박 사 학 위 논 문

Phase II Study of Docetaxel, Cisplatin, and S-1 Triplet Combination Chemotherapy in Patients with Advanced Gastric Cancer

계 명 대 학 교 대 학 원

의 학 과

장 원 영

지도교수 김 진 영

2 0 2 0 년 8 월

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지도교수 김 진 영

이 논문을 박사학위 논문으로 제출함

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계 명 대 학 교 대 학 원

의학과 내과학 전공

장 원 영

장원영의 박사학위 논문을 인준함

주 심 박 건 욱

부 심 김 진 영

부 심 도 영 록

부 심 허 미 화

부 심 김 종 광

계 명 대 학 교 대 학 원

2 0 2 0 년 8 월

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장 원 영

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1. Introduction

Gastric cancer is the fifth most common cancer and the third most common cause of cancer related death globally (1). In Korea, gastric cancer ranks second in cancer incidence and third in cancer mortality (2). Standard chemotherapy for advanced gastric cancer (AGC) employs first-line 5-fluorouracil (5-FU) or its derivatives plus platinum agent combination regimens. Despite the worldwide adoption of two-drug fluorinated platinum-based chemotherapy as optimal initial chemotherapy for AGC, there is uncertain benefit for adding a third chemotherapy agent. Trastuzumab, human epidermal growth factor receptor 2 (HER-2) monoclonal antibody, is added to first-line chemotherapy in HER2-positive disease. The addition of trastuzumab to standard chemotherapy significantly improved all endpoints of overall response rate (ORR), progression-free survival (PFS), and overall survival (OS) in the ToGA trial (3). However HER-2 overexpression is observed in less than 30%, current survival of patients with AGC is still not good. Docetaxel is a good candidate agent for triplet combination strategy because this drug has demonstrated efficacy in patients with metastatic or recurrent AGC, either as a single agent or as a doublet chemotherapy. In 2006, the V325 phase 3 trial reported the superiority of triplet chemotherapy with docetaxel, cisplatin, and fluorouracil (DCF) over doublet chemotherapy with cisplatin plus fluorouracil for patients with AGC; the median OS was 9.2 months versus 8.6 months with a risk reduction of 32%, in an era where few options for second-line treatment were available. However, this triplet regimen has not been accepted globally as a standard treatment due to its severe hematological toxicity, 82% incidence of grade 3 - 4 neutropenia and 29%

incidence of febrile neutropenia, and small survival benefit (4).

Many modified DCF regimens that aim to reduce toxicity while retaining the efficacy of DCF have been investigated in patients with metastatic or recurrent AGC. S-1, an oral xuoropyrimidine derivative developed in Japan, is active against AGC as a single agent or in combination with cisplatin in phase III trials. These trials suggested that S-1 was not inferior to 5-FU, with less toxicity, and can replace 5-FU for the treatment of AGC (5,6). Docetaxel, cisplatin, and S1 (DCS) combination chemotherapy has replaced DCF as a triplet regimen. First reported in 2007, the DCS triplet regimen had a higher ORR than S-1 plus cisplatin (7). In this phase 1 study, patients received oral S-1 40 mg/m^2 bid on days 1-14, intravenous cisplatin 60 mg/m^2 and docetaxel 60, 70 or 80 mg/m^2 depending on dose-limiting toxicity (DLT) on day 8 every three weeks. The recommended dose of docetaxel was defined as 60 mg/m^2. The DLT was neutropenia. A phase II study showed quite high clinical efficacy, with an 87.1% total response rate, including 3.2% showing complete response, 25.8% of patients achieving down-staging, and 22.6% undergoing a conducted curative surgical treatment (8). Because intravenously administered docetaxel effectively penetrates ascites, a systemic regimen involving docetaxel would be ideal for treating patients with peritoneal metastasis (PM). This phase II DCS therapy (oral S-1 40 mg/m^2 bid on days 1-14, intravenous cisplatin 60 mg/m^2 and docetaxel 60 mg/m^2 depending on DLT on day 8 every three weeks) also showed a high incidence of grade 3/4 hematologic toxicities, such as 77.4% neutropenia, as well as grade 3 non-hematologic toxicities, such as 35.3% anorexia and 32.3% nausea. To reduce DLT and achieve best response rate, we conducted a phase II study of modified DCS, using a reduced dose of docetaxel.

