Infusional 5-Fluorouracil, Etoposide, and Cisplatin(FEP) in advanced and relapsed gastric cancer

Joohyuk Sohn

Department of Medicine
The Graduate School, Yonsei University

Infusional 5-Fluorouracil, Etoposide, and Cisplatin(FEP) in advanced and relapsed gastric cancer

Directed by Professor Hyuncheol Chung

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Joohyuk Sohn

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This certifies that the Master's Thesis of

Joohyuk Sohn is approved.

Thesis Supervisor: Hyuncheol Chung

Jaekyung Roh: Thesis Committee Member#1

Sunghoon Noh: Thesis Committee Member#2

The Graduate School Yonsei University

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Abstract

Infusional 5-Fluorouracil, Etoposide, and Cisplatin(FEP) in advanced and relapsed gastric cancer

Joohyuk Sohn

Purpose: We evaluated the efficacy and tolerability of the combination chemotherapy including infusional Fluorouracil(5-FU), Etoposide, and Cisplatin in patients with advanced/relapsed gastric cancer.

Patients and Methods: A total of 89 patients with advanced/relapsed gastric cancer were enrolled between 1990.7-2000.9 for the study. Primary endpoints were progression-free and overall survival. Secondary endpoints were response rate, response duration, and toxicity. Patients were either recurred after curative surgery or finished on a palliative surgery. The treatment schedule was as following: 5-FU 1000mg/m^2 and Etoposide 100mg/m^2 were delivered for 3 consecutive days and Cisplatin 80mg/m^2 on day2, which was repeated every 3weeks.

Results: The median time to progression and overall survival was four and eight months, respectively. One year progression-free and overall

survival rates were 10% and 33%, respectively. The overall response rate for 25 eligible patients with measurable disease was 20%(5/25, CR 2, PR 3) with median response duration of 7 months. Median ADIs of 5FU, Etoposide, and Cisplatin were 700 mg/m^2/week, 70 mg/m^2/week, and 21 mg/m^2/week, respectively. Median RDIs of 5FU, Etoposide, and Cisplatin were 0.70, 0.70, and 0.63 respectively. All the prognostic factors including performance status, initial relapse site, age, gender, histology, previous chemotherapy history, and palliative surgery were not significant in the univariate analysis. Hematologic and nonhematologic toxicities were tolerable.

Conclusion: FEP regimen showed similar therapeutic results and acceptable toxicity to the other combination studies. This regimen could be used as one of the options for advanced gastric cancer chemotherapy for the patients who couldn't be a candidate for doxorubicin-based regimens.

Key Words: gastric cancer, 5-fluorouracil, etoposide, cisplatin

Infusional 5 - Fluorouracil, Etoposide, and Cisplatin(FEP) in advanced and relapsed gastric cancer

Directed by Professor **Hyun Cheol Chung**

Department of Medicine
The Graduate School, Yonsei University

Joo Hyuk Sohn

I . INTRODUCTION

Gastric carcinoma is the most common cancer and leading cause of death in Korea. Though it is increasing to detect an early gastric cancer according to increased frequency of gastroscopy, locally advanced or metastatic gastric cancer still remains a greater portion at diagnosis. Our institute has been performing radical gastrectomy with extended regional lymph dissection (D2 resection) as a standard operation in a patient with advanced gastric cancer.[1]

5 - FU has demonstrated improvement of overall survival and quality of life in patients with advanced gastric cancer compared with best supportive care[2, 3]. Since MacDonald et al. has reported 42% response rate with the combination of 5 - FU, Doxorubicin, and Mitomycin (FAM) in

1980[4], FAM combination chemotherapy was a standard regimen for comparative analysis in several phase III trials.[5, 6] But, not only subsequent several reports have not shown response rate as high as an initial report[5], but also no survival benefit has been demonstrated compared to 5-FU alone.[6]

Since 1983, cisplatin appeared as a chemotherapeutic agent with a modest efficacy against disseminated gastric cancer. It showed about 25% response rate as a single drug, [7] and was combined with other drugs producing FAP (5-FU, Doxorubicin, Cisplatin), ECF(Epirubicin, Cisplatin, 5-FU), and EAP(Etoposide, Doxorubicin, Cisplatin) combination regimens. FAP showed 19-50% response rate in several studies[8, 9] and ECF produced at least as good as those achieved with the FAP regimen.[10] In particular, ECF regimen in which 5-FU was administered as a protracted venous infusion showed better survival benefit and response rate over FAMTX (5-FU, Doxorubicin, Methotrexate) regimen and was insisted to be regarded as a standard regimen in advanced gastric cancer.[10]

