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Phase II multi-institutional prospective randomised trial comparing S-1 + paclitaxel with S-1 + cisplatin in patients with unresectable and/or recurrent advanced gastric cancer

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BACKGROUND: A combination of S-1 and cisplatin has been shown to be effective with acceptable safety for the first-line treatment of far-advanced gastric cancer in Japan. This is the first randomised phase II trial to compare S-1 + paclitaxel with S-1 + cisplatin in this setting.

METHODS: Patients with unresectable and/or recurrent advanced gastric cancer were randomly assigned to receive one of the two regimens: S-1 ($40\,mg\,m^{-2}$ twice daily) on days 1–14 plus paclitaxel ($60\,mg\,m^{-2}$) on days 1, 8, and 15 of a 4-week cycle (S-1 + paclitaxel) or S-1 ($40\,mg\,m^{-2}$ twice daily) on days 1–21 plus cisplatin ($60\,mg\,m^{-2}$) on day 8 of a 5-week cycle (S-1 + cisplatin). The primary end point was the response rate (RR). Secondary end points included progression-free survival (PFS), overall survival (OS), and safety.

RESULTS: A total of 83 patients were eligible for safety and efficacy analyses. In the S-1 + paclitaxel and S-1 + cisplatin groups, RRs (52.3% vs 48.7%; $P = 0.74$) and median PFS (9 vs 6 months; $P = 0.50$) were similar. The median OS was similar in the S-1 + paclitaxel and S-1 + cisplatin groups (16 vs 17 months; $P = 0.84$). The incidence of grade 3 or higher haematological toxicity was 19.0% with S-1 + paclitaxel and 19.5% with S-1 + cisplatin. The incidence of grade 3 or higher non-haematological toxicity was 14.2% with S-1 + paclitaxel and 17.1% with S-1 + cisplatin.

CONCLUSION: S-1 + paclitaxel was suggested to be a feasible and effective non-platinum-based regimen for chemotherapy in patients with advanced gastric cancer. Our results should be confirmed in multicenter, phase III-controlled clinical trials.

Translational Therapeutics

Gastric cancer is the second most common cause of cancer-related mortality worldwide. Patients with unresectable or recurrent gastric cancer have extremely poor outcomes, with 5-year survival rates of <5%. Various chemotherapeutic agents have been used in the hope of improving overall survival (OS), progression-free survival (PFS), response rate (RR), and quality of life in patients with advanced gastric cancer.

The SPIRITS trial established that S-1 + cisplatin is a standard first-line regimen for advanced gastric cancer in Japan (Koizumi et al, 2003; Koizumi et al, 2008). This randomised phase III study compared OS between patients who were given S-1 + cisplatin and those who were given S-1 alone (Koizumi et al, 2008). Median OS was significantly longer in the S-1 + cisplatin group than in the S-1 alone group. On the other hand, the S-1 + cisplatin group had more toxic events, such as neutropenia, anaemia, nausea, and

anorexia; however, there was no treatment-related mortality. Subsequently, the JCOG 9912 study confirmed that oral S-1 could replace infusional 5-fluorouracil without compromising efficacy or causing excessive toxicity (Boku et al, 2009). Based on these findings, S-1 + cisplatin has been recognised as a standard chemotherapy regimen for advanced gastric cancer in Japan. However, no alternative standard regimen is currently available for this indication. Some patients with impaired renal function cannot receive S-1 + cisplatin as a first-line treatment for advanced gastric cancer. Therefore, other regimens with low toxicity are needed.