2. Materials and Methods

2.1. Study Design:

This trial was a single-arm phase II study evaluating triplet combination chemotherapy with DCS in AGC patients who were not treated with chemotherapy except adjuvant chemotherapy. The primary end point was ORR, and the secondary end points were OS, PFS, response duration, and assessment of toxicity. The investigation was performed in accordance with the Declaration of Helsinki, and the protocol was approved by the institutional review boards of Keimyung University Dongsan Medical Center (No. 2011-11-031).

2.2. Patient Eligibility:

Patients with pathologically proven unresectable recurrent or metastatic gastric adenocarcinoma were assessed for eligibility. The major inclusion criteria were as follows: measurable disease based on Response Evaluation Criteria in Solid Tumors (RECIST) version 1.0, age 18 - 70 years, an Eastern Cooperative Oncology Group (ECOG) performance status of 0 - 2, adequate bone marrow function (defined by an absolute neutrophil count of 1500 /mm^3 or greater, a platelet count of (100,000 /mm^3 or greater), adequate renal function (serum creatinine level below 1.5 mg/dL or creatinine clearance > 60 mL/min), and adequate hepatic function (bilirubin level below 2.0 mg/dL, and aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels threefold or less of the reference value). Prior radiotherapy was permitted if it had been

completed at least 1 year before enrollment of the patient into the study. Patients in whom adjuvant chemotherapy containing cisplatin had been completed at least 1 year before recruitment were enrolled. However, patients with recurrence after adjuvant S-1, docetaxel-based chemotherapy were not eligible for the study regardless of the time to recurrence. Patients with brain metastasis, obvious bowel obstruction, or serious gastrointestinal bleeding were excluded. Each patient provided written informed consent before study enrollment.

2.3. Assessment:

At the time of enrollment, all patients had a medical history assessment and physical examination, including evaluation of performance status, complete blood cell counts, serum chemistry profiles, creatinine clearance, urinalysis, electrocardiogram, chest X-ray and computed tomography (CT), or magnetic resonance imaging scan. Complete blood cell counts, liver function tests, and renal function tests were assessed at least once per cycle during treatment. CT scanning and imaging of measurable disease were performed every two cycles. Adverse events were assessed according to the National Cancer Institute Common Toxicity Criteria (NCI-CTC, version 4.0).

2.4. Treatment Schedule:

S-1 was administered orally at 40 mg/m^2 twice daily on days 1-14, a dose calculated according to the patient's body surface area as follows: < 1.36 m^2, 50 mg; 1.36-1.57 m^2, 60 mg; 1.58-1.78 m^2, 65 mg; 1.79-1.92 m^2, 70 mg; 1.93-2.07 m^2, 75 mg; and > 2.08 m^2, 80 mg. Cisplatin was

administered by intravenous infusion for 2 h at 60 mg/m^2 in 5% glucose, followed by docetaxel (Taxotere®) at 40 mg/m^2 in 5% glucose on day 1. Prophylactic dexamethasone and anti-histamine were prescribed to prevent potential hypersensitivity reactions to docetaxel. To avoid cisplatin-induced renal dysfunction, adequate hydration of normally more than 2000 mL of normal saline on day 1 was administered. Antiemetic prophylactics were routinely used to prevent nausea and vomiting when cisplatin was administered according to American Society of Clinical Oncology (ASCO) guidelines. Granulocyte colony stimulating factor was administered to treat neutropenic events. Cycles were repeated every three weeks. Treatment with this regimen was continued for six cycles. Patients received at least two cycles of DCS unless disease progression was noted. Subsequently, patients with no sign of disease progression were then given a two more cycles, with a maximum of eight cycles as per investigator's decision.

