항암화학요법으로 완전관해가 된 말기 식도암 환자 1례

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80세 남자가 한 달전부터 점차 심해지는 삼킴곤란을 주소로 내원하였다. 환자는 특이 과거력은 없었으며, 상기 증상에 대하여 타 병원에 내원하여 시행한 상부위장관조영술에서 중부식도에서 약 5 cm 크기의 불규칙적인 경계로 내강이 좁아져 있었으며, 부분적으로 통과장애가 있어 식도암 의증하에 본원으로 전원되었다. 본원에서 시행한 내시경에서 절치하방 약 25 cm에서부터 33 cm까지 길게 이어지는 내강을 약 3분의 2 정도 차지하는 궤양융기형의 병변이 관찰되어 조직검사를 시행하였다. 조직검사에서는 식도암(편평세포암)으로 진단되었으며, 흉부전산화단층촬영에서는 다발성 림프절전이가 있어 T4N3M0(IIIC)로 진단되었다. 보호자 수술 거부하여 고식적인 항암화학요법을 시작하였다. 항암화학요법에 치료 반응을 보여 6차 DP까지 시행하였으며, 추적 관찰 결과 흉부전산화단층촬영에서 종양의 재발이나 전이의 증거는 없었다. 위내시경에서도 일부 반흔을 남기고 호전되었으며, Lugol 용액을 도포한 후에도 불염되는 부분없이 완전관해 상태를 보여 현재까지 추적 관찰 중이다.

말기 식도암의 경우 항암화학요법만으로는 관해 되는 경우가 드물지만, 본 증례에서는 말기식도암에서 항암치료만으로 현재까지 완전관해를 유지하고 있는 드문 경우로 보고하는 바이다.

삼킴곤란을 주소로 내원한 80세 남자
(항암화학요법으로 완전관해가 된
말기식도암 환자 1례)

(80/M) **외래초진:** 2013.9.27

- Chief complaint

Swallowing difficulty

Onset) 약 한달 전

(80/M)

외래초진: 2013.9.27

- **Present illness**
  - 평소 특별히 진단받은 질환 없음
  - 약 한달 전부터 연하곤란있어 개인 병원에서 시행한 상부위장관 조영술에서 식도암 의증하에 진단 및 치료 위해 전원됨

과거력

- HTN/DM/pul.Tb/Hepatitis (-/-/-/-)
- Operation History (-)

사회력

- Alcohol : 소주 1병/일 X 40 년 -> 최근 중단
- Smoking : 2pack X 50yrs -> 4년 전 중단

계통적 문진

- 전신 전신 위약감 / 피로감 (+/-)
  발열 / 오한 (-/-) 발한 (-)
  두통 / 어지러움 (-/-)
  체중감소 (-)

- 심혈관계 흉통 / 흉부 불편감 (-/+)
  심계항진 (-)

- 호흡기계 기침 / 가래 / 콧물 (-/-/-)
  호흡곤란 / 운동시 호흡곤란 (-/-)

계통적 문진

- 복부 식욕부진 / 오심 / 구토 (+/-/-)
  설사 / 변비 (-/-)
  복부 불편감 / 복통 (-/-)
  흑색변 / 혈변 / 토혈 (-/-/-)

- 비뇨/생식기계

  배뇨통 / 혈뇨 (-/-)
  빈뇨 / 다뇨 / 야간뇨 (-/-/-)