Paclitaxel is a taxane derivative that was originally isolated from Taxus brevifolia, a type of Western yew (Wani et al, 1971). Paclitaxel has activity against a broad range of tumour types, including breast, ovarian, and lung cancers (Holmes et al, 1991; Einzig et al, 1992; Chang et al, 1993). Paclitaxel is also an effective drug for gastric cancer, with RRs ranging 20–28% in single-agent phase II studies (Ajani et al, 1998; Ohtsu et al, 1998; Yamada et al, 2001; Yamaguchi et al, 2002). The recommended dosage of paclitaxel in Japan was determined to be $210\,mg\,m^{-2}$ once every 3 weeks (Yamaguchi et al, 2002). Recently, good results have been

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obtained with a weekly regimen of paclitaxel in patients with ovarian cancer and gastric cancer (Fennelly et al, 1997; Hironaka et al, 2006). To further improve outcomes, many phase II studies have been performed to evaluate the safety profile and efficacy of weekly paclitaxel-based combination regimens for advanced and metastatic gastric cancer (Sakamoto et al, 2009). In 2006, we performed a phase I/II study of weekly paclitaxel combined with S-1 in patients with unresectable and/or recurrent advanced gastric cancer (Mochiki et al, 2006). The RR was 54.1%, and the median survival time was 15.5 months. Our results showed that S-1 + paclitaxel is effective and well tolerated (Mochiki et al, 2006). To confirm our findings, we planned the present randomised phase II study to compare the efficacy and safety of S-1 + paclitaxel with those of S-1 + cisplatin, currently the standard treatment in Japan, in patients with advanced gastric cancer.

PATIENTS AND METHODS

Patients

Patients between 20 and 75 years of age who had advanced, unresectable, histologically confirmed adenocarcinoma of the stomach were eligible for enrolment in this study. Eligible patients also had to have measurable or evaluable lesions, the ability to orally intake medications, an Eastern Clinical Oncology Group performance status of 0 or 1, and adequate liver, kidney, and bone marrow functions, similar to our previous study (Mochiki et al, 2006). Patients were excluded if they had brain metastases, significant gastrointestinal bleeding, serious comorbidity, concomitant use of drugs that potentially interact with S-1 (flucytosine, allopurinol, warfarin, or phenytoin), or an inability to comply with the protocol requirements. Pregnant women were also excluded.

Study design and randomisation

This randomised, open-label, phase II study was conducted at six institutions in Gunma and Saitama Prefectures in Japan between January 2006 and November 2010. The protocol was approved by the ethics committee of each participating institution, and all patients gave written informed consent. The primary end point of the study was the clinical response (RR) to the study treatment (S-1 + paclitaxel) as compared with the response to the control treatment (S-1 + cisplatin) in patients with advanced gastric cancer. Secondary end points were median OS, PFS, and safety. These variables were compared between the treatment groups.

A central data centre confirmed patient eligibility, and eligible patients were randomly assigned to treatment automatically according to stratification factors (prior therapy and performance status). Randomisation was centrally performed by the Coordination Centre of Gunma University.

Treatment regimens

Patients who were assigned to the S-1 + paclitaxel group received S-1 orally ($40\,mg\,m^{-2}$ twice daily) on days 1–14 plus paclitaxel ($60\,mg\,m^{-2}$) as an intravenous infusion on days 1, 8, and 15 of a 4-week cycle (Mochiki et al, 2006). Patients who were assigned to the S-1 + cisplatin group received S-1 orally ($40\,mg\,m^{-2}$ twice daily) on days 1–21 plus cisplatin ($60\,mg\,m^{-2}$) as an intravenous infusion on day 8 of a 5-week cycle (Koizumi et al, 2003).

Before treatment with paclitaxel in the S-1 + paclitaxel group, patients received an antihistamine (e.g., diphenhydramine hydrochloride 50 mg), dexamethasone 8 mg, and cimetidine 300 mg (or a comparable H2 blocker) to prevent paclitaxel-related hypersensitivity reactions. To reduce the risk of cisplatin-induced renal damage in the S-1 + cisplatin group, patients received hydration with 1500 ml of 5% glucose before treatment with cisplatin. Furosemide was given 30 min before starting the cisplatin infusion, and hydration with 4000 ml of 5% glucose, 24 g NaCl, 1.2 g KCl and

$0.8\,g$ $CaCl_2$ was continued for 48 h. Treatment was discontinued at the onset of disease progression, severe toxic effects, or at the patient's request.