2.5. Dose Modifications:

Dose modifications were done according to the study protocol. Initiation of the next course was postponed until recovery and fulfillment of the following criteria: ANC 1500 /mm^3 and platelets 100,000 /mm^3. Docetaxel, cisplatin, and S-1 doses were reduced when the following adverse events occurred in the previous course: febrile neutropenia, grade 4 neutropenia, grade 4 thrombocytopenia, grade 2 or higher elevated AST/ALT, and grade 3 or 4 fatigue. The S-1 dose was reduced in the event of grade 3 or 4 diarrhea, or grade 3 stomatitis. The dosage of S-1 was reduced by 60 mg/m^2/day for related grade 3-4 toxicity, for the second occurrence of the same grade 3 toxicity, or for

the third occurrence of the same grade 2 toxicity. The doses of docetaxel and oxaliplatin were reduced by 50% of the initial dose for related grade 4 toxicity, for the second occurrence of the same grade 3 toxicity, or for the third occurrence of same grade 2 toxicity. Treatment was delayed for up to 2 weeks if patients had insufficient hepatic, cardiac, renal, or bone marrow function (i.e., ANC < 1,500 /mm^3, platelets < 100,000 /mm^3, fever with grade 3 to 4 neutropenia, or non-hematologic toxicity grade 3). Treatment was discontinued if recovery did not occur within 14 days.

2.6. Statistical Analysis:

According to Simon's optimal two-stage design (9), 35 patients were required for enrollment to test the null hypothesis that the true ORR is 20% versus the alternative hypothesis that the true ORR is at least 45%, at a significance level of 0.05 with a power of 90%. If six or more responses were observed among 19 patients in the first stage, the study was continued with additional patients included. As the drop-out rate was assumed to be 10%, the number of patients necessary for sufficient statistical power was calculated to be 39.

The intention-to-treat (ITT) population included all of the patients, and the per-protocol (PP) population excluded those patients who received treatment for less than six weeks for reason other than disease progression or death. The duration of a complete response (CR) or partial response (PR) was defined as the time from the first day that measurement criteria were met for complete response or partial response until the first documentation of progressive disease or recurrence (by referencing the smallest measurements recorded since the treatment

started). We measured OS as from the date of first administration of DCS chemotherapy to the date of the death or last follow-up. We measured PFS as from the date of first administration of DCS chemotherapy to the date of detection of progression or death from any cause. The time to the event end points was analyzed with Kaplan - Meier survival methods. All P values lower than 0.05 were considered to indicate statistical significance.

3. Results

3.1. Patient Characteristics:

From July 2011 to June 2016, 26 patients who met the inclusion criteria were enrolled in this study. The demographic and pathologic characteristics of the patients are described in Table 1. The median age was 53 years (range 35-68 years). Twenty-two patients (84.6%) were male, and only one patient (3.8%) had an ECOG performance status of 2. Twenty-three patients (88.5%) had metastatic disease. Twenty-two (84.6%) had an initial diagnosis of stage 4 AGC, and 4 patients (15.4%) had recurrent gastric cancer after curative surgery with adjuvant chemotherapy. Twenty patients (76.9%) had poorly differentiated adenocarcinoma, and the most common metastatic sites were the peritoneum (46.2%), distant lymph nodes (38.4%), and the liver (23.0%). The median number of metastatic organs was 2 (range 0 - 3).

3.2. Treatment Delivery:

A total of 142 cycles of DCS chemotherapy (median 6; range 1 - 8 per patient) were administered. Three patients had to discontinue use of S-1, because of grade 3/4 fatigue and diarrhea and they received increased doses (130%) of docetaxel and cisplatin doublet therapy for 3 of 6 cycles. One patient did not complete the first cycle of chemotherapy because of loss to follow-up. Seventeen patients (65.4%) received six or more cycles of chemotherapy. Five patients (19.2%) required dose reductions or delays. The mean relative dose intensities (ratio of the

dose received to the dose planned) of docetaxel, cisplatin, and S-1 for all of the cycles administered were 1.03 (95% confidence interval (CI) 0.99 - 1.06), 1.0 (95% CI 0.98 - 1.02), and 0.92 (95% CI 0.84 - 1.0), respectively. The most common reasons for dose reduction and delay were grade 3/4 neutropenia and diarrhea.

