SD). Survival probabilities were estimated using the Kaplan Meier method and compared with the log-rank test. Multivariate survival analysis and calculation of hazard ratios (HR) were performed using a Cox proportional regression hazard model including all covariates that were significant on univariate analysis. Probability (*p*) values were considered to be statistically significant at the <0.05 level.

The mean±standard deviation (SD) follow-up period was 16.5±10.3 months.

Results

Patients' characteristics. In total, 113 patients with AGC were enrolled in this study between July 2007 and March 2012. Of these, 35 were 75 years old or more and 78 patients were younger than 75 years. The patient characteristics were compared between the two groups and are listed in Table I. All patients had locally advanced or metastatic lesions, with the lymph nodes, peritoneum, liver and other organs as the predominant sites of metastases. There were no significant differences in gender, ECOG performance status, site of primary tumor, macroscopic type, tumor diameter, depth of invasion, lymph node metastasis, histological type, clinical stage, disease status, metastatic sites, number of involved organs, or prior treatment between the elderly group and the non-elderly group.

Treatment administration. The 113 patients were administered a total of 562 courses, with a median of four (range, 2-16). The docetaxel dose was reduced to 35 mg/m^2 in 24 patients (21.2%), and stepwise to 30 mg/m^2 in 25 patients (22.1%), according to the dose-reduction criteria (30 patients had recurring grade 2 or 3 neutropenia, 11 patients had grade 4 neutropenia, six patients had grade 3 anorexia, and two patients had grade 3 neutropenia with fever). There was a significant difference in the incidence of dose reduction between the elderly group and the non-elderly group (24/35 *versus* 25/78, $p<0.001$). Moreover, there was a significant

Table I. *Patients' characteristics*.

Characteristic	Elderly (n=35)	Non-elderly (n=78)	*p*-Value
Age (years)			
Mean	77.8±3.6	64.6±7.9	<0.001
Range	75-91	37-74	
Gender			0.656
Male	24 (68.6)	57 (73.1)	
Female	11 (31.4)	21 (26.9)	
ECOG performance status			0.761
0	30 (78.9)	70 (89.7)	
1	5 (21.1)	8 (10.3)	
Glasgow prognostic score			0.861
0	16 (45.7)	33 (42.3)	
1	10 (28.6)	21 (26.9)	
2	9 (25.7)	24 (30.8)	
Neutrophil lymphocyte ratio			0.208
<5.0	24 (68.6)	62 (79.5)	
>5.0	11 (31.4)	16 (20.5)	
Site of primary tumor			0.201
Upper third	8 (22.9)	34 (43.7)	
Middle third	7 (20.0)	10 (12.8)	
Lower third	11(31.4)	20 (25.6)	
Entire	9 (25.7)	14 (17.9)	
Macroscopic type			0.050
Well-defined	18 (51.4)	25 (32.1)	
Ill-defined	17 (48.6)	53 (67.9)	
Tumor diameter (mm)			0.738
<5.0	4 (11.4)	13 (16.7)	
≥5.0 to <10	23 (65.7)	50 (64.1)	
≥10	8 (22.9)	15 (19.2)	
Depth of invasion			0.633
T1,2	2 (5.7)	6 (7.7)	
T3	22 (62.9)	54 (69.2)	
T4	11 (31.4)	18 (23.1)	
Lymph node metastasis			0.869
N0	2 (5.7)	4 (5.1)	
N1	8 (22.9)	17 (21.8)	
N2	12 (34.3)	33 (42.3)	
N3	13 (37.1)	24 (30.8)	
Histological type			0.309
Differentiated	20 (57.1)	35 (44.9)	
Undifferentiated	15 (42.9)	43 (55.1)	
Stage			0.999
III	7 (20.0)	15 (19.2)	
IV	28 (80.0)	63 (80.8)	
Disease status			
Newly-diagnosed	33 (94.3)	72 (92.3)	
Recurrent	2 (5.7)	6 (7.7)	
Locally advanced disease	8 (22.9)	20 (25.6)	
Metastatic disease	27 (77.1)	58 (74.4)	
Metastatic sites			0.238
Lymph nodes	32 (91.4)	67 (85.9)	
Peritoneum	8 (22.9)	29 (37.2)	
Hematogenous	14 (40.0)	21 (26.9)	
No. of involved organs			0.924
1	1 (2.9)	3 (3.8)	
2	18 (51.4)	42 (53.8)	
3	16 (45.7)	33 (42.3)	
Prior treatment			0.999
None	33 (94.3)	72 (92.3)	
Gastrectomy	2 (5.7)	6 (7.7)	

ECOG: Eastern Cooperative Oncology Group.