Response and toxicity criteria

Tumour response was assessed objectively after each course of treatment, according to the Response Evaluation Criteria in Solid Tumours. OS was estimated from the date of study entry to the date of death or the last follow-up visit according to the Kaplan–Meier method. The log-rank test was used to compare survival between treatment groups. Progression free survival was measured from the date of study entry to the first objective observation of disease progression or death from any cause. Adverse events were evaluated according to the Common Terminology Criteria for Adverse Events, version 4.0.

Follow-up schedule

Disease progression and the development of new lesions were evaluated as needed by abdominal radiography, abdominal and thoracic computed tomography, and measurement of the tumour markers carcinoembryonic antigen (CEA) and CA 19–9, performed at baseline and at least every 4–5 weeks during treatment. Responses were evaluated every 8 weeks or earlier in patients who had an evidence of treatment failure. Physical examinations, complete blood counts, serum chemical analyses, and other laboratory tests were performed before treatment and at least every 2 weeks during treatment.

Statistical analysis

The required sample size was estimated according to the criteria of Simon et al (1985). We estimated that 36 patients per treatment group would allow selection of the better treatment with 90% accuracy, given that the absolute difference in the RR of the better treatment is at least 15%, with an expected baseline RR of 50%. To compensate for the possible enrolment of ineligible patients, the sample size was set at 80 (40 patients per group).

The Kaplan–Meier estimates and a Cox proportional hazards model were used to analyse time-event variables. The distributions of discrete variables were compared between the two treatment groups with the use of the χ^2-test or Fisher's exact test as appropriate. To compare continuous variables, the Mann–Whitney U-test for nonparametric data was used. All the tests were two-sided, and P values < 0.05 were considered to indicate statistical significance. SPSS software (SPSS Inc., Chicago, IL, USA) was used for statistical analyses.

RESULTS

Patient characteristics

Between January 2006 and November 2010, a total of 83 patients (61 men and 22 women) were registered at six hospitals. In all, 42 patients were assigned to S-1 + paclitaxel and 41 patients were assigned to S-1 + cisplatin. The characteristics of the assessable patients, including sex, median age, performance status, histological type, prior therapy, and sites of metastasis, are shown in Table 1. The mean age of the patients was 63.3 years in the S-1 + paclitaxel group and 63.0 years in the S-1 + cisplatin group. The baseline characteristics were well balanced between the two treatment groups.

Response rate

The confirmed RR was 52.3% (22 out of 42) in the S-1 + paclitaxel group (95% confidence interval (CI), 39–61%) and 48.7% (20 out

Table 1 Characteristics of patients

	S-1 + paclitaxel	S-1 + cisplatin	*P*-value
Sex: male/female	31/11	30/11	0.48
Mean age ± s.e.; years	63.3 ± 1.4	63.0 ± 1.3	0.91
Performance status 0/1	38/4	39/2	0.42
Histological type			
Intestinal	16	16	0.47
Diffuse	26	25	
Prior therapy			
None	33	33	0.73
Gastrectomy	2	3	
Gastrectomy + chemotherapy	7	5	
Site of metastasis			
Liver	14	12	0.57
Lymph nodes	40	33	
Peritoneum	11	8	

Table 2 Overall response to treatment

|	S-1 + paclitaxel	S-1 + cisplatin	*P*-value
CR	1	0	0.72
PR	21	20	
SD	12	10	
PD	6	8	
NE	2	3	

Abbreviations: CR = complete response; NE = inevaluable; PD = progressive disease; PR = partial response; SR = stable disease.

of 41) in the S-1 + cisplatin group (95% CI, 39–61%) (Table 2). All the responses were partial, except for one complete response (CR) in the S-1 + paclitaxel group. The RR in the S-1 + paclitaxel group was slightly, but not significantly, higher than that in the S-1 + cisplatin group ($P = 0.74$). The tumour control rate (CR + partial response + stable disease) was 80% (34 out of 42) in the S-1 + paclitaxel group and 73% (30 of 41) in the S-1 + cisplatin group.