3.3. Toxicity:

Seventeen patients (65.4%) completed the six planned cycles of DCS. The reasons for chemotherapy discontinuation were patient refusal (n = 1), delayed recovery from an adverse event (n = 1), and disease progression (n = 7). Toxicities during treatment are listed in Table 2. The common hematologic toxicities were anemia (76.9%), neutropenia (53.8%), and thrombocytopenia (23.1%). Among them, grade 3 or 4 adverse events that occurred in more than 10% of the patients were neutropenia (23.1%), diarrhea (15.5%), and anemia (11.5%). No patient experienced grade 3 or 4 febrile neutropenia. In addition, one patient had a grade 3 pulmonary embolism, and another patient had a grade 3 pneumonia. All treatment related toxicities resolved with appropriate management, and no treatment related deaths occurred.

3.4. Response to Chemotherapy:

Of the 26 patients, 25 patients were eligible for response evaluation. One patient was not available for response evaluation because of loss during follow-up. Tumor responses are summarized in Table 3. A total of 142 cycles of DCS chemotherapy (median 6; range 1 - 8 per patient) were administered. All 26 patients had measurable lesions, with CR

achieved in 1, PR achieved in 16, and SD achieved in seven patients. The confirmed ORR was 65.4% in the ITT population (n = 26) and 68.0% in the PP population (n = 25). The disease control rate was 92.3% in the ITT population and 96.0% in the PP population. The median time to response was 1.4 months (95% CI 1.1-1.7 months] and median duration of response was 5.6 months (95% CI 1.7-12.9 months). At the time of survival analysis, the median follow-up period for censored (surviving) patients was 11.2 months (range 1.7 - 80.0 months). The median PFS was 7.2 months (95% CI 6.0-8.3 months), and the median OS was 11.0 months (95% CI 7.8-14.0 months) in the ITT population (Figure 1&2). Of the 26 patients, 4 patients (15.4%) received conversion surgery because of disappearing distant metastasis and/or down-staging (Table 4). Two of 4 patients who received conversion surgery underwent curative gastrectomy. The metastatic lesions in 2 patients completely disappeared after surgical gastrectomy with lymph node. Another 2 patients showed residual tumor at the time of surgery, one in the retroperitoneal place and the other in the mesocolon.

Table 1A. Baseline Characteristics of Patients

Patients characteristics	N	%
Number of patients	26	
Median age, years (range)	53(35-68)	
Sex		
Male	22	84.6%
Female	4	15.4%
ECOG performance status		
0-1	25	96.2%
2	1	3.8%
Histology		
Moderate	6	23.1%
Poor	20	76.9%
Prior therapy		
Palliative surgery	3	11.5%
Surgery + adjuvant chemotherapy	4	15.4%
None	19	73.1%
Clinical stage (AJCC)		
Stage 4	26	100%
T category		
T2	2	7.7%
T3	7	26.9%
T4a	10	38.5%
T4b	7	26.9%
N category		
N0	1	3.8%
N1	5	19.2%
N2	5	19.2%
N3	15	57.7%
M category		
M0	3	11.5%
M1	23	88.5%

Table 1B. Baseline Characteristics of Patients (continued)

Patients characteristics	N	%
Peritoneal carcinomatosis		
Yes	12	46.2%
No	14	53.8%
Number of metastases		
0	4	15.4%
1	9	34.6%
2	6	23.1%
≥3	7	26.9%
Involved organ		
Peritoneum	12	46.2%
Distant lymph node	10	38.4%
Liver	6	23.0%
Bone	4	15.4%
Lung	3	11.5%
Adrenal gland	2	7.6%
Ovary	1	3.8%
Others	2	7.6%

AJCC: The American Joint Committee on Cancer; ECOG: Eastern Cooperative Oncology Group.