Table II. *Treatment-related factors*.

Characteristic	Elderly (n=35)	Non-elderly (n=78)	*p*-Value
Number of administered courses	5.1±2.8	4.9±2.9	0.299
Any dose reduction			<0.001
Presence	24 (68.6)	25 (32.1)	
Absence	11 (31.4)	53 (67.9)	
Assessment of response after 2 courses			0.648
PR/CR	21 (60.0)	41 (52.6)	
SD	11 (31.4)	26 (33.3)	
PD	3 (8.6)	11 (14.1)	
Gastrectomy after chemotherapy			0.579
Presence	4 (11.4)	14 (17.9)	
Absence	31 (88.6)	64 (22.1)	
Second-line chemotherapy			0.454
Presence	18 (51.4)	42 (53.8)	
Absence	17 (48.6)	36 (46.2)	
Third-line chemotherapy			0.174
Presence	3 (8.6)	16 (20.5)	
Absence	32 (91.4)	62 (79.5)	
Reason of discontinuation			0.814
Tumor progression	24 (68.6)	63 (80.8)	
Gastrectomy	3 (8.6)	7 (9.0)	
Personal convenience	0 (09	1 (1.2)	

PR: Partial response, CR: complete response, SD: stable disease, PD: progressive disease.

difference in the degree of dose reduction (35 mg/m^2/30 mg/m^2) between the two groups (18/6 *versus* 16/9, $p<0.001$).

Treatment administration was delayed in 97 (17.3%) out of the 562 courses, with the course intervals being delayed for more than 7 days. The major causes of delayed administration were treatment-related toxicity, including neutropenia for 76/562 (13.5%) courses and anorexia for 18/562 (3.2%) courses, as well as personal convenience for 3/562 (0.5%) courses. There was no significant difference in the cause of delayed administration (neutropenia/anorexia/personal convenience) between the elderly group and the non-elderly group (58/14/2 *versus* 18/4/1, $p=0.916$). The reasons for discontinuations of the first-line treatment were tumor progression (87/113 patients, 77.0%), surgery with curative intent (10/113 patients, 8.9%) and personal convenience (1/113 patients, 0.9%) There was no significant difference in the distribution of the reasons between the two groups (Table II).

Response and survival analysis. Out of the 113 patients who were assessable for tumor response and survival, 61 (54.0%) showed a PR and one (0.9%) showed a complete response (CR), resulting in an overall response rate of 54.9% [95% confidence interval (CI)=45.7-64.0%]. A CR was observed

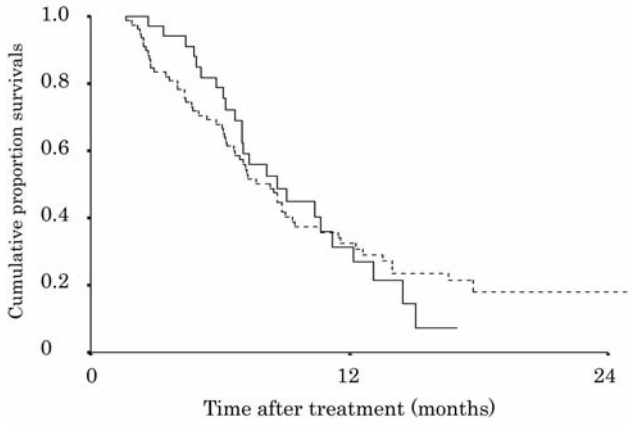

Figure 1. *Progression-free survival time according to age. No significant differences were observed in the median survival time between the elderly group (solid-line) and the non-elderly group (dotted-line) (8.0 months versus 9.0 months, p=0.965).*