Etoposide, an inhibitor of topoisomerase II was initially used as combination chemotherapy for advanced gastric cancer. EAP (Etoposide, Doxorubicin, Cisplatin) regimen was initially reported as a response rate

up to 60-70%, but showed a severe hematologic toxicity especially neutropenia.[11, 12] And it's subsequent phase III study comparing with FAMTX showed overall response rate of 20% with a median survival of 6.1 months.[13]Another combination, ELF(Etoposide, Leucovorin, 5-FU) was reported as an overall response of 53% with a median survival of 11.0 months[14], but showed no survival benefit over FAMTX or FP(5-FU, Cisplatin) regimens in a recent trial.[15]

Even though 5-FU, Etoposide, and Cisplatin showed modest activity in lots of combination trials, FEP combination has rarely been reported since Ajani et al. had reported small numbered phase II study in 1991.[16-18] There were reports about synergistic effects between not only etoposide and cisplatin but also 5-FU and cisplatin in an experimental models.[19-21]

Based on these background, our institute has used FEP (5-FU, Etoposide, Cisplatin) regimen for relapsed gastric cancer patients after radical operation (with or without adjuvant chemotherapy, mostly 5-FU and Doxorubicin),[1] and palliatively resected patients. This study was designed to evaluate the treatment efficacy and feasibility of FEP combination chemotherapy in patients with advanced/relapsed gastric cancer.

II. PATIENTS AND METHODS

1. Patient Eligibility

We designed to perform FEP regimen for the relapsed patients after curative surgery (with or without adjuvant chemotherapy) and palliatively resected patients. Relapse was documented by tissue biopsy whenever possible or by CT scan. “Palliative operation” included palliative resection or bypass surgery. Palliative resection was defined as the surgical resection of a primary tumor (D2 type resection) either when the residual tumors remained grossly in the neighboring organs, lymph nodes, peritoneum, or when the tumors remained microscopically in the resection margin.[22]

Eligibility criteria were as follows: age ≤ 75 years; histologically proven adenocarcinoma; performance status of grade 0 - 2 according to the Eastern Cooperative Oncology Group scale, adequate baseline organ function (WBC count ≥ 4 000 cells/μL, platelet count ≥ 100, 000 cells/μL, serum bilirubin level ≤ 2 mg/dL, and serum creatinine level ≤ 1.5 mg/dL); no concurrent uncontrolled medical illness. Eighty - nine patients were enrolled between July 1990 and September 2000. All the patients were grouped as follows. 1) Relapsed patients who have been treated with

curative gastrectomy and adjuvant chemotherapy (54 patients). 2) Relapsed patients who have been treated with curative gastrectomy alone (9 patients). 3) Palliatively operated patients due to locally advanced disease (26 patients) (Table 1).

2. Chemotherapy Schedule

The FEP chemotherapy was commenced according to the following schedule within 4 weeks after the patients were diagnosed as recurred or palliatively resected. Continuous IV infusion of 5-FU at a dose of 1000mg/m^2 and etoposide at a dose of 100mg/ m^2 intravenously for 120 min were administered for 3 consecutively days and cisplatin 80mg/m^2 was given as a 1-hour infusion with adequate hydration on day 2. The cycles were repeated every 3week. Prophylactic antiemetics were given according to local policy. Since 1994, granulocyte colony-stimulating factor (G-CSF) has been used not on a prophylactic but a therapeutic purpose. Chemotherapy was continued until the disease progression or the patient's refusal (maximum 12 cycles).

3. Toxicity

Toxicity was evaluated and graded according to WHO criteria. The

dose was reduced by 25% when there was grade III/IV nonhematologic toxicity or grade III/IV hematologic toxicity existed with fever or sustained more than one week. Subsequent cycle was delayed until complete recovery of the toxicity.

4. Response and follow up

During the course of chemotherapy, patients were given physical examinations and complete blood counts. At the end of every 3 cycles, response evaluation was performed that included chest X-ray, abdominopelvic computed tomography scan or radiological ultrasonography, bone scan, liver function test. During the follow-up period, any suspected recurrence was confirmed by biopsy, if possible. Typical nodules in liver or lung by image studies, and lytic areas in the radioisotope bone scan and plain X-ray were considered as recurrence without histologic confirmation. We used telephone and postcards in query for the follow-up of lost patients. The median follow-up duration was 6 months (range, 1-54 months).

The primary endpoints of the study were progression-free survival and overall survival. Progression-free survival was defined as the time from the start of chemotherapy to the progression of cancer. Overall

survival was defined as the time from the start of chemotherapy to the date of death or to the last follow-up date. Deaths from all causes were considered in the analysis of overall survival.