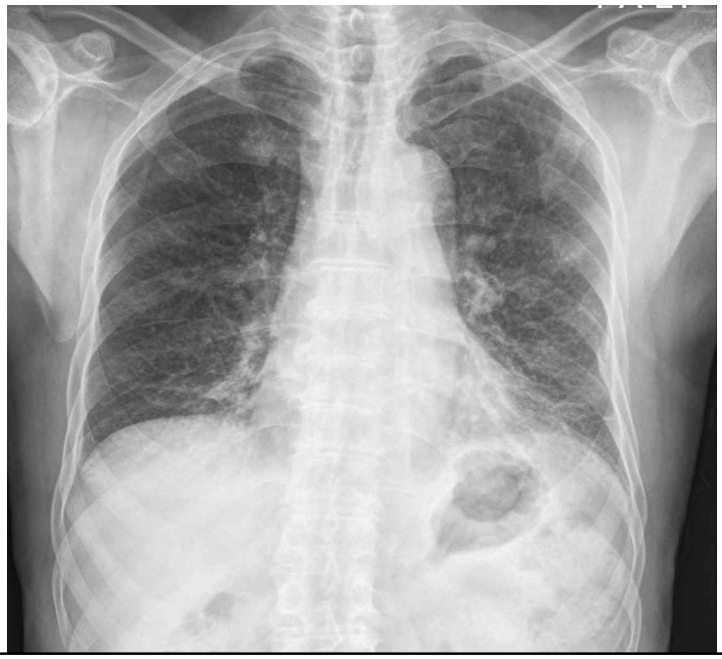
신체 검사

활력 징후	120/70 mmHg – 68회/분 – 20회/분 – 36.5℃
전신 상태	의식: 명료
두 경 부	경정맥 확장 (-/-) 임파절 종대 (-/-)
눈	동공 반사 (+/+) 결막 : 분홍색 공막 : 하얀색
흉부 청진	깨끗한 호흡음 천명 / 나음 (- / -) 규칙적 심음 잡음 (-)

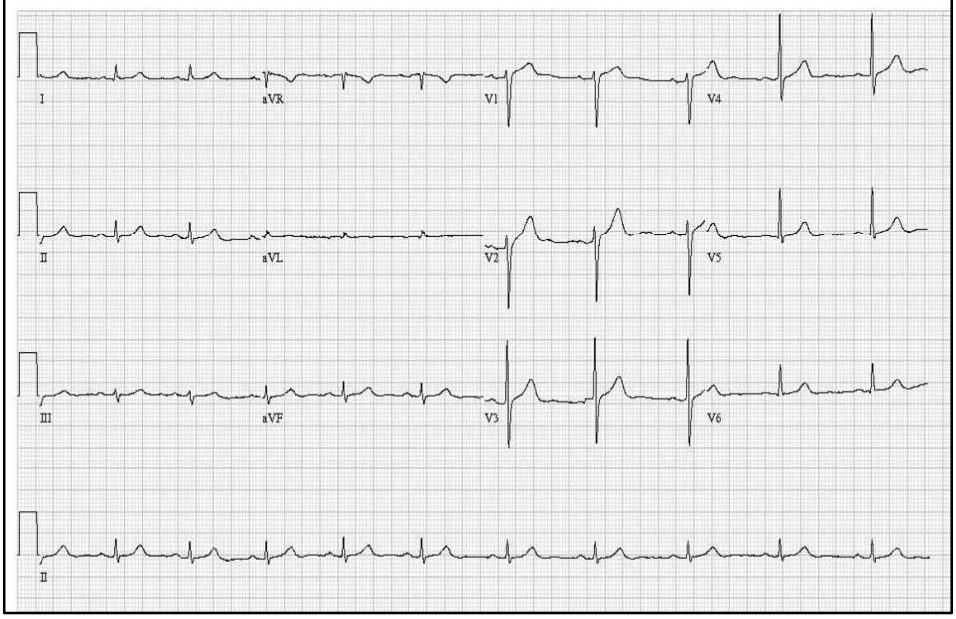
신체 검사

복부	부드럽고 편평함
	정상 장음
	배꼽주위 압통 / 반발통 (-/-)
	간 비대/비장 비대/종물의 촉지 (-/-/-)
등	늑골 척추각 압통 (-/-)