Table 2. Observed Adverse Events Associated with Chemotherapy

Adverse events	All grade		Grade 3/4	
	N	%	N	%
Hematologic				
Neutropenia	14	53.8%	6	23.1%
Febrile neutropenia	2	7.7%	0	
Anemia	20	76.9%	3	11.5%
Thrombocytopenia	6	23.1%	0	
Bilirubin	0		0	
AST/ALT	1	3.8%	1	3.8%
Creatinine	1	3.8%	0	
Non-hematologic				
Diarrhea	9	34.6%	4	15.4%
Nausea/vomiting	5	19.2%	2	7.7%
Anorexia	5	19.2%	1	3.8%
Fatigue	4	15.4%	1	3.8%
Stomatitis	2	7.7%	0	
Infection	3	11.5%	1	3.8%
Pulmonary embolism	1	3.8%	1	3.8%

ALT: alanine aminotransferase; AST: aspartate aminotransferase.

Table 3. Treatment Efficacy

Treatment efficacy	N	%
Complete remission (CR)	1	3.8%
Partial remission (PR)	16	61.5%
Stable disease (SD)	7	26.9%
Progressive disease (PD)	1	3.8%
Response rate (95% CI)		65.4%

Table 4. Patients with Conversion Surgery

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4
Sex	M	M	M	M
Age, years	47	58	53	38
ypT	3	4a	2	4b
ypN	1	0	3b	2
Sites of metastasis	Liver	Peritoneum	Distant LN	Pancreas, colon
Cycles	6	4	6	6
Response	PR	PR	PR	PR
Time to response	1.4	2.8	1.4	1.4
Response duration	57.7	17.7	8.4	7.4
PFS	59.1	20.5	9.8	8.8
OS	62.7	48.7	15.9	10.0
Type of resection	Total gastrectomy with partial hepatectomy	Total gastrectomy	Total gastrectomy	Total gastrectomy with distal pancreatectomy
LN dissection	D2	D2	D2	D2
Residual tumor	No	No	Yes (retroperito-neum)	Yes (mesocolon)

LN: lymph node; OS: overall survival; PFS: progression free survival; PR: partial response.

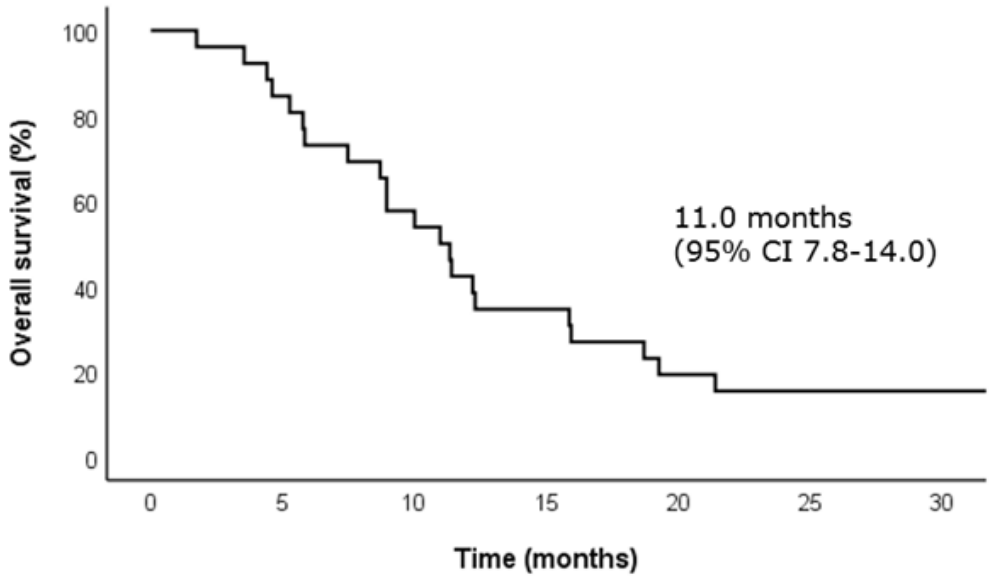

Figure 1. Kaplan-Meier analysis for overall survival (OS). In survival analysis, the median OS was 11.0 months (95% CI 7.8-14.0 months) in the ITT (intention-to-treat) population.