The secondary endpoints were response rate, duration and toxicity. Response rate and duration were obtained when a measurable lesion was present. The objective responses to treatment, which includes complete remission, partial remission, stable disease, and progressive disease, were defined by the WHO criteria. Only patients with bi-dimensionally measurable mass (eg, hepatic or lung metastasis or lymph node) more than 20mm × 20 mm were considered assessable for objective response.

5. Actual Dose Intensity and Relative Dose Intensity

Actual dose intensity was defined as the amount of administrated dose per week and calculated as below.

$$\text{ADI } (\text{mg/m}^2/\text{week}) = \frac{\text{total delivered dose of each drug}(\text{mg/m}^2)}{\text{chemotherapy duration}(\text{week})}$$

Relative dose intensity (RDI) implies that actual dose intensity versus planned dose intensity. It was calculated by dividing the ADI by the

planned DI. Mean dose intensity of FEP regimen was calculated.

6. Statistics and Data Analysis

Survival curves were analyzed using the Kaplan-Meier method. The significance of survival difference between groups was analyzed by the log-rank test. In order to identify prognostic factors and the risk associated with them, univariate and multivariate analyses were performed using the Cox regression analysis model.

III. RESULTS

1. Patients Characteristics

A total of 89 patients were enrolled in this study. The median age of the patients were 52 years (range;18 - 75). ECOG performance status was 0 – 1 in 80 patients and 2 in 9 patients. Stage III was the most frequent initial cancer stage in relapsed patients. Poorly differentiated adenocarcinoma was most common in either relapsed or palliatively operated groups, followed by moderately differentiated and signet ring cell type. Peritoneal recurrence was the most common initial presentation followed by hematogenous recurrence in relapsed patients. The detailed patient characteristics are listed in Table 1.

Table. 1. Patient Characteristics

Characteristic	Relapsed Group		Palliative surgery group	Total
	Previous adjuvant chemotherapy group (n = 54)	No adjuvant chemotherapy group (n = 9)	(n = 26)	(n = 89)
Gender (M:F)	39:15	6:3	16:10	61:28
Age, years				
Median	50	53	53	52
Range	29 - 72	36 - 68	18 - 75	18 - 75
ECOG				
0 - 1	47	8	25	80
2	7	1	1	9
Stage when diagnosed				
I	2	5	0	7
II	8	1	0	9
III	27	2	3	32
IV	17	1	23	41
Differentiation (Histology)				
Well	3	0	1	4
Moderate	11	1	5	17
Poor	29	7	16	52
Signet ring cell	10	1	3	14
Mucinous	1	0	1	2
Undifferentiated	0	0	0	0
Initial recur site				
Local	5	2	-	7
Peritoneal	20	3	-	23
Hematogenous (liver, lung, bone)	14	2	-	16
Lymph node	10	1	-	11
Multiple sites	5	1	-	6

2. Progression-free and Overall Survival

Among the total 89 patients, 3 patients stopped chemotherapy due to patients' refusal and 6 patients could not continue the chemotherapy because of the side effects. At the time of the last follow-up date, 76 patients have progressed and 5 patients have not. The median progression-free survival duration of the total patients was 4 months (95% CI; 3-5 months) (Fig. 1).

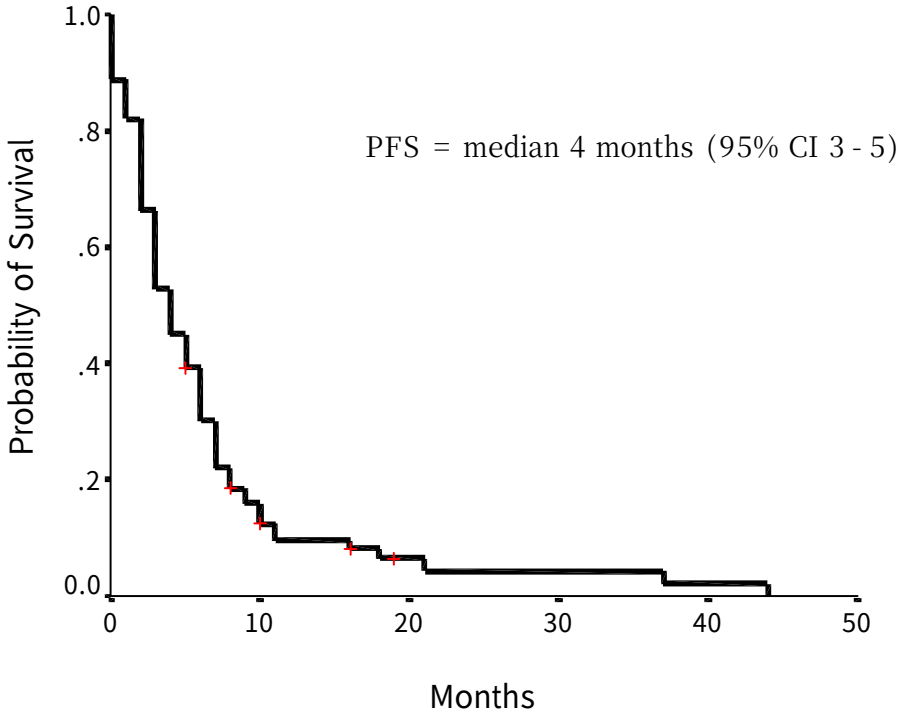

Figure 1. Progression-free survival curves of the total patients (n=89)