단순 흉부 사진 2013.10.11



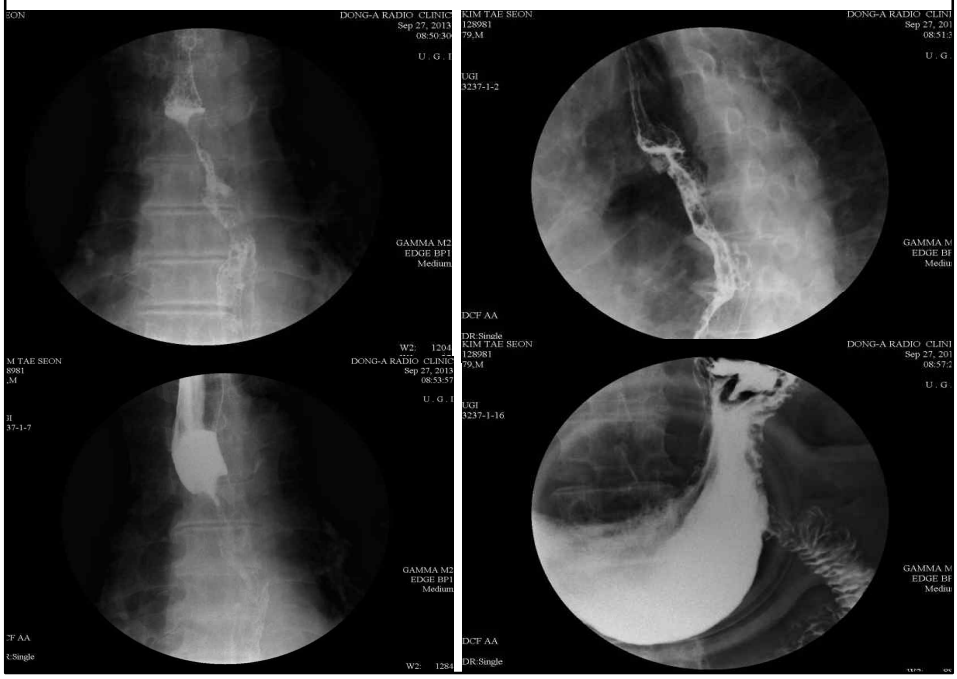
EKG 2013.10.23



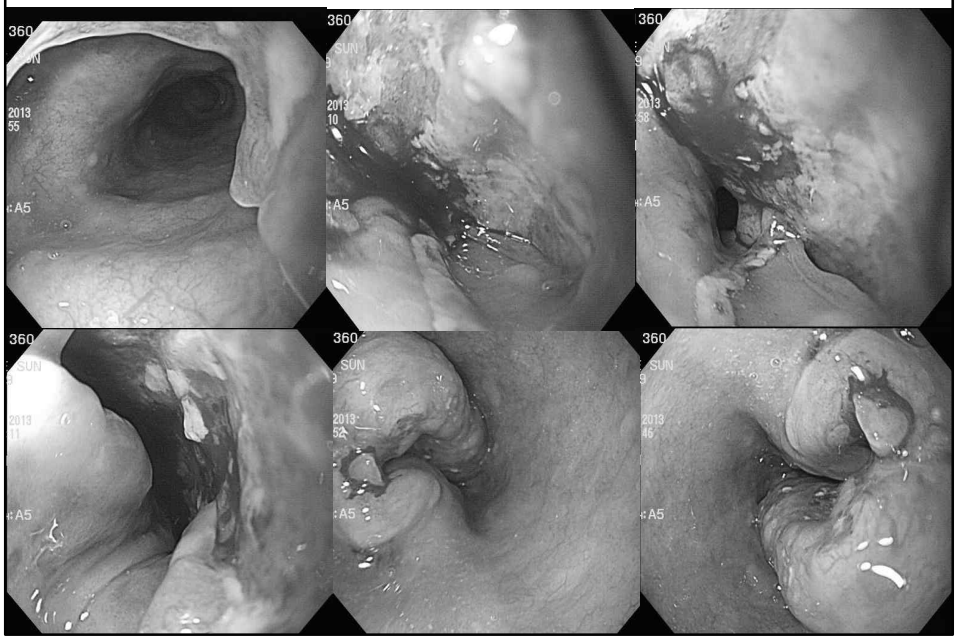
Laboratory test 2013.10.11

Complete Blood Count			
WBC	6,650 (/uL)	Hct.	51.2 (%)
Hb	17.6 (g/dl)	Seg. Neutro	40.2 (%)
Platelet	227 (10^3/Ul)		
Chemistry			
AST/ALT/ALP	14/20/74 (IU/L)	BUN/Cr	10.7/0.93 (mg/dl)
TP/Albumin	7.4/4.1 (g/dl)	Na/K/Cl	137/4.1/101.4 (mEq/L)
LDH	216 (IU/L)	CRP	<0.1 (mg/dl)
T.Bilirubin	0.7 (mg/dl)	T.Chol	165 (mg/dl)
Coagulation Proflie			
PT	12.8 (sec)	aPTT	37.7 (sec)
PT(INR)	1.04		

