A Long-term Survival Case of First Line FOLFOX, Second Line FOLFIRI Chemotherapy in Patient With Gastric Cancer Stage IV

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63세 남자 환자가 내원 수 개월 전부터 소화불량을 느껴 지역병원을 내원하여 시행한 내시경 소견에서 위암 진단 받았으나, 재검사 위해 내원 3주 전 연세의대 세브란스병원 내원하여 저분화형 위선암종, Borrman III형의 종괴가 위각부에 있고, 좌측 빗장위 림프절 전이가 있음을 진단받고 항암치료 권유받았으나, 연고지 관계로 고신대학교 복음병원 소화기내과로 전원되었다. 내원 당시 혈압 130/80 mmHg, 심박수 70회/분, 호흡수 20회/분, 체온 섭씨 36.6도로 측정되었고, 5년 전 양안 녹내장 수술받은 외에 특이과거력은 없었고, 동생이 위암으로 사망한 가족력이 있었다. 내원 당시 좌측 빗장위 림프절이 촉지되었고, 혈액검사에서는 AST 56 IU/L, ALT 64 IU/L, r-GTP 75 U/L로 상승된 이외에 특이사항이 없었다. CEA는 2.78 ng/ml, CA19-9은 26.54 U/ml였다. 입원하여 시행한 상부위장관 내시경 검사에서 위각부에 약 3×3 cm의 융기되고 중심부의 출혈을 동반한 궤양이 있는 Borrmann III형의 종괴가 관찰되었다. 조직검사에서 병리 판독은 adenocarcinoma, poorly differentiated 였고, 복부 CT에서는 내시경에서 관찰되었던 병변부위와 동일한 부위에 위벽이 두꺼워져 있었고, perigastric, paraaortic lymph node enlargement도 저명하게 관찰되었다. 병기는 진행성 위암 4기로 진단하여 palliative FOLFOX-4 항암치료를 2008년 1월 28일부터 2-3주 간격으로 시행하였고, 종괴의 크기가 점차 줄어들던 중 2009년 4월 21일 19차 FOLFOX-4 항암치료 시행 후 Oxaliplatin에 의한 severe thrombocytopenia (Platelet 2000/ul) 발생하여 FOLFIRI로 palliative chemotherapy regimen을 변경하였다. 2009년 5월 21일 1차 FOLFIRI 항암치료를 시작하였고, 전신쇠약감과 오심으로 인해 Irinotecan 용량을 75%로 감량하여 3-4주 간격으로 항암치료 진행하여 2012년 6월 4일에 41차 FOLFIRI 항암치료를 마쳤고, 복부 CT 추적검사와 위내시경 추적 검사항 원발 병소가 더 이상 관찰되지 않았다 PET CT에서는 좌측 빗장위 림프절에서 hypermetabolic 소견이 관찰되었다. 2013년 2월 14일 좌측 빗장위 림프절이 커져서 내원하여 동시항암화학방사선 치료를 시행하였다. 이후 흉부 CT에서 림프절 크기의 변화는 없었으나, PET CT에서 hypermetabolic uptake는 감소하였다. 2014년 3월 11일 경부 CT상 좌측 빗장위 림프절이 크기가 증가하여 다시 43차 FOLFIRI 항암치료를 시작하였고, 2014년 7월 현재 46차 FOLFIRI 항암치료를 진행 중이다.

Brief History : 63/M

• **C/C**

Dyspepsia for several months

• **P/I**

– 2007년 12월, 수 개월간의 소화불량으로 통영 세계로병원에서 위내시경 시행하여 위암 진단받고 추가 검사 위해 서울로 전원

– 2008년 1월 연세대 세브란스병원에서

AGC Borrmann III with Lt. supraclavicular node metastasis (adeno-carcinoma, poorly differentiated) 진단 후 항암치료 권유 받았으나, 연고지 관계로 08년 1월 24일 본원으로 내원함.