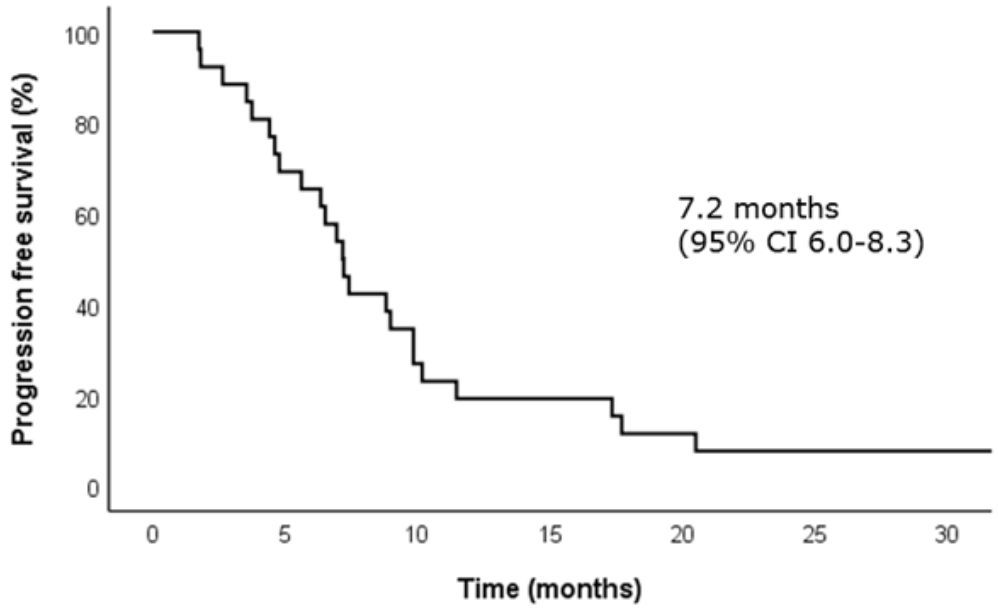

Figure 2. Kaplan-Meier analysis for progression free survival (PFS). In survival analysis, the median PFS was 7.2 months (95% CI 6.0-8.3 months) in the ITT (intention-to-treat) population.

4. Discussion

The best choice of first-line chemotherapy in patients with HER-2 negative AGC is still debated, although a platinum-based regimen is generally used in clinical practice with scientific evidences. Wagner et al. (10) reported that a significant survival benefit with the combination chemotherapy compared with single agent chemotherapy. In addition, triplet regimen combination chemotherapy such as docetaxel based regimen (DCF) showed a better survival than a doublet regimen chemotherapy, but with a higher grade of hematologic toxicity (4). Veer et al. also showed that taxane based triplet regimen (taxane, fluorouracil and cisplatin, or oxaliplatin) was better efficacy for PFS than a doublet regimen (11). One of the triplet regimen for AGC, the original DCS therapy was first conducted by Takayama et al. with a very good response rate of 88%, but it also had severe toxicities (7). Hence, we used modified dose of docetaxel that was evaluated in a multicenter phase III study for AGC and in a phase II study in preoperative chemotherapy for gastric cancer with extensive lymph node metastasis (12,13).

We conducted to investigate the clinical efficacy of DCS and the degree of adverse event after dose modification for docetaxel in a DCS regimen. A previous phase II study described the high clinical efficacy of a DCS regimen with 87.1% ORR showing 7.5 months of PFS and 22.9 months of OS (8). However, toxicities were also high, with incidences of 77.4% for neutropenia and 35.5% for anorexia, as the most common grade 3/4 hematologic and non-hematologic toxicities, respectively (8). In this study, the modified DCS also showed a high clinical efficacy with 65.4% ORR including one case of CR and 15.3% for a conversion