외부 UGI series 2013.9.27



Duodenoscopy 2013.10.1



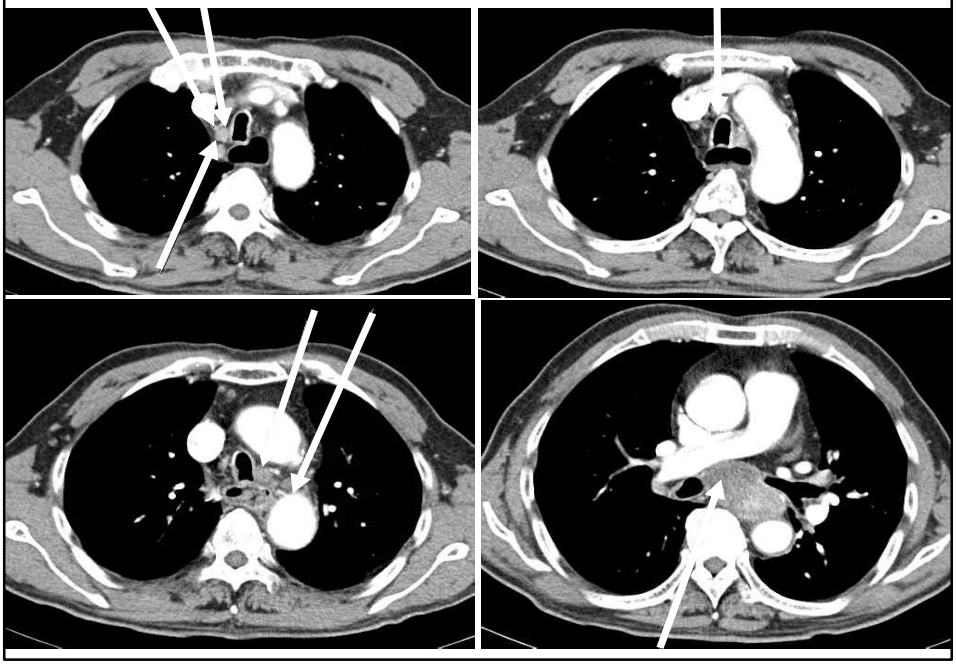
Endoscopic biopsy

◎ 병리 진단

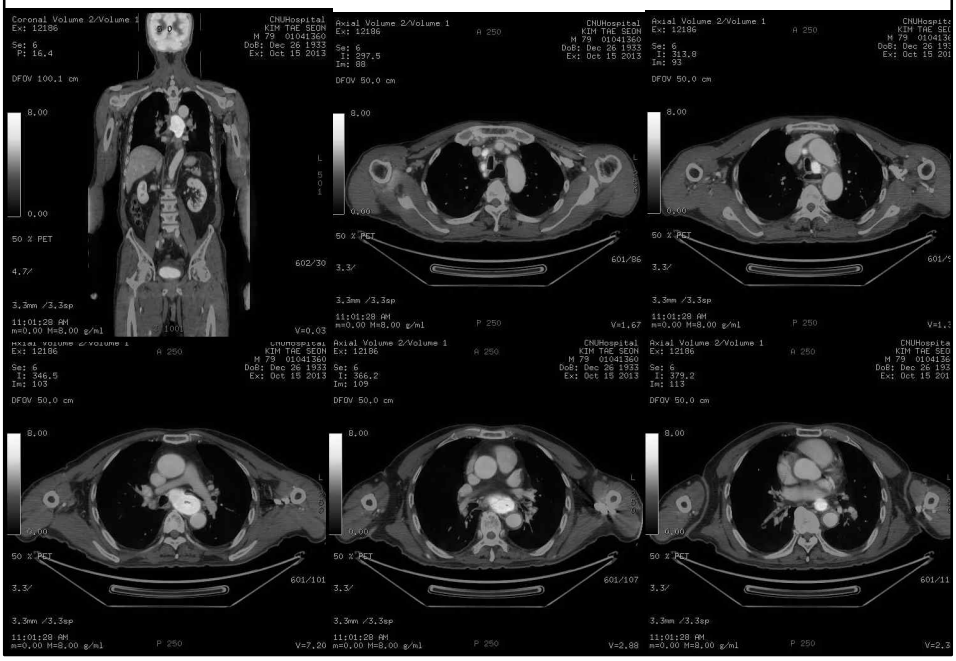
Esophagus, endoscopic biopsy;

Squamous cell carcinoma

Chest CT 2013.10.18



PET 토르소 2013.10.15



Assessment & Plan

평가

1. Esophageal cancer T4N2M0 [IIIc]

계획

1. 고식적 항암 화학치료 시행

2. chest CT 및 Duodenoscopy 추적 관찰(반응 평가)