Progression-free survival and overall survival

The median PFS was 9 months in the S-1 + paclitaxel group (95% CI, 6–12 months) and 6 months in the S-1 + cisplatin group (95% CI, 4–9 months; Figure 1). The hazard ratio for disease progression or death (S-1 + paclitaxel/S-1 + cisplatin) was 0.84 (95% CI, 0.50–1.4). When the treatment groups were compared by log-rank test, there was no significant difference in median PFS ($P = 0.50$). At a median follow-up of 14 months, the median OS was 16 months in the S-1 + paclitaxel group (95% CI, 15–22 months) and 17 months in the S-1 + cisplatin group (95% CI, 11–23 months); the hazard ratio for death (S-1 + paclitaxel/S-1 + cisplatin) was 0.94 (95% CI, 0.55–1.63). Efficacy of the treatments thus appeared to be similar (log-rank test; $P = 0.84$; Figure 2). The estimated survival rates at 1 and 2 years were 70% and 26%, respectively, in the S-1 + paclitaxel group and 63% and 30%, respectively, in the S-1 + cisplatin group.

A total of 14 patients (S-1 + paclitaxel, 6 patients; S-1 + cisplatin, 8 patients) underwent gastrectomy after chemotherapy and had no critical chemotherapy-related adverse effects. On average, the number of administered courses of chemotherapy before surgery was 5.1 (range 2–15) in the S-1 + paclitaxel group and 4.1 (range 2–8) in the S-1 + cisplatin group. Total gastrectomy was performed in 13 patients and distal gastrectomy was done in 1. The six patients in the S-1 + paclitaxel group had a median survival of 28
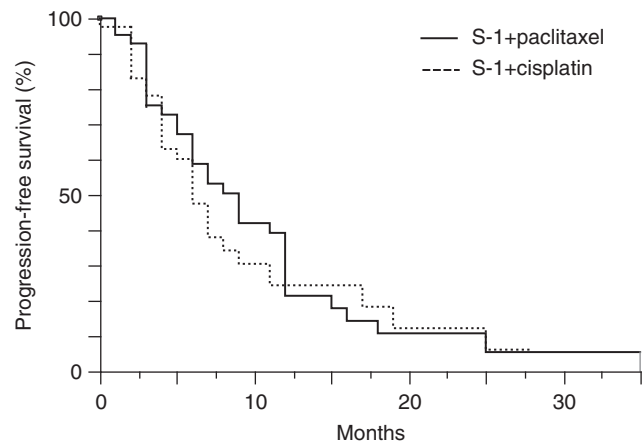
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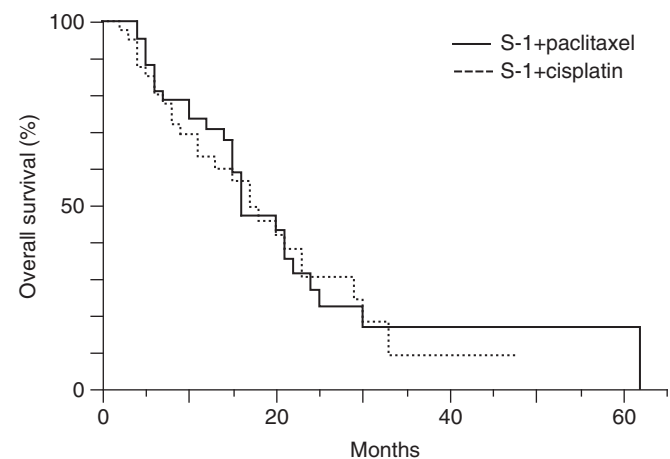
Figure 2 Overall survival.

months (range 21–60), and two patients were alive at the time of this analysis. The eight patients in arm C had a median survival of 25.5 months (range 11–48), and all were alive at the time of this analysis. Responses of all the patients who underwent gastrectomy were partial.