Brief History: 63/M

■ **Past History**

- DM/HTN/TB/Hepatitis (-/-/-/-)
- Glaucoma operation, 5 years ago

■ **Social History**

- Alcohol: (-)
- Smoking: (-)

■ **Family History**

- Brother, stomach cancer

Review of System

- **General**
  - General weakness/Fatigue/Weight loss (- /- /-)
- **Head and Neck**
  - Headache/Dizziness (- /-)
  - **Lt. neck node swelling/throat discomfort (+/+)**
- **Respiratory system**
  - Cough/Sputum/Dyspnea/DOE/Hemoptysis (- /- /- /- /-)
- **Cardiovascular system**
  - Chest pain/Palpitation (- /-)
- **GI system**
  - Anorexia/Nausea/Vomiting/Diarrhea/Constipation (- /- /- /- /-)
  - Acid regurgitaion/Epigastric soreness/Post prandial epigastric discomfort (- /- /-)
  - Hematemesis/Melena/Hematochezia (- /- /-)
  - Bowel habitus change/Tenesmus (- /-)
- **Urinary system**
  - Dysuria/Frequency/Hematuria/Norturia (- /- /- /-)

Physical Examination

- **General appearance**
  - Alert mentality/Not ill-being appearance
- **HEENT**
  - Sclera: non- icteric/Conjunctiva: not pale/Tongue : non-dehydrated
  - **Neck node: palpable, Lt**
- **Chest**
  - Symmetry, deformity (-)
  - Breath sound: clear/Heart sound: regular, murmur (-)
- **Abdomen**
  - Soft, normo-active bowel sound
  - Palpable liver or spleen (-) /Palpable mass (-)
  - Tenderness/Rebound tenderness (-/-)
- **Extremity**
  - Pretibial pitting edema (-/-)

Vital Sign

- BP: 130/80 mmHg
- HR: 78 회/분
- RR: 20 회/분
- BT: 36.6 ℃

Initial Laboratory Findings

- **WBC/Hb/Hct/PLT** 7,800/uL / 14.3 g/dL / 39.9% / 134,000/uL
- **BUN/Creatinine/Sodium/Potassium** 11 mg/dL / 1.0 mg/dL / 142 meq/L / 4.6 meq/L
- **Total Protein/Albumin** 6.9 g/dL / 4.0 g/dL
- **Total Bilirubin/Direct Bilirubin** 0.7 mg/dL / 0.3 mg/dL
- **Alk Phosphatase/r-GTP/AST/ALT/LDH** 75 IU/L / 75 U/L / 56 IU/L / 64 IU/L / 394 IU/L
- **PT/PTT** 10.3 sec / 28.6 sec
- **ESR/HS-CRP** 4 mm/hr / 0.27 mg/dL
- **CEA/CA19-9** 3.78 ng/ml / 26.54 U/ml

2008. 01. EGD & Pathology

• **EGD**

At the angle

a about 3*3cm sized

poorly circumscribed

infiltrating mass with ulceration

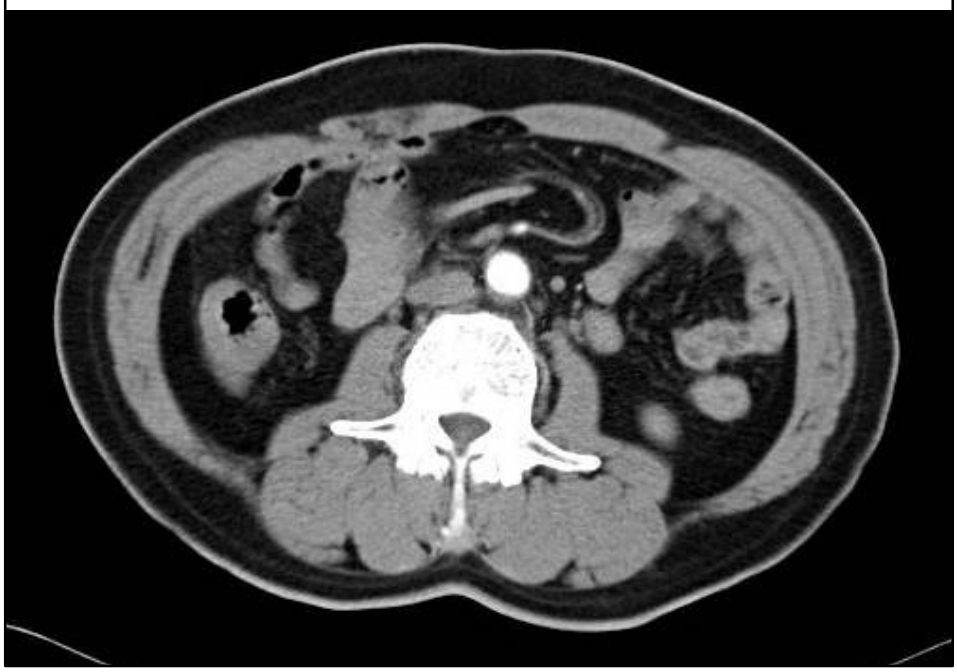
which margin blended into the surrounding mucosa and the base