Brief follow up History

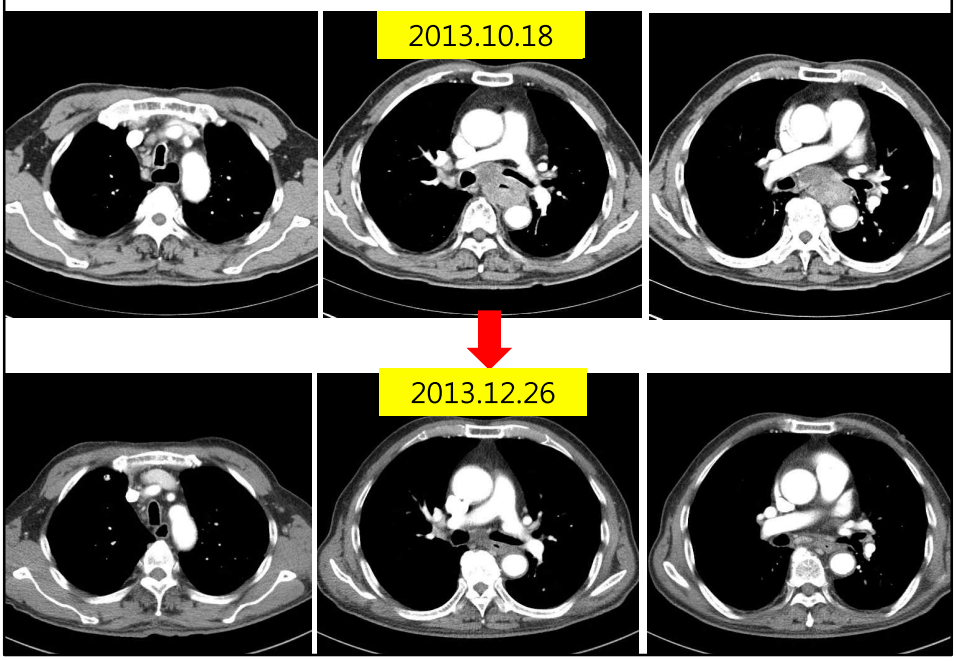
항암화학 치료 시행

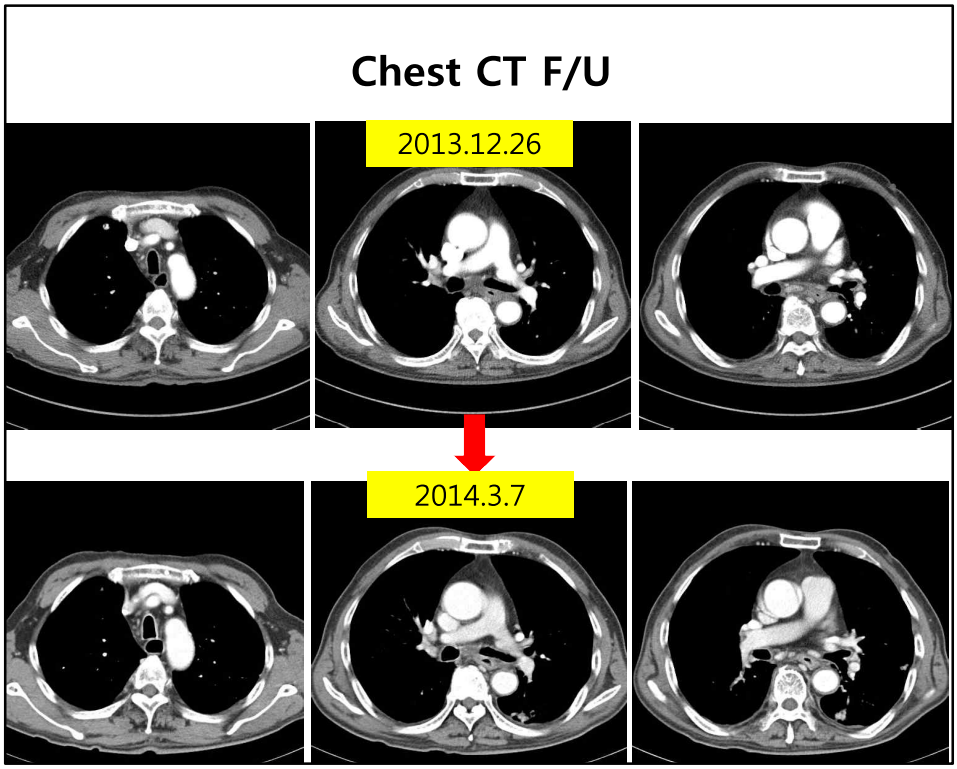
- 2013.10.25~2013.12.10) #1~3. DP (q 3wks)