Toxic effects

The median number of administered cycles of chemotherapy was 5 (range 2–30) in the S-1 + paclitaxel group and 4 (range 1–15) in the S-1 + cisplatin group. Myelosuppression was the most frequent toxic effect in both groups (Table 3). In the S-1 + paclitaxel group, grade 3 or 4 haematological toxicity occurred in 19.0% (8 out of 42) of the patients and grade 3 or 4 non-haematological toxicity occurred in 14.2% (6 out of 42) of the patients. The most common types of severe (grade 3 or 4) haematological toxicity were leucopenia (3 patients, 7.1%), neutropenia (3 patients, 7.1%), and anaemia (2 patients, 4.7%) (Table 3). The most common types of all grade non-haematological toxicity were peripheral neuropathy (7 patients, 16.6%), anorexia (6 patients, 14.2%), diarrhoea (5 patients, 11.9%), nausea (5 patients, 11.9%), and stomatitis (5 patients, 11.9%). In the S-1 + cisplatin group, grade 3 or 4 haematological toxicity occurred in 19.5% (8 out of 41) of the patients and grade 3 or 4 non-haematological toxicity occurred in 17.1% (7 out of 41). The frequent types of severe (grade 3 or 4) haematological toxicity were neutropenia (4 patients, 9.7%), leucopenia (3 patients, 7.5%), and anaemia (2 patients, 5%) (Table 3). There was one episode of febrile neutropenia. The most

Table 3 Toxic effects and number of patients with toxicity

Grade	S-1 + paclitaxel		S-1 + cisplatin	
	1-2	3-4	1-2	3-4
Haematological toxicity				
Leucopenia	10	3	11	2
Neutropenia	10	3	6	4
Anaemia	3	2	8	2
Thrombocytopenia	1	0	8	0
Non-haematological toxicity				
Anorexia	6	0	12	2
Nausea	5	0	10	2
Diarrhoea	3	2	9	1
Fatigue	3	0	6	0
Stomatitis	4	1	3	0
Peripheral neuropathy	4	3	2	0
Hypoalbuminemia	2	0	6	0
Bilirubin	1	0	1	0
AST/ALT	2	0	0	1
Hyperkalemia	3	0	0	0
Hyponatremia	0	0	0	1

Abbreviations: ALT = alanine aminotransferase; AST = aminotransferase.

common types of all grade non-haematological toxicity were anorexia (14 patients, 34.1%), diarrhoea (10 patients, 24.3%), and nausea (12 patients, 29.2%). Treatment was discontinued during the first course of S-1 + cisplatin in three patients because of grade 3 liver dysfunction, grade 3 anorexia, and grade 4 neutropenia, respectively. There was no treatment-related death or severe delayed toxicity in either group. The overall incidence of grade 3 or 4 toxic effects did not differ significantly between the treatment groups ($P = 0.53$).

DISCUSSION

The efficacy of S-1-based combination chemotherapy in advanced gastric cancer has been assessed in a number of phase I/II studies. The SPIRITS trial, a phase III study, established S-1 + cisplatin as a standard first-line regimen for advanced gastric cancer in Japan (Koizumi et al, 2008). However, the FLAGS trial, a non-Asian global phase III study, concluded that S-1 + cisplatin did not prolong the OS of patients with advanced gastric or gastroeso-phageal adenocarcinoma as compared with cisplatin + infusional fluorouracil, but did have a significantly better safety profile (Ajani et al, 2010). Cisplatin can cause renal toxicity, emesis, and peripheral neuropathy, and the intravenous hydration required during its use lengthens outpatient visits and can necessitate overnight admission. Consequently, drug combinations, such as S-1 + cisplatin, are considered too toxic for elderly patients or patients with a poor performance status. S-1 + cisplatin regimens also have other limitations. Therefore, alternative drug combina-tions with similar efficacy but lower toxicity than S-1 + cisplatin are needed. Our previous phase I/II study showed that a combination of S-1 + paclitaxel is highly effective in advanced and recurrent gastric cancer, with an acceptable and manageable toxicity profile (Mochiki et al, 2006). This combination regimen produced promising results, with an overall RR of 54.1%, a median time to progression of 9.5 months (95% CI, 5–11.6 months), and a median OS of 15.5 months) (95% CI, 11.6–19.4 months). Haematological and non-haematological toxicities associated with S-1 + paclitaxel were generally mild. Based on the positive results of our previous study, we initiated the present randomised phase II trial to compare S-1 + paclitaxel with S-1 + cisplatin in a similar setting.