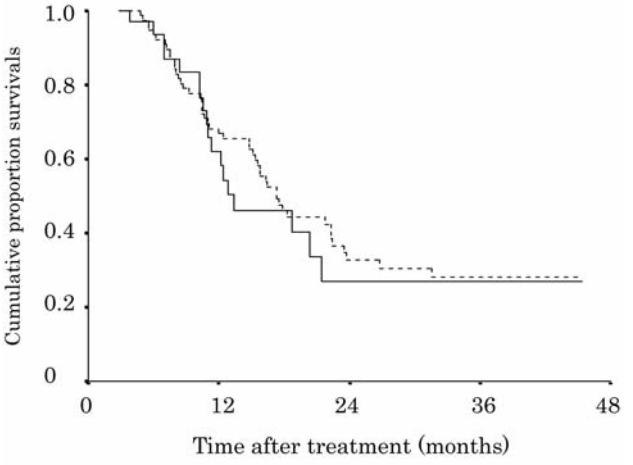

Figure 2. *Overall survival time according to age. No significant differences were observed in the median survival time between the elderly group (solid-line) and the non-elderly group (dotted-line) (13.4 months versus 17.3 months, p=0.502).*

in one patient with multiple lung metastases after curative gastrectomy. Overall, the disease was stable in 37 patients (32.7%) and progressive in 14 (12.4%) at the end of the two courses. There was no significant difference in the overall response rate between the elderly group and the non-elderly group (60.0% *versus* 52.6%), p=0.648). The overall response rates according to the metastatic site were as follows: 23/38 (60.5%) for peritoneal metastases, 21/33 (63.6%) for liver metastases and 59/107 (55.1%) for lymph-node metastases. The overall response rates according to thehistological type were as follows: 35/55 (63.6%) for differentiated-type adenocarcinoma and 27/58 (46.6%) for undifferentiated-type adenocarcinoma. The overall response rates according to the number of organs involved were: 2/4 (50.0%), 32/60 (53.3%) and 28/49 (57.1%) in patients with one, two and three involved organs, respectively.

A total of 60 patients (53.1%) received second-line chemotherapies: 52 irinotecan-based, seven S-1-based, and five paclitaxel-based regimens. A total of 19 of these patients also received third-line chemotherapies, all of which were paclitaxel-based regimens. There were no significant differences in the incidence of second-line and third-line treatments between the two groups (Table II).

The median PFS was 8.0 months (95% CI=7.0-10.0 months). There was no significant difference in the median PFS between the two groups (9.0 months *versus* 8.0 months, p=0.965) (Figure 1). The median OS was 17.3 months (95% CI=14.7-19.8 months) with a 1-year survival rate of 65.5%. There was no significant difference in the median OS between the elderly group and the non-elderly group (13.4 months *versus* 17.3 months, p=0.502) (Figure 2). Survival time in patients administered second-line treatments were calculated. The median survival time (MST) after administration of second-line treatment was 10.0 months (95% CI=7.0-13.0 months) in 60 patients. There was no significant difference in the MST after second-line treatments between the two groups [7.0 months (95% CI=3.0-12.0 months) *versus* 10.0 months (95% CI=7.0-13.0 months), p=0.7201] (Figure 3).

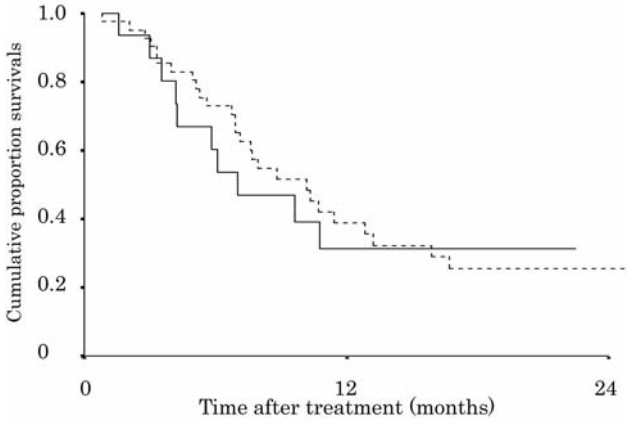

Figure 3. *Median survival time after administration of second-line treatment according to age. There was no significant difference in the MST after second-line treatments between the elderly group (solid-line) and the non-elderly group (dotted-line) (7.0 months versus 10.0 months, p=0.7201).*

Prognostic factors. Cox proportional hazard regression model for PFS revealed that assessment of responses after two courses, Glasgow prognostic factor (GPS), and number of courses independently influenced adverse prognosis. Moreover, Cox proportional hazard regression model for OS showed that third-line chemotherapy, assessment of

Table III. *Cox proportional regression hazard model for progression-free survival and overall survival.*