surgery. The median PFS (7.2 months) was not inferior to that of DCS (7.5 months). Neutropenia, the most common grade 3/4 toxicities, were present in 23.1% of patients, less toxic than previous DCS (77.4%), and grade 3/4 febrile neutropenia was not present in modified DCS. In addition, neutropenia was usually short lasting, and its incidence was reduced by prophylactic G-CSF. Non-hematological toxicities also showed a trend of reduced toxicity. Grade 3/4 diarrhea was observed in 15.4% of patients (16.1% for DCS), nausea and vomiting in 7.7% of patients (32.3% for DCS), and anorexia in 3.8% of patients (35.5% for DCS). Although each of three drugs had the shared myelosuppressive effect, these finding suggests that dose reduction of decetaxel had relieving effects of hematologic and non-hematologic toxicities. In addition, despite the high development of toxicities, the median cycles of DCS regimen was 6 with favorable compliance. Hence, dose modification for decetaxel in DCS regimen had a positive effect in both hematologic and non-hematologic toxicities, representing equivalent efficacy and less toxicity in patients with advanced gastric cancer.

In a phase I study with DCS regimen which was designed to evaulate the optima dose and DLT, the recommended dose of cisplatin was determined to be 70 mg/m^2 (14). However, the reduced dose of cisplatin with 60 mg/m^2 was used in the present phase II study, since other phase II study of DCS therapy reported that grade 1 or higher renal dysfunction occurred in 26% of the patients (15). This reduced dose of cisplatin was related to less toxicity, with no change in the response rate.

Generally, high ORRs achieved by various other combination regimens for AGC have failed to translate into major survival benefits (16-18). In this study, the median OS was estimated to be 11 months, which is inferior and disappointing compared with that reported for the DCS

regimen (22.9 months). In the original DCS study, good survival data may be partly influenced by adjuvant surgery performed in 29.0% of the patients. The survival benefit of chemotherapy followed by radical surgery in the conversion from unresectable to resectable gastric cancer has been reported. Triplet combination chemotherapy was developed as a regimen with high antitumor effect. Conversion therapy combined with intensive chemotherapy is a strategy that looks promising as a possible cure for unresectable AGC. These findings suggest that a triplet DCS regimen is suitable for attempting conversion therapy with a high anti-tumor effect sufficient to eliminate distant metastasis, including micro-metastasis. In our study, two patients received curative conversion therapy, they showed survival benefit over two years. DCS with a reduced dose of docetaxel may offer short-term control of AGC, and influence sequential curative conversion therapy by its high disease control capacity.

Our study has some limitations. Primarily, we did not successfully recruit and retain enough patients. This may lead to a reduced statistical power. Second, our patients were young and had a relatively good general status, as only one patient had a performance status of 2. Third, three patients had to discontinue use of S-1 because of grade 3/4 fatigue and diarrhea, and they received increased doses (130%) of docetaxel and cisplatin doublet therapy for 3 of 6 cycles.

In conclusion, modified DCS triplet combination chemotherapy, using a reduced dose of docetaxel (40 mg/m^2), appears to be effective as a first-line treatment in AGC and has an acceptable safety profile, but close monitoring of adverse events is also needed. The high response rate and long PFS of this regimen enabled treatment with a curative intent, even in a metastatic setting. To confirm the therapeutic practicality of modified DCS regimen for the first-line chemotherapy of

patients with AGC, we should further evaluate long-term patient safety and survival in DCS therapy with longer follow-up times and larger sample sizes.

5. Summary

With the high prevalence of AGC, it remains a common cause of cancer-related mortality worldwide. Systemic chemotherapy is regarded as the main treatment option for AGC with the survival benefit. Although triple agents chemotherapy in AGC have been active and many trials have been performed, there is no accepted first-line treatment against AGC. To achieve best response rate with minimal DLT, we conducted a phase II study of triple combination chemotherapy with modified DCS, using a reduced dose of docetaxel. This trial was a single-arm phase II study evaluating triplet combination chemotherapy with DCS in AGC patients who were not treated with chemotherapy except adjuvant chemotherapy. In survival analysis, the median PFS was 7.2 months and the median OS was 11.0 months in the ITT population. The common hematologic toxicities were anemia, neutropenia, and thrombocytopenia. No patient experienced grade 3 or 4 febrile neutropenia. All treatment related toxicities resolved with appropriate management, and no treatment related deaths occurred. The combination chemotherapy with modified DCS may be less toxic and was effective for patients with AGC.