The progression-free survival duration of the each different group was expressed in Fig. 2. The median progression-free survival duration was 3 months (95% CI, 2 to 4 months) for the relapsed group with previous chemotherapy, 2 months (95% CI, 1 to 3 months) for the relapsed group without previous chemotherapy, and 6 months (95% CI, 4 to 8 months) for the palliatively operated group (Fig.2). The 6 months progression-free survival rate of the total patietns were 30% with the subgroup results as following; 23% for relapsed patients and 48% for palliatively operated patients.

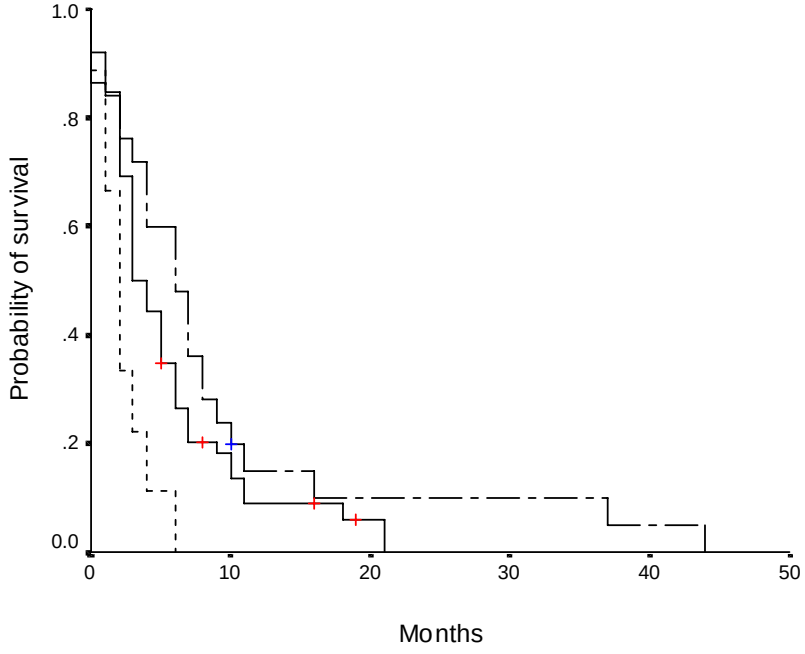

Figure 2. Progression free survival curves of the total patients according to treatment groups

——— Recurrent cancer group with previous chemotherapy (n=52): 3 mo.

- - - - - Recurrent cancer group without previous chemotherapy (n=9): 2 mo.

—·— Post palliative chemotherapy group (n=26): 6 mo.

The median overall survival duration of the total 89 patients was 8 months (Fig. 3). The results of the subgroups were 8 months (95% CI, 5.2 to 10.8 months) for relapsed group with previous chemotherapy, 7 months for relapsed group without chemotherapy (95% CI, 0 to 21 months), and 9 months (95% CI, 7.0 to 11.0 months) for palliatively operated patients (Fig. 4). But, there was no significant difference between relapsed and palliatively operated group in terms of overall survival (P value = 0.33, by log rank test). The one year overall survival rate of the total patients was 34% with little difference between relapsed and palliatively operated group.