Variable	χ^2	Hazard ratio (95% CI)	*p*-Value
Progression-free survival			
Assessment of responses after 2 courses	47.624		0.001
SD/PR,CR		1.306 (0.786-2.171)	
PD/PR,CR		17.485 (7.695-39.734)	
GPS	18.355		0.001
1/0		1.688 (0.959-2.971)	
2/0		3.587 (1.995-6.450)	
Number of course	6.594		0.037
5 to 8/2 to 4		0.968 (0.590-1.587)	
9 or more/2 to 4		0.317 (0.130-0.769)	
Overall survival			
Third-line chemotherapy	10.413		0.001
Absence/presence		0.277 (0.127-0.604)	
Assessment of responses after 2 courses	12.240		0.002
SD/PR,CR		1.388 (0.805-2.394)	
PD/PR,CR		3.900 (1.819-8.362)	
Gastrectomy after chemotherapy	9.757		0.002
Yes/no		0.144 (0.043-0.486)	
GPS	9.331		0.009
1/0		0.755 (0.396-1.438)	
2/0		1.882 (1.039-3.407)	

95% CI: 95% Confidence interval; SD: stable disease, PR: partial response, CR: complete response, PD: progressive disease; GPS: Glasgow prognostic score

responses after two courses, gastrectomy after chemotherapy and GPS were independent prognostic factors. However, age was not found to be an independent prognostic factor in either analysis (Table III).

Toxicity. All patients were assessable for toxicity. Among the hematological toxicities at grade 3 and 4, neutropenia was most frequently observed (39 patients, 34.5%), followed by leukopenia (28 patients, 24.8%). Ten patients were classed as having grade 4 neutropenia. All patients were manageable by administering G-CSF, followed by dose reduction according to the criteria described above. Most non-hematological toxicities were of grade 1 or 2, with the exception of four patients who had grade 3 anorexia. The most common non-hematological toxicities were alopecia (85 patients, 75.2%), anorexia (53, 46.9%), nausea (45, 39.8%) and general fatigue (38, 33.6%). Other non-hematological toxicities were less frequent (Table IV), and all were controllable with optimal treatments.

Table IV. *Toxicity.*

Toxicity	No. of patients (%)	
	Grade 1-2	Grade 3-4
Hematological		
Leukopenia	44 (38.9)	28 (24.8)
Neutropenia	33 (29.2)	39 (34.5)
Anemia	15 (13.3)	0
Thrombocytopenia	2 (1.8)	0
Non-hematological		
Alopecia	85 (75.2)	-
Anorexia	53 (46.9)	6 (5.3)
Nausea	45 (39.8)	0
General fatigue	38 (33.6)	0
Skin	18 (15.9)	0
Vomiting	16 (14.2)	0
Diarrhea	15 (13.3)	0
Peripheral neuropathy	9 (8.0)	0
Liver dysfunction	8 (7.1)	0

Table V. *Toxicity according to age.*

Toxicity	Grade 1-2		Grade 3-4	
	Elderly n (%)	Non-elderly n (%)	Elderly n (%)	Non-elderly n (%)
Hematological				
Leukopenia	16 (45.7)	28 (35.9)	10 (28.6)	18 (23.1)
Neutropenia	16 (45.7)	17 (21.8)	13 (37.1)	26 (33.3)
Anemia	5 (14.3)	10 (12.8)	0	0
Thrombocytopenia	1 (2.9)	1 (1.3)	0	0
Non-hematological				
Alopecia	27 (77.1)	58 (74.4)	-	-
Anorexia	20 (57.1)	33 (42.3)	3 (8.6)	3 (3.8)
Nausea	15 (42.9)	30 (38.5)	0	0
General fatigue	16 (45.7)	22 (28.2)	0	0
Skin	6 (17.1)	12 (15.4)	0	0
Vomiting	5 (14.3)	11 (14.1)	0	0
Diarrhea	5 (14.3)	10 (12.8)	0	0
Peripheral neuropathy	3 (8.6)	6 (7.7)	0	0
Liver dysfunction	2 (5.7)	6 (7.7)	0	0

The comparison of toxicities according to age is shown in Table V. Among the hematological toxicites, grade 1 or 2 neutropenia was significantly frequent in the elderly group (45.7% *versus* 21.8%, $p=0.0097$), whereas the frequency of other grade 1 or 2 hematological toxicities did not differ between the elderly and non-elderly group. In particular, the incidence of grade 2 neutropenia was significantly higher in the elderly group than in the non-elderly group (grade1/grade 2: 5/11 *versus* 12/5, $p=0.038$). Moreover, there were no

significant differences in grade 3 or 4 hematological toxicities between the two groups. Among the non-hematological toxicities, the incidence of toxicities at any grade did not differ between the two groups although the incidence of anorexia and general fatigue tended to be more frequent in the elderly group. There were no treatment-related deaths.