infiltrated with cancer was noted

• **Pathology**

Adenocarcinoma, poorly differentiated

2008.01.28 Abd. CT



Routine Chemotherapy

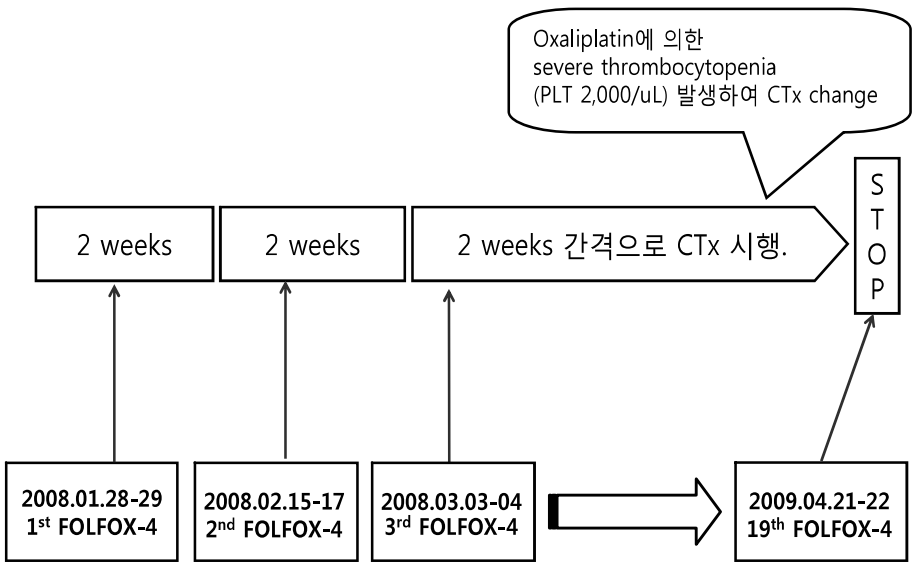
1st line, FOLFOX-4 chemotherapy

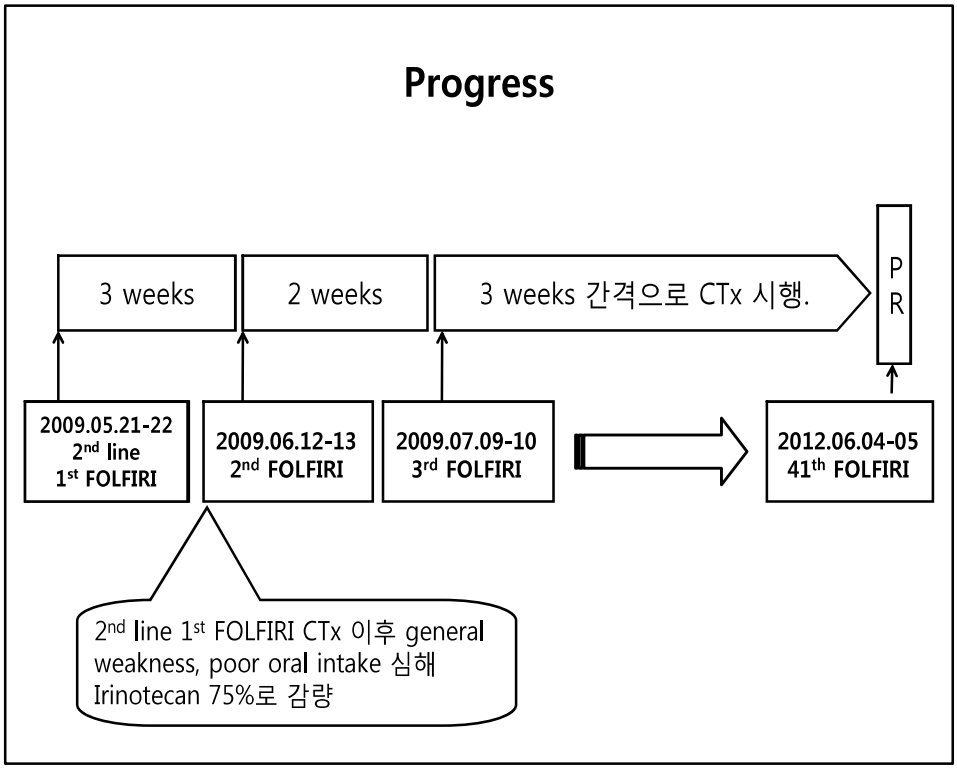
	D1	D2	-	D15
Oxaliplatin 85 mg/m^2 for 2 hrs	o		-	Next CTx.
Leukovorin 200 mg/m^2 for 2 hrs	o	o	-	
5-FU (Bolus) 400 mg/m^2 for bolus	o	o	-	
5-FU (Continuous) 600 mg/m^2 for 22 hrs	o	o	-	