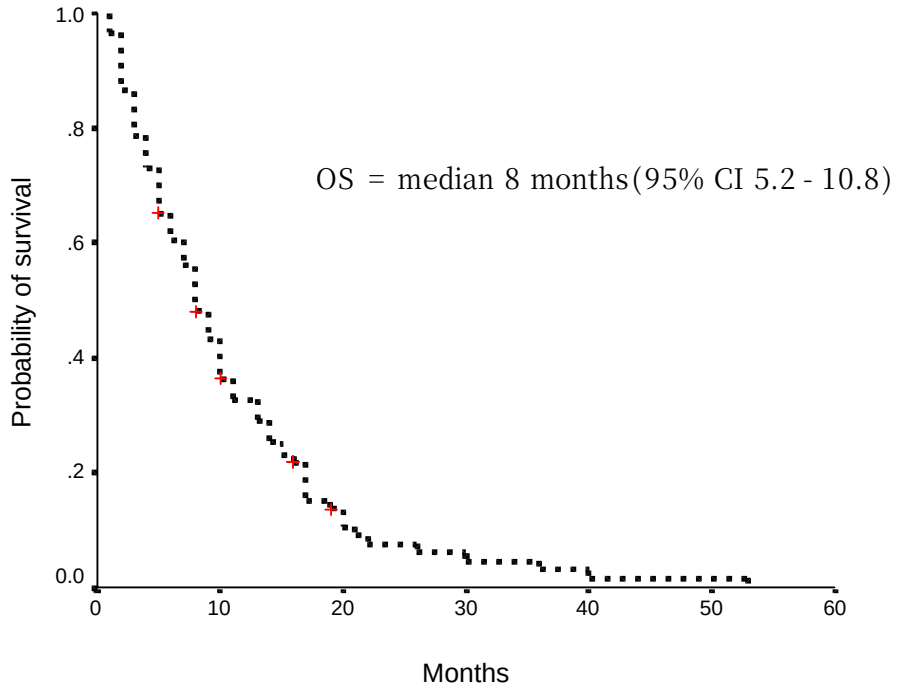

Figure 3. Overall survival curves of the total patients (n=89)

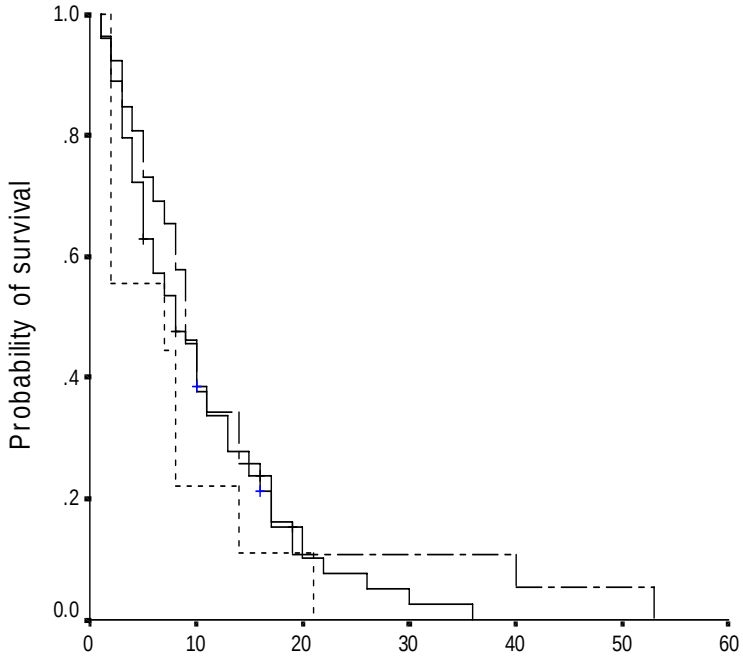

Figure 4. Overall survival curves of the total patients according to treatment groups

——— Recurrent cancer group with previous chemotherapy (n=54): 8mo.

– – – – Recurrent cancer group without previous chemotherapy (n=9): 7mo.

—·— Post palliative chemotherapy group (n=26): 9 mo.

3. Response rate

Twenty-five patients had a measurable lesion and the other 64 patients did not. The best response to treatment for the 25 patients who had a measurable lesion among the total of 63 relapsed patients is presented in Table 2. The response rate was 20% (5/25). Two complete responses and three partial responses were observed. The median response duration was 7 months (range, 4 – 24 months). All the responsive patients had lymph node recurrences (3 para-aortic, 2 supra-clavicular lymph nodes) (Table 2).

Table 2. Treatment efficacy in patients with measurable lesion

	Relapsed Group			
	Previous chemotherapy group	No adjuvant chemotherapy group	Palliative Op. group	Total
CR	2	0	-	2
PR	3	0	-	3
SD	6	1	-	7
PD	10	3	-	13
Response rate	5/21	0/4	-	5/25
Response duration (median)	7 mo.	-	-	7mo.
(range)	(4 - 24)			(4 - 24)

4. Toxicity

The toxicities of the FEP regimen were generally tolerable and reversible. Nonhematologic toxicities such as nausea, vomiting, mucosities, alopecia, and diarrhea were the mainstay of the toxicities. Hematologic toxicities were not significant as shown in Table 3. There was one treatment-related death due to septic shock. There were another six treatment-related complications such as 2 neuropathies, 1 nephrotoxicity, 2 septic shock, and 1 microangiopathic hemolytic anemia, which had made their patients fail to continue FEP chemotherapy further. One of the two patients who had been complicated with septic shock, has come to the treatment-related death.