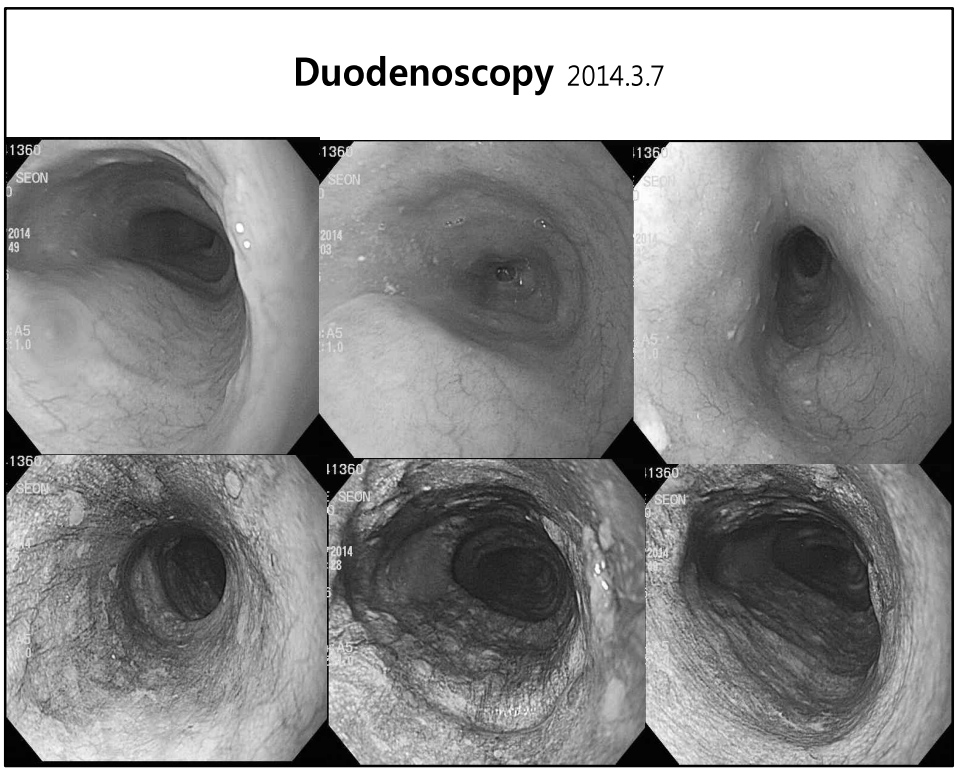
Regimen	Dose	Duration
Docetaxel	70 mg/m^2	D1 (1 hrs)
Cisplatin	60 mg/m^2	D1 (2 hrs)

- 2013.12.26) Chest CT : PR
- 2014.1.3~2014.2.18) #4~6. DP
- 2014.3.7) Chest CT : T0N0Mx
- GFS : CR