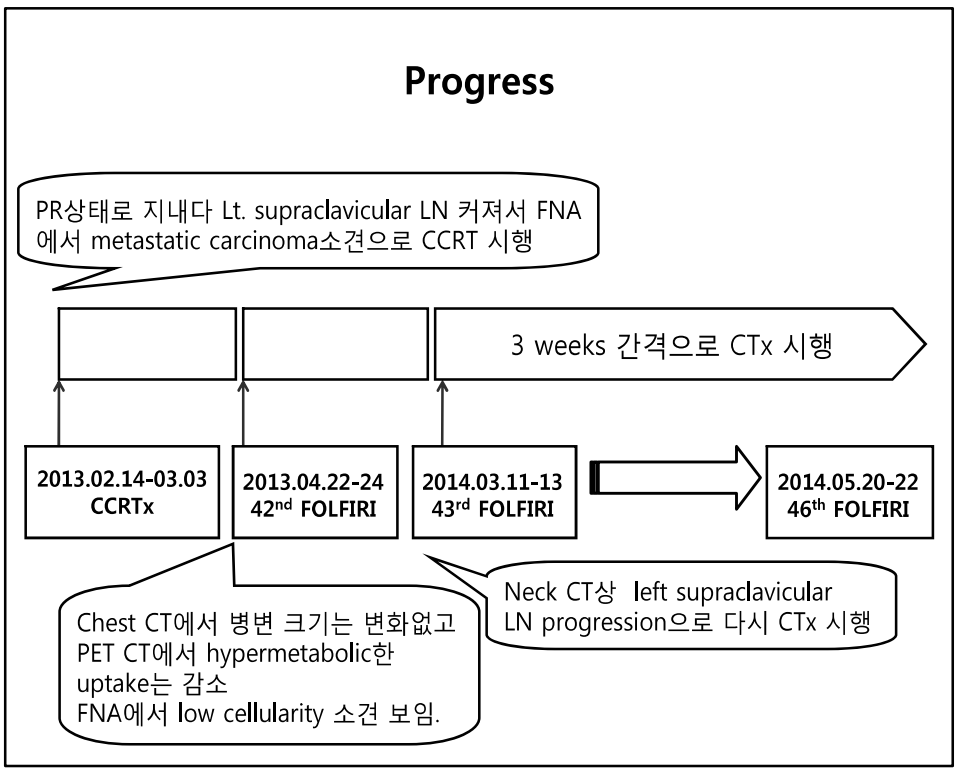
2nd line, FOLFIRI chemotherapy

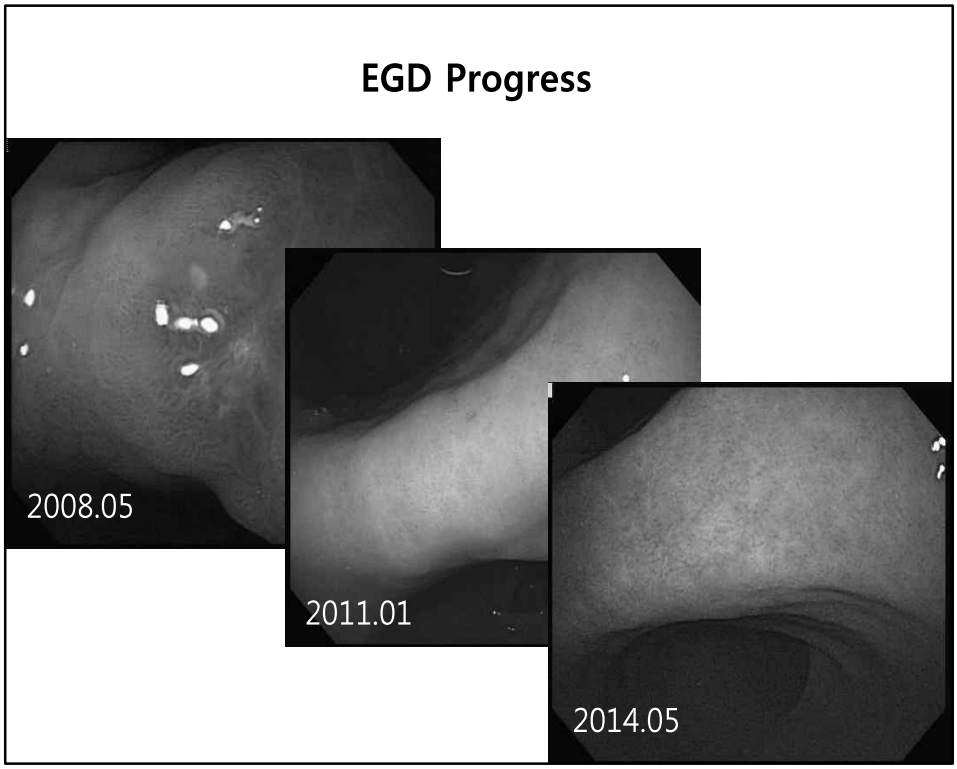
	D1	D2	-	D15
Irinotecan 160 or 180 mg/m^2 for 2 hr	o		-	Next CTx.
Leukovorin 200 mg/m^2 for 2 hrs	o	o	-	
5-FU (Bolus) 400 mg/m^2 for bolus	o	o	-	
5-FU (Continuous) 600 mg/m^2 for 22 hrs	O	O	-	