Discussion

The current study shows that biweekly docetaxel and S-1 combination chemotherapy offers satisfactory antitumor effects, with an acceptable and manageable toxicity profile for AGC in the elderly.

Previously, we conducted a phase I and II study of biweekly combination treatments in order to develop a more effective and safe therapy for AGC in an outpatient setting (18, 19). We assessed the toxicities during the first and second courses to develop a safety regimen and, subsequently, the recommended docetaxel dose was identified as being 40 mg/m^2, with a response rate of 57.1% in the phase I study. The response rate was similar in the phase II study, at 57.8%. This optimised dose intensity of S-1 and docetaxel was higher than in previous studies, but the mean number of courses for each patient was comparable (22-24).

The overall response rate and MST in our phase II study were similar to those of previous studies. However, we observed less frequent hematological toxicities compared with earlier studies, and most non-hematological toxicities were of grade 1 or 2 and were controllable in an outpatient setting. Therefore, the current regimen appeared to be satisfactorily active for AGC.

In the present study, we continued this combination treatment for 113 patients with AGC, and compared the therapeutic outcomes between patients aged less than and more than 75 years of age, in order to evaluate feasibility of the treatment for elderly patients. A previous study showed that S-1 monotherapy was effective, with minimal adverse events for AGC in the elderly (25). Other studies revealed that weekly cisplatin, 5-FU, and folic acid (PLF) offered acceptable survival times in all of 58 elderly patients (26), while weekly oxaliplatin, 5-FU, and leucovorin (OXALF) achieved satisfactory survival times in all of 42 patients in spite of high incidences of neutropenia (27). A phase I/II trial with docetaxel and S-1 for patients with AGC concluded that the dose of docetaxel should be graded according to patient age because the incidence of febrile neutropenia was relatively high (28).

Previously, several reports have evaluated the therapeutic outcomes of combination docetaxel and S-1 treatment for AGC (22-24). However, the precise treatment protocols differed between studies. We conducted the present study to obtain satisfactory therapeutic outcomes with lesser toxicities in an outpatient clinic. In particular, our observed incidences of leukopenia and neutropenia were relatively low compared to other studies. As a result, our elderly patients tolerated the treatment regime as well as the non-elderly patients. In this study, higher incidence of grade 2 neutropenia forced dose reduction of docetaxel in the elderly group. As a result, it was possible to continue this chemotherapy in the non-elderly group, although dose intensity was reduced. However, PFS and OS did not differ between the two groups. Therefore, it may be important to continue these regimens until disease progression could be confirmed, or patients could tolerate chemotherapeutic treatments in the elderly.

A pooled analysis of three previous clinical trials of 1,080 patients with esophago-gastric cancer revealed that performance status and advanced disease, rather than age were independent prognostic factors for survival (29). In that previous study, elderly patients achieved acceptable response and survival rates, with low toxicities. An Italian group reported similar results and concluded that elderly patients not suffering from co-morbid disease may be suitable candidates for full doses of chemotherapy (30). However, it is necessary to reduce doses with caution in the elderly, in order to perform treatments safely and effectively.

Second-line treatment after failure of the first-line treatment is important to improve overall survival in patients with AGC. In the present study, more than half of the enrolled patients underwent second-line chemotherapies, and the MST of second-line treatment was 10.0 months. Subsequently, second-line treatments greatly increased survival in this study. The MST of second-line chemotherapies did not differ between the elderly and non-elderly groups, suggesting that second-line treatment could be recommended for elderly patients of favorable performance status and with less serious co-morbid diseases. In previous studies focusing on the therapeutic outcomes of elderly patients, the impact of second-line treatment was not fully discussed. However, it is important to evaluate this in a large number of patients.

Multivariate analysis revealed that age was not a prognostic factor. Therefore, this treatment is appropriate for elderly gastric cancer patients with eligibility.

In conclusion, biweekly docetaxel and S-1 combination chemotherapy in an outpatient setting, offered favorable survival benefits with controllable tolerance, according to the appropriate dose-reduction criteria for therapy of AGC in the elderly. It will be necessary to conduct a large-scale comparative study between elderly and non-elderly patients because of the limited patient sample size of the present study.

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