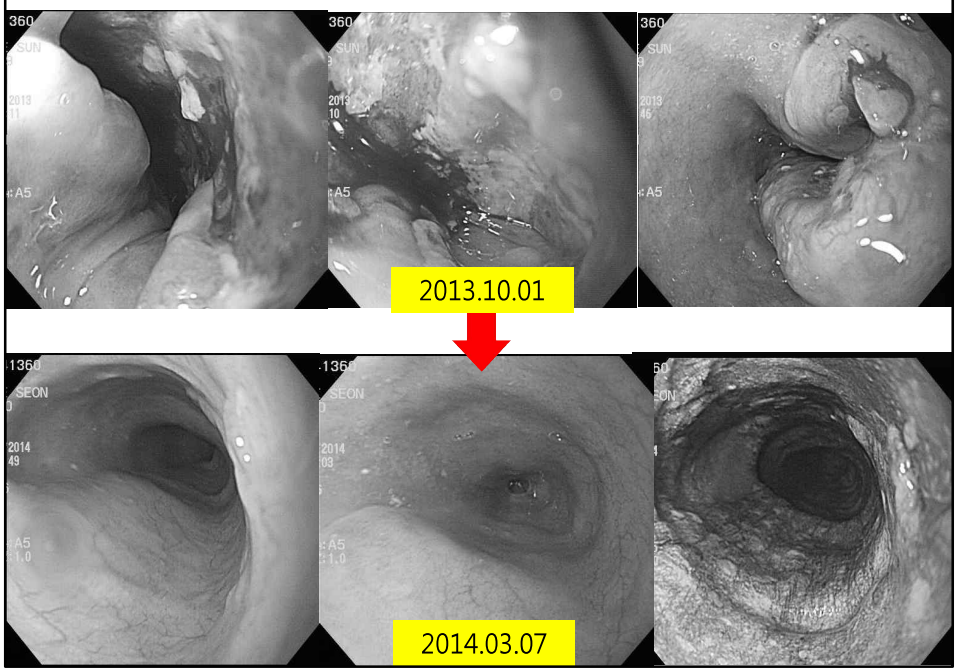
Chest CT F/U



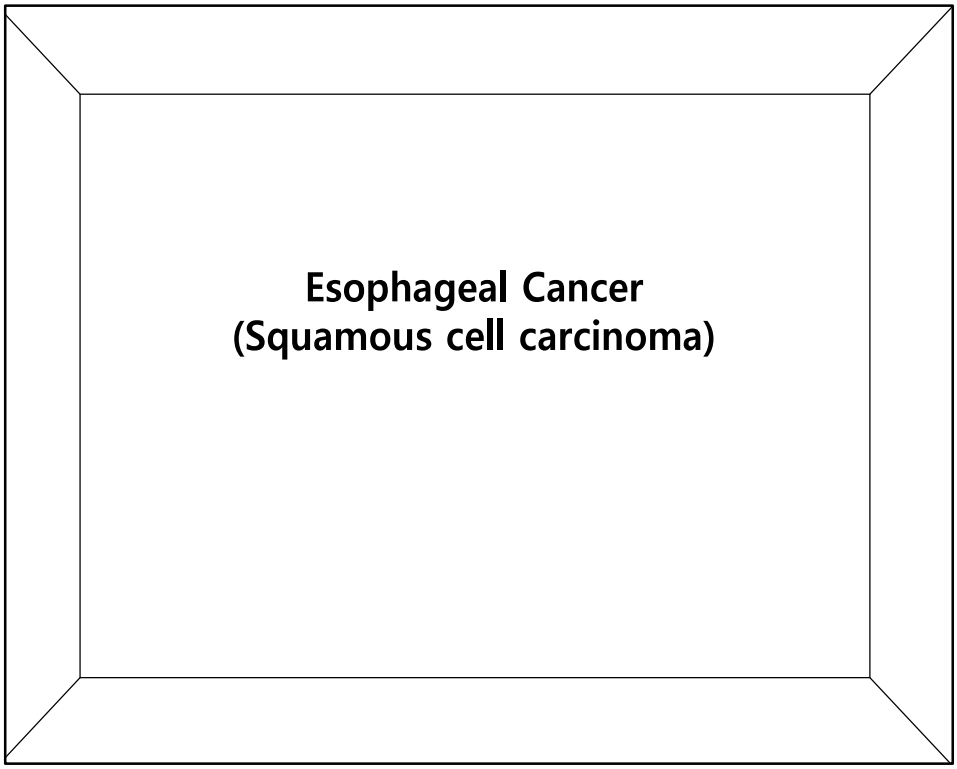

Chest CT F/U
2013.12.26
2014.3.7


Duodenoscopy 2014.3.7

Duodenoscopy F/U



- 현재는 외래에서 추적관찰하며, 복부 CT 및 내시경 시행 예정으로 항암화학치료 3차 더 계획하였으나, 환자 전신위약감으로 현재 보류하고 있는 상태임



Docetaxel and cisplatin as first-line treatment for patients with metastatic esophageal cancer: a pilot study.

Laack E[1], Andritzky B, Dürk H, Burkholder I, Edler L, Schuch G, Boeters I, Görn M, Lipp R, Horst H, Popp J, Hossfeld DK.

- 16명의 chemotherapy-naïve metastatic esophageal cancer 환자 대상 (male 15, Female 1)
- 평균 나이 : 58.5세 / median ECOG Performance : 1
  - 11명 : Esophageal cancer / 5명 : Gastroesophageal junction
- Docetaxel 75 mg/m^2 Cisplatin 80 mg/m^2 (q 3 wks)
  - median cycle 3 (1-6)

Results

Overall response rate : 31.3% (SqCC : 4/10 adenoca. : 1/5)

Median overall survival : 29.6wks Median progression survival 18.6wks

Toxicity(Hematologic & Non-hematologic) : moderate

ORIGINAL ARTICLE

A multi-center phase II study of docetaxel plus cisplatin as first-line therapy in patients with metastatic squamous cell esophageal cancer