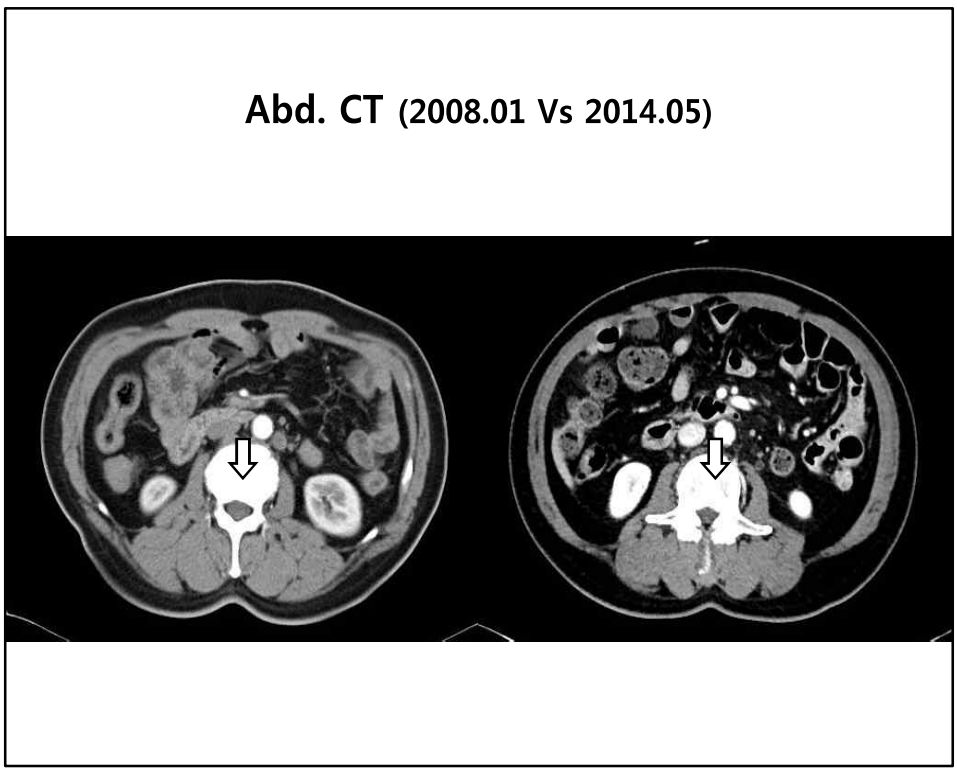
Progress



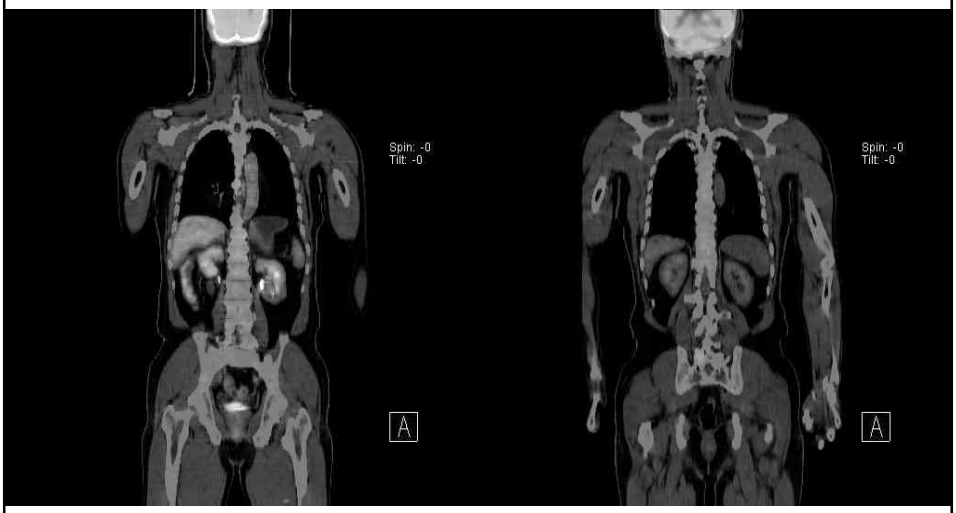

Progress
3 weeks
2 weeks
3 weeks 간격으로 CTx 시행.
PR
2009.05.21-22
2nd line
1st FOLFIRI
2009.06.12-13
2nd FOLFIRI
2009.07.09-10
3rd FOLFIRI
2012.06.04-05
41th FOLFIRI
2nd line 1st FOLFIRI CTx 이후 general weakness, poor oral intake 심해
Irinotecan 75%로 감량


Progress
PR상태로 지내다 Lt. supraclavicular LN 커져서 FNA에서 metastatic carcinoma소견으로 CCRT 시행
3 weeks 간격으로 CTx 시행
2013.02.14-03.03
CCRTx
2013.04.22-24
42nd FOLFIRI
2014.03.11-13
43rd FOLFIRI
2014.05.20-22
46th FOLFIRI
Chest CT에서 병변 크기는 변화없고
PET CT에서 hypermetabolic한
uptake는 감소
FNA에서 low cellularity 소견 보임.
Neck CT상 left supraclavicular
LN progression으로 다시 CTx 시행


EGD Progress
2008.05
2011.01
2014.05


Abd. CT (2008.01 Vs 2014.05)

PET. CT (2012.07 & 2013.04)



Journal Review

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Long-term Survival and Prognostic Factors in Patients with Metastatic Gastric Cancers Treated with Chemotherapy in the Japan Clinical Oncology Group (JCOG) Study

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Background: The long-term survival of patients after chemotherapy for advanced gastric cancer remains unclear. The aim of this analysis was to investigate prognostic factors for patients with metastatic gastric cancer treated by chemotherapy, and to identify the characteristics of long-term survivors.