Table 3. Hematologic toxicity

		Relapsed Group			
		Previous chemotherapy group (n=54)	No adjuvant chemotherapy group (n=9)	Palliative operation group (n=26)	Total (n=89)
Anemia	1	4(7.4)	1(11.1)	2(7.7)	7(7.4)
	2	9(16.7)	2(22.2)	3(11.5)	14(14.7)
	3	3(5.6)	1(11.1)	0(0.0)	4(4.2)
	4	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Neutropenia	1	3(5.6)	0(0.0)	3(11.5)	6(6.3)
	2	11(20.4)	0(0.0)	6(23.1)	17(17.9)
	3	5(9.3)	1(11.1)	1(3.8)	7(7.4)
	4	1(1.9)	0(0.0)	0(0.0)	1(1.1)
Thrombocytopenia	1	1(1.9)	0(0.0)	0(0.0)	1(1.1)
	2	3(5.6)	0(0.0)	0(0.0)	3(3.2)
	3	0(0.0)	0(0.0)	1(3.8)	1(1.1)
	4	0(0.0)	0(0.0)	0(0.0)	0(0.0)

5. Dose Intensity

The median number of cycle of the total patients was four (range, 1 – 12). In subgroup analysis, the median number of cycle was 4 (range, 1 - 12) in relapsed group and 5 (range, 1 - 11) in palliatively operated group. The median chemotherapy duration of the total patients was 18 weeks (range, 3 – 54). Dose reductions were done in 10 cases due to either hematologic or nonhematologic toxicities. There was no cancer-unrelated death during and after the chemotherapy. Twelve patients have been treated on another chemotherapy after FEP chemotherapy because of disease progression. Dose intensites of each drug are as follows; 5-FU 702 mg/m^2/week, Etoposide 70.2 mg/m^2/week, and Cisplatin 21.1 mg/m^2/week. The median dose intensity of the FEP combination regimen was 0.67. Dose intensity and relative dose intensity are listed in Table 4. Relative dose intensity and chemotherapy cycle number were inversely correlated. Median RDI of the patients who has been treated on chemotherapy repeatedly has decreased until the cycle number 9, but the patients who have been treated more than 10 cycles showed relatively high RDI.(Fig.5.)

. Table 4. Dose intensity and Relative dose intensity

	Dose intensity (mg/m^2/week)	Relative dose intensity
5 - FU	702 (406 - 1000)	0.70(0.4 - 1.0)
Etoposide	70.2(40.6 - 100)	0.70(0.4 - 1.0)
Cisplatin	21.1(12.3 - 34.5)	0.63(0.4 - 1.0)
FEP	-	0.67(0.4 - 1.0)

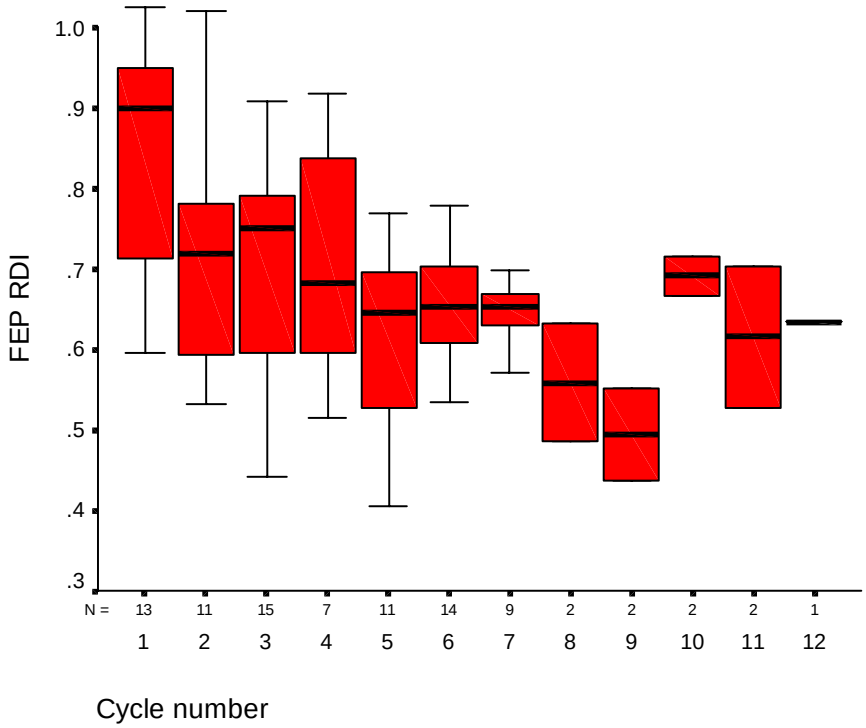

Figure 5.Relative dose intensities of the FEP chemotherapy corresponding to cycle numbers.
(N; number of patients who have completed the cycle of FEP chemotherapy.)