To our knowledge, this is the first randomised trial to compare S-1 + paclitaxel with S-1 + cisplatin in patients with unresectable and recurrent gastric cancer. Although this was a phase II study and had limited power to detect significant differences between the treatment groups, we could estimate the relative efficacy and safety of the two regimens. To assess the primary end point (RR), all images were reviewed and all responses were confirmed. The RR was 52.3% in the S-1 + paclitaxel group and 48.7% in the S-1 + cisplatin group, suggesting that both regimens have similar activity in patients with unresectable and recurrent gastric cancer. The RRs for S-1 + paclitaxel and S-1 + cisplatin are largely consistent with the results of previous studies in advanced gastric cancer (Koizumi et al, 2003; Mochiki et al, 2006). Furthermore, median PFS and OS were also similar for both regimens in this study. The promising median survival time obtained in the present study (16 months) raises hope that S-1 + paclitaxel may improve survival outcomes in patients with advanced gastric cancer. The longer median OS in our study may have been related to the good performance status of many patients. Performance status was 0 or 1 in all patients; no patient had a performance status of 2. Survival outcomes in our study are consistent with the results of phase II studies of similar regimens of S-1 + paclitaxel in patients with advanced gastric cancer (Narahara et al, 2008; Lee et al, 2009; Ueda et al, 2010). Lee et al (2009) obtained an RR of 40% and a median survival time of 12.1 months with a combination regimen of weekly paclitaxel and S-1 in advanced gastric cancer. Nakajo et al (2008) reported a median OS of >17.0 months in their feasibility study of paclitaxel and S-1 in 52 patients with advanced gastric cancer treated at a single institution. In the present study, combination therapy with S-1 and weekly paclitaxel was associated with very tolerable levels of gastrointestinal toxicity as well as high antitumour effectiveness. Furthermore, the survival outcomes with S-1 + paclitaxel were similar to those reported for S-1 + docetaxel, another S-1 taxane-based regimen (Yoshida et al, 2006). It is not necessarily surprising that taxanes + S-1 markedly improved outcomes in patients with advanced and metastatic gastric cancer because patients eligible to receive a combination of paclitaxel and oral agents must have the possibility of oral intake, suggesting that they are in better general condition.

Human epidermal growth factor receptor 2 (HER2) is an important biomarker and a key driver of tumourigenesis in gastric cancer, with studies showing overexpression in 7–34% of tumours (Tanner et al, 2005; Gravalos and Jimeno, 2008). The ToGA study recently showed that the addition of trastuzumab to chemotherapy improves survival in patients with advanced gastric or gastro-oesophageal junction cancer as compared with chemotherapy alone (Bang et al, 2010). The ToGA study also found that OS was longer in patients with high expression of HER2 protein than in those with low expression. Information on the HER2 status of the patients in our study is unfortunately unavailable. However, recent studies have also shown an association of HER-2-positive tumours with poor outcomes and aggressive disease (Tanner et al, 2005; Gravalos and Jimeno, 2008). Further studies are thus needed to address the issue of whether HER2 has an effect on outcomes in gastric cancer and to determine whether it confers a good or poor prognosis.

Studies of patients with gastric cancer who receive chemother-apy before gastrectomy may show a survival benefit with the use of perioperative chemotherapy as compared with chemotherapy alone. Neoadjuvant (preoperative) chemotherapy is attractive for a number of reasons, including good compliance of patients with preoperative treatment, higher surgical cure rates as a result of tumour downstaging, and sparing patients with biologically aggressive disease from induction chemotherapy. The MAGIC trial showed that neoadjuvant chemotherapy resulted in tumour downstaging, significantly improved OS from 23–36%, and did not increase the rate of postoperative complications (Cunningham et al, 2006). However, favourable outcomes have been obtained

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after gastrectomy with R0 resection in patients with resectable as well as those with unresectable disease (Satoh *et al*, 2006). These results stress the importance of precise preoperative staging to identify patients most likely to benefit from neoadjuvant chemotherapy and of using a feasible and highly effective chemotherapeutic regimen.