Methods: Six hundred and forty three patients were enrolled in four phase II studies and one phase III study by the Japan Clinical Oncology Group between January 1985 and April 1997. By adjusting patients' eligibility between the five studies, 497 patients (77%) were selected for the analysis. Univariate and multivariate analyses were performed using log-rank tests and Cox's proportional hazard model, respectively.

Journal Review

Table 5. Relative risk of prognostic factors

Variable	*n*	RR	95% CI	*P*-value
Age (years)				
<60	219	–		
≥60	278	1.16	0.97–1.40	0.2
Gender				
Male	364	–		
Female	133	0.93	0.75–1.14	0.5
Performance status				
0	174	–		
1	235	1.16	1.08–1.25	<0.01
2	85			
Histological type				
Intestinal	228	–		
Diffuse	266	1.13	0.97–1.30	0.11
Macroscopic type				
Scirrhous	137	–		
Non-scirrhous	360	1.27	1.02–1.25	0.04
History of gastrectomy				
Yes	84	–		
No	413	1.01	0.92–1.10	0.9
No. of metastatic sites				
1	315	–		
2	148	1.32	1.14–1.53	0.01
≥3	34			

Journal Review

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Multivariate Prognostic Factor Analysis in Locally Advanced and Metastatic Esophago-Gastric Cancer—Pooled Analysis From Three Multicenter, Randomized, Controlled Trials Using Individual Patient Data

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Authors' disclosures of potential conflicts of interest are found at the end of this article.