6. Prognostic factors for survival

Univariate and multivariate analyses of prognostic factors for both progression-free and overall survivals were accomplished. All the factors including performance status, age, gender, histology, response, relative dose intensity, previous chemotherapy and surgery type were not significant in terms of both progression-free (Table 5), and overall survivals (Data not shown).

Table 5. Prognostic factors for progression-free survival

	Univariate analysis (p value)
ECOG (0,1 vs 2)	0.39
Initial relapsed site (local recur vs metastasis)	0.23
Age(>50 vs <50)	0.32
Gender(M vs F)	0.43
Histology (adenocarcinoma vs others)	0.40
Previous chemotherapy history	0.59
Recurrent vs Palliative operation	0.07

IV. DISCUSSION

In a phase II clinical trial, advanced gastric cancer is not an easy tumor to study treatment response, because most of the patients presents or relapse as a peritoneal carcinomatosis. In these cases, it is hard to find a measurable lesion and to evaluate the treatment response. Moreover, lung and liver metastasis usually occur when the patients have a so poor performance status that they could not be involved in a clinical trial. Considering these points, we adapted a progression-free survival and overall survival as primary endpoints. Under these circumstances, we have enrolled two kinds of patients, which were composed of relapsed or palliatively operated patients.

5-FU, mitomycin, doxorubicin, cisplatin, etoposide, and methotrexate are the active drugs in advanced gastric cancer as a single agent showing the modest efficacy range of 11 – 30% with short response duration.[16] Their combinations showed better results in various regimens in phase II trials. However, results observed in subsequent randomized trials were less convincing with response rates staying in the range of 20-25%, with median time to progression not exceeding 5 months. Thereafter, there has been no outstanding regimen fulfilling the requirements, which are a total response rate (CR + PR) more than 50% with prolonged response duration, median overall survival time more than 12 months and CR rate

more than 10%. Our results have not reached to these criteria to be a standard regimen in advanced and relapsed gastric cancer. But as the National Comprehensive Cancer Network has proposed, 5-FU or cisplatin based combinations could be used as an acceptable regimen for advanced gastric cancer, [26] especially, in patients to whom doxorubicin could not be administered. Cisplatin has been reported to be also effective in advanced gastric cancer patients who already pre-treated with other active agents.[27, 28]

It has been difficult to access which combination regimen is most effective in advanced gastric cancer. FAMTX regimen was initially reported 58% of response rate, with subsequent modest response of 30-40%. EAP regimen showed 64% of initial response rate. But, subsequent studies found it to be less active with high rate of toxicity. The EORTC FAMTX regimen showed 41% response rate comparing to 9 % in FAM. These results led clinicians to question the benefit of chemotherapy in advanced gastric cancer.

An impressive response rate of 71% with 12% complete response was obtained in a phase II trial with ECF regimen.[12] In a phase III trial comparing to FAMTX, ECF regimen showed superior response rate (45% versus 21%) and a superior median time to progression (7.4 months versus 3.4 months). However, only modest activity was observed with no

single combination was associated with a survival advantage when compared with the others in an EORTC phase III trial comparing 3 regimens; FAMTX, ELF, and FP.[15]

Our experience with combination of 5-FU, etoposide, and cisplatin would seem quite favorable for relapsed or palliatively operated gastric canrcinoma where 4 months of progression-free, and 8 months of overall survival duration, and 34% of one-year survival rate. These results were similar to previous other combinations such as ELF, FUP, FAMTX or ECF which were recently reported as median survival of 5.7-8.9 months and 21-36% of one-year survival in a large scaled randomized clinical trials.[10, 15]

In our cohorts, there are several considerable factors, which could act as an either positive or negative direction in terms of survival. First, 5-FU has already been used as adjuvant chemotherapy as a bolus (5-FU, Doxorubicin) in 54 relapsed patients. The combination of epirubicin, cisplatin, and prolonged infusion of 5-FU showed encouraging response rate in phase II trial (71%) and phase III trial (45%) comparing to FAMTX. In that phase III trial, one cisplatin and 5-FU (ECF) regimen was superior to FAMTX whereas another cisplatin and 5-FU (FP) regimen showed no benefit over FAMTx. One possible explanation of this paradox is a prolonged 5-FU infusion. Based on this data and the