Overall, treatment compliance and safety were good in both treatment arms, and there were no treatment-related deaths in our study. Both agents were associated with minimal myelosuppression, and the most common haematological toxic effects were leucopenia and neutropenia. In general, S-1 + paclitaxel had a better safety profile and was better tolerated than S-1 + cisplatin. S-1 + cisplatin was characterised by a higher incidence of grade 1 or 2 haematological toxicity, especially anaemia and thrombocytopenia, as compared with S-1 + paclitaxel. One episode of febrile neutropenia occurred in one patient treated with S-1 + cisplatin. Non-haematological toxicity profiles differed between S-1 + paclitaxel and S-1 + cisplatin. The major difference was the higher incidences of anorexia and nausea among the patients treated with S-1 + cisplatin. In contrast, the S-1 + paclitaxel regimen had tolerable gastrointestinal toxicities as well as high antitumour effectiveness. Less than 15% of our patients had grade 3 or higher gastrointestinal toxicities, including anorexia, nausea, and diarrhoea. As compared with S-1 + cisplatin, however, S-1 + paclitaxel has been shown to be more often associated with peripheral neuropathy. Peripheral neuropathy, which usually begins to develop after four cycles of treatment, may have clinical implications; it causes numbness and paraesthesia in a glove- and stocking-like distribution. Severe neurotoxicity precludes long-term treatment with paclitaxel (Sakamoto *et al*, 2009). Therefore, early detection and symptomatic relief are essential clinically. Both haematological and non-haematological toxicities of S-1 + paclitaxel were generally manageable, and most patients could continue treatment in an outpatient setting. With cisplatin-based regimens, patients must receive intravenous infusions to ensure adequate hydration and prevent cisplatin-induced renal damage. S-1 + paclitaxel might therefore be better suited for treatment on an outpatient basis than cisplatin-based chemotherapy. A high RR coupled with a better quality of life is considered an advantage of S-1 + paclitaxel.

S-1 is approved in Japan, China, Taiwan, Korea, and Singapore for the treatment of gastric cancer and more recently has been approved in 27 European countries for the management of advanced gastric cancer (Blum *et al*, 2011). In initial clinical trials

of S-1 in the United States and Europe, diarrhoea occurred as dose-limiting toxicity. In early Japanese clinical trials, however, myelosuppression developed as dose-limiting toxicity (Lenz *et al*, 2007). Differences in dose tolerance between Asians and other populations are probably caused by polymorphisms in the CYP2A6 gene (Blum *et al*, 2011). Lower dose intensity may thus explain why S-1 is not always as effective in Western countries as it has been in Japan. There are also marked geographic differences in the prevalences of gastric cancer subtypes. Intestinal-type distal gastric cancer related to *Helicobacter pylori* is predominant in Asia, whereas proximal and diffuse subtypes of gastric cancer are most common in Europe and North America. There are also marked regional differences in how gastric cancer is treated. In Europe, triplet therapy with epirubicin, cisplatin, and fluorouracil (ECF) is widely used on the basis of the results of two randomised studies (Webb *et al*, 1997; Ross *et al*, 2002). The REAL-2 trial is the largest randomised controlled study to date to compare first-line chemotherapy regimens for advanced oesophago-gastric cancer in the United Kingdom (Cunningham *et al*, 2008). The results showed that triplet therapy with epirubicin, oxaliplatin, and capecitabine is at least as efficacious as ECF, with the additional advantages of a more convenient mode of administration (no requirement for hydration) and an acceptable toxicity profile. Because of these appreciable differences between Japan and Western countries, our results may be applicable only to Asian patients with gastric cancer and cannot be directly extrapolated to a Western population.

CONCLUSION

In conclusion, this is the first randomised trial to compare the efficacy and safety of S-1 + paclitaxel with those of S-1 + cisplatin in patients with far-advanced gastric cancer. As a randomised phase II study, our protocol had limited power to directly compare efficacy between the treatment groups. However, our results suggest that both the regimens are active and well-tolerated treatments for unresectable and/or recurrent advanced gastric cancer and indicate that S-1 + paclitaxel merits further evaluation as a reference arm in a subsequent phase III trial.

Conflict of Interest

Translational Therapeutics

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