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A B S T R A C T

Purpose
To identify baseline prognostic factors and assess whether pretreatment quality of life (QoL) predicts survival in patients with locally advanced or metastatic esophago-gastric cancer.

Patients and Methods
Between 1992 and 2001, 1,080 patients were enrolled into three randomized, controlled trials assessing fluorouracil-based combination chemotherapy. All patients were required to complete the European Organization for Research and Treatment of Cancer core QoL questionnaire before random assignment.

Results
Of the 1,080 patients randomly assigned, 979 (91%) died. Four independent poor prognostic factors were identified by multivariate analysis: performance status ≥ 2 (hazard ratio [HR], 1.58; 99% CI, 1.25 to 1.98), liver metastases (HR, 1.41; 99%CI, 1.14 to 1.74), peritoneal metastases (HR, 1.33; 99%CI, 1.01 to 1.74) and alkaline phosphatase ≥ 100 U/L (HR, 1.41; 99% CI, 1.14 to 1.76). A prognostic index was constructed dividing patients into good (no risk factor), moderate (one or two risk factors) or poor (three or four risk factors) risk groups. One-year survival for good, moderate, and poor risk groups were 48.5%, 25.7%, and 11%, respectively, and the survival differences among these groups were highly significant ($P < .00001$). Compared with the good risk group, the moderate risk group had nearly twice the risk of death, and the poor risk group had 3.6-fold increased risk of death. Pretreatment physical ($P = .0001$), role functioning ($P < .001$), and global QoL ($P < .001$) predicted survival.

Journal Review

Table 3. Multivariate Baseline Prognostic Model

Factors	Hazard Ratio	99% CI	P
Performance status			
0-1	1		
2-3	1.575	1.251 to 1.981	< .0001
Liver metastases	1.409	1.139 to 1.743	< .0001
Peritoneal metastases	1.329	1.013 to 1.743	.007
Alkaline phosphatase ≥ 100 U/l	1.412	1.136 to 1.755	< .0001
Borderline significant factors			
Hemoglobin ≤ 11 g/L			.011
White blood cell			.06
Previous esophagectomy or gastrectomy			.054

Journal Review

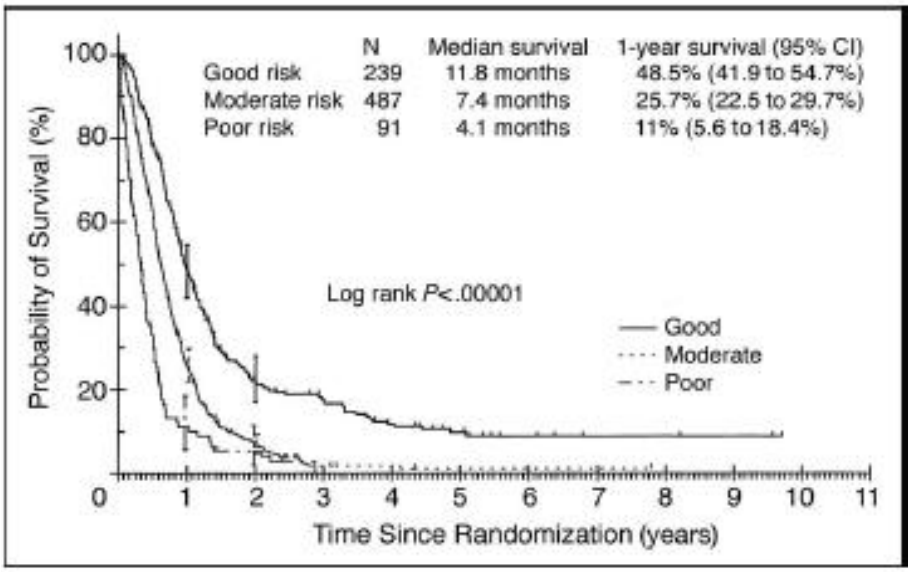

Fig 2. Overall survival by prognostic index (n = 817).