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Phase II Study of Decetaxel, Cisplatin, and S-1 Triplet Combination Chemotherapy in Patients with Advanced Gastric Cancer

Jang, Won Young

Department of Internal medicine
Graduate School

Keimyung University

(Supervised by Professor Kim, Jin Young)

(Abstract)

Despite the worldwide adoption of two-drug fluorinated platinum-based chemotherapy as optimal initial chemotherapy for advanced gastric cancer (AGC), there is uncertain benefit for adding a third chemotherapy agent. To reduce the incidence of adverse events, we conducted a phase II study of modified triplet regimen using docetaxel, cisplatin, and S-1 (DCS), using a reduced dose of docetaxel. This was a single-arm phase II study evaluating triplet combination chemotherapy with DCS in AGC patients who were not treated with chemotherapy. Of the 26 patients, 25 patients were eligible for response evaluation. The confirmed ORR was 65.4% and disease control rate was 92.3% in the intention-to-treat (ITT) population. The median time to response was 1.4 months (95% CI

1.1-1.7 months) and median duration of response was 5.6 months (95% CI 1.7-12.9 months). At the time of survival analysis, the median PFS was 7.2 months (95% CI 6.0-8.3 months), and the median OS was 11.0 months (95% CI 7.8-14.0 months) in the ITT population. Grades 3 or 4 included adverse events of neutropenia (23.1%), diarrhea (15.5%), and anemia (11.5%). In conclusion, modified DCS triplet combination chemotherapy, using a reduced dose of docetaxel, was effective against AGC with less toxicity.

진행성 위암 환자에서 Doxetaxel과 Cisplatin과 S-1 복합화학요법에 대한 2상 임상 연구

장 원 영
계명대학교 대학원
의학과 내과학 전공
(지도교수 김 진 영)

(초록)

위암은 전 세계적으로 5번째로 흔하며 3번째로 사망률이 높은 암으로 알려져 있다. 본 연구의 목적은 진행성 위암에 있어서 아직 효과가 잘 알려지지 않은 3제 복합화학요법 중 하나인 docetaxel, cisplatin, 그리고 S-1(DCS) 치료의 효과를 알아보고, docetaxel 용량 조절을 통하여 약제 부작용의 빈도 감소여부에 대하여 확인해보고자 함이다. 본 연구는 2011년 7월부터 2016년 6월까지 계명대학교 동산의료원에 내원한 환자 중 진행성 위암으로 진단을 받은 환자를 대상으로 실시하였다. 총 26명의 환자가 연구기간에 포함되었고 이 중 반응평가는 25명의 환자에서 시행되었다. 분석 대상군 중 치료에 대한 전체 반응률은 65.4% 이었으며, 질병 조절률은 92.3%로 나타났다. 생존분석에서 전체생존기간의 중앙값은 11개월이었고, 무진행 생존기간의 중앙값은 7.2개월로 나타났다. 등급 3 or 4의 부작용은 호중구 감소증이 23.1%, 빈혈이 11.5%, 설사가 15.5%로 나타났다. 진행성 위암 환자에서 용

량 조절된 DCS 치료의 효과를 확인할 수 있었고, 부작용의 빈도가 감소함을 확인할 수 있었다. 이러한 결과를 토대로 약제 부작용에 대한 적절한 모니터링과 관리를 통해 부작용을 줄이고 복합항암요법의 효과를 극대화 하는데 대한 추가 연구가 필요할 것으로 생각된다.

□ 저자 약력

1986년 대구 출생
계명대학교 의과대학 의학과 졸업
계명대학교 대학원 의학과 석사
계명대학교 동산의료원 소화기내과 전임의
계명대학교 동산의료원 소화기내과 임상조교수 (현)

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