experience of different action mechanism of 5-FU between bolus and infusion in colon cancer, we considered infusion of 5-FU as a positive factor even in patients with previous 5-FU bolus treatment. Second, Etoposide has been tried in metastatic gastric cancer patients with previous naive chemotherapy resulting in favorable outcomes. On the contrary, Japanese trial with etoposide showed poor response in gastric cancer patients with previous chemotherapy.[23] Third, palliative resection has shown beneficial effect on survival in locally advanced or metastatic gastric cancer.[22, 24, 25] Our institute has also reported the improved survival and quality of life with the combination of modified FAM chemotherapy plus palliative resection in a patients with advanced gastric cancer.[22] Better survival of the palliatively operated group compared to that of relapsed group could be explained by the lesser tumor burden due to surgery. "A" area in the Fig.2 and Fig.4 indicates the patients who have been undertaken a near radical surgery. Fourth, twelve patients had received second-line chemotherapy after progression with FEP, which might have benefit on survival with this treatment.

In gastric cancer, a correlation between dose escalation and tumor response has not validated yet. But a recent EORTC trial showed the importance of dose intensity and response rate, which suggested the importance of feasibility in each regimen. In that trial, the response rate

of FAMTX was only 12%, which was explained by the fact that only 57% of the patients received the intended dose of doxorubicin. ELF and FP regimen also showed 41% and 42% of compliance in each regimen. In our trial, as shown in Fig. 5, dose intensities have declined with the increase of chemotherapy cycle number. The median dose intensities of FEP were around 0.7, which suggest that toxicities were within acceptable range.

Under these backgrounds, It would be required that FEP be used for a randomized controlled phase III studies as a first or second line chemotherapy in patients with advanced gastric cancer. In addition, taxanes and irrontecan, that showed significant antitumor activity in advanced gastric cancer, [29 - 31] lacking cross - resistance to cisplatin and 5 - FU need to be evaluated further in randomized trials.

This study demonstrated that FEP regimen could be used to advanced and relapsed patients on a palliative aim. Comparable survival advantage and tolerable toxicity made us to design phase III studies comparing with FAM regimen, which is mostly used regimen in our institute. The fact that responses were prominent in lymph node metastasis also should be evaluated in the future

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국문요약

진행성 혹은 재발한 위암 환자에서 5-Fluorouracil, Etoposide, 그리고 Cisplatin(FEP) 정주요법의 효과

손 주 혁

연세대학교 대학원 의학과

(지도교수 **정현철**)

목적: 진행성 그리고 재발성 위암환자에서의 정주 5-Fluorouracil(5-FU), Etoposide, 그리고 Cisplatin 3 제 병용요법의 효능과 독성을 평가하고자 한다.

환자와 방법: 이 연구를 위해 1990.7-2000.9 사이에 진행성 그리고 재발성 위암 환자 89 명이 등록되었다. 일차적인 목표는 무 진행 생존기간과 전체 생존 기간이다. 이차적인 목표는 반응율, 반응기간 그리고 독성이다. 대상환자는 근치적 절제술 후 재발하거나 보존적 수술을 시행한 환자를 대상으로 하였다. 치료 계획은 다음과 같다.; 5-FU 1000mg/m^2과 Etoposide 100mg/m^2 는 3 일간 투여 되었고 Cisplatin 80mg/m^2 은 2 일째 투여 되었으며 이러한 치료는 3 주간격으로 반복되었다.

결과: 무진행 생존기간과 전체 생존기간은 각각 4 개월과 8 개월이었다. 1 년

무진행 생존율과 전체 생존율은 각각 10%와 33%였다. 측정 가능한 병변을 지닌 25 명의 환자의 반응율은 20%(5/25, 완전관해 2 명, 부분관해 3 명) 이었고 반응기간의 중앙값은 7 개월이었다. 5FU, Etoposide,와 Cisplatin 의 실제 용량 강도의 중앙값은 각각 700 mg/m^2/week, 70 mg/m^2/week, 그리고 21 mg/m^2/week 이었다. 5FU, Etoposide,와 Cisplatin 의 상대 용량강도의 중앙값은 각각 0.70, 0.70, 그리고 0.63 이었다. 수행상태, 처음 재발위치, 나이, 성별, 조직학적 분류, 전의 항암 약물 요법 유무 그리고 보존적 수술 유무 등 모든 예후인자를 단순변량 분석을 시행하였으나 통계학적으로 유의하지 않았다. 혈액학적 그리고 비혈액학적 독성은 심하지 않았다.

결론: FEP 병용요법은 지금까지의 다른 복합항암요법과 비교하여 유사한 치료 결과와 독성에 대한 순응도를 보였다. 이 요법은 doxorubicin 에 근거한 항암약물요법의 대상이 되지 않는 진행성 위암 환자에 있어서 하나의 치료 방법으로 사용될 수 있을 것이다.

핵심되는 말) 위암, 5 - fluorouracil, etoposide, cisplatin