Journal Review

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Original Article Open Access

Modified FOLFIRI as Second-Line Chemotherapy after Failure of Modified FOLFOX-4 in Advanced Gastric Cancer

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Purpose
The purpose of this study was to evaluate efficacy and toxicity of irinotecan, leucovorin and 5-fluorouracil (FOLFIRI) as second-line treatment after failure of oxaliplatin, leucovorin and 5-fluorouracil (FOLFOX) for advanced gastric cancer.

Materials and Methods
Patients who received modified FOLFOX-4 as first-line treatment and then received sequential modified FOLFIRI for disease progression were included in this study. The modified FOLFIRI regimen consisted of irinotecan 150 mg/m² in a 90-minute intravenous infusion on day 1, leucovorin (LV) 20 mg/m² and 5-fluorouracil (5-FU) 400 mg/m² as a bolus followed by 600 mg/m² as a 22-hour infusion on days 1 and 2 with the same dose of 5-FU/LV of modified FOLFOX-4 every 2 weeks.

Journal Review

Table 3. Efficacy of FOLFIRI

Response	No. of patients (%)	95% confidence interval
Complete response	0 (0)	-
Partial response	3 (9.4)	0-20.1
Stable disease	11 (34.4)	17.0-51.8
Progressive disease	10 (31.2)	14.3-48.2
Not assessable	8 (25)	-

FOLFIRI, irinotecan, leucovorin and 5-fluorouracil.

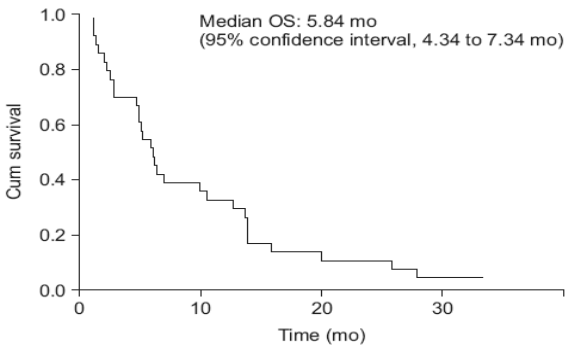

Fig. 2. Overall survival (OS) curve.

Journal Review

Table 4. Phase II studies on irinotecan, 5-FU, and LV combination chemotherapy for advanced gastric cancer

	Previous chemotherapy	No. of previous chemo-regimen	Regimen	RR (%)	SD (%)	TTP (mo)	OS (mo)
Lorizzo et al. [16]	Not restricted, fluoropyrimidine based, regimen (71.43%) included, no FOLFOX	1	I 180 mg/m² D1 LV 200 mg/m² bolus D1 5-FU 400 mg/m² bolus, 2,400 mg/m² over 46 hr	21	21	4	5
Assersohn et al. [15]	Not restricted, fluoropyrimidine based, regimen (97.4%) included, no FOLFOX	1	I 180 mg/m² D1 LV 125 mg/m² bolus D1 5-FU 400 mg/m² bolus, 1,200 mg/m² over 48 hr	29	34	3.7	6.4
Seo et al. [14]	Not restricted, fluoropyrimidine based, regimen (75%) included, modified FOLFOX (29%) included	1	I 180 mg/m² D1 LV 200 mg/m² bolus D1, 2 5-FU 400 mg/m² bolus, 600 mg/m² over 22 hr D1, 2	18	29	3.2	9.1
Kim et al. [18]	Fluoropyrimidine based regimen	≥1	I 150 mg/m² D1 LV 20 mg/m² bolus D1, 2 5-FU 3,000 mg/m² over 48 hr	18.2	18.2	2.3	5.1
Kim et al. [17]	Not restricted, modified FOLFOX (52.6%) included	≥1	I 150 mg/m² D1 LV 20 mg/m² bolus D1, 2 5-FU 400 mg/m² bolus, 600 mg/m² over 22 hr D1, 2	10	36.7	3.3	10.9
This study	Modified FOLFOX	1	I 150 mg/m² D1 LV 20 mg/m² bolus D1, 2 5-FU 400 mg/m² bolus, 600 mg/m² over 22 hr D1, 2	9.1	34.4	2	5.84

5-FU, 5-fluorouracil; LV, leucovorin; RR, response rate; SD, stable diseases; TTP, time to progression; OS, overall survival; I, irinotecan; D, day.