Jin Young Kim · Young Rok Do · Keon Uk Park · Min Kyung Kim · Kyung Hee Lee · Sung Hwa Bae · Hun Mo Ryoo · Jin Ho Baek · Hong Suk Song

- 2004 ~2007
- Untreated metastatic squamous cell esophageal cancer 39명 대상
- Docetaxel 70 mg/m^2 + Cisplatin 70 mg/m^2 (q 3wks)
- Median age : 65세 Median number of cycle : 3 (0-6)
- Results : 34명이 반응 평가
  -> CR 3명(7.7%) PR 10명(25.6%) SD 11명(28.2%) PD 10명(25.6%)
  -> Objective response rate 33.3% / Median PFS : 5.0 month
  Median survival : 8.3 month
  -> Toxicity : Grade 3/4 Neutropenia 20.5%/10.3%
  Grade 3 Infection 2.6%

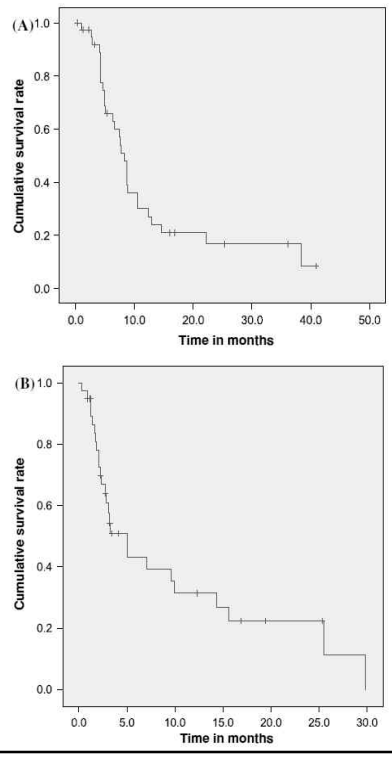


Table 3 Efficacy result

Response	Number of patients
Complete response	3 (7.7%)
Partial response	10 (25.6%)
Stable disease	11 (28.2%)
Progressive disease	10 (25.6%)
Objective tumor response	33.3%

Table 4 Adverse reactions according to NCI-CTC grade

	Grade (% of patients, $n = 39$)[a]			
	1	2	3	4
Hematologic				
Leukopenia	12 (30.8)	4 (10.3)	4 (10.3)	
Neutropenia	4 (10.3)	2 (5.1)	8 (20.5)	4 (10.3)
Anemia	12 (30.8)	13 (33.3)	1 (2.6)	
Thrombocytopenia	1 (2.6)			
Non-hematologic				
Nausea	3 (7.7)	6 (15.4)	1 (2.6)	
Vomiting	3 (7.7)	2 (5.1)		
Fatigue	1 (2.6)	3 (7.7)		
Dysphagia	3 (7.7)	3 (7.7)		
Anorexia	2 (5.1%)	1 (2.6)		
Diarrhea	2 (5.1)	1 (2.6)		
Infection		1 (2.6)	1 (2.6)	
Pain	1 (2.6)	1 (2.6)		
Edema	1 (2.6)			

[a] NCI-CTCAE v 2.0

Chemotherapy for locally advanced unresectable and metastatic esophageal and gastric cancer

1) Single agent chemotherapy

- Older single agent : Bleomycin, mitomycin-C, methotrexate, 5-FU, etoposide, cisplatin, doxorubicin (<6 month)
- Newer agents
  : Taxanes, irinotecan and vinorelbine, Oral fluoropyrimidines

Studies evaluating newer single agents chemotherapy in locally advanced and metastatic esophageal and gastric cancers

Drug	Cancer type	Author	N	RR (percent)
Paclitaxel 24 hour infusion	Esophageal	Ajani, J; 1994	50	32
	Gastric	Ajani, J; 1998	18	23
Paclitaxel weekly short infusion	Esophageal	Ilson, D; 2007	102	15
	Gastric	Kii, T; 2006	26	14
Docetaxel	Esophageal (1st and 2nd-line)	Muro, K; 2004	50	20
	Gastric	Mavroudis, D; 2000	30	20
Irinotecan	Esophagogastric	Enzinger, P; 2005	43	14
	Gastric	Kohne, C; 2003	40	20
Vinorelbine	Esophageal SCC (1st and 2nd-line)	Conroy, T; 1996	46	15
	Esophagogastric adenocarcinoma (1st and 2nd line)	Kulke, M; 2006	29	7

N: number of patients; RR: objective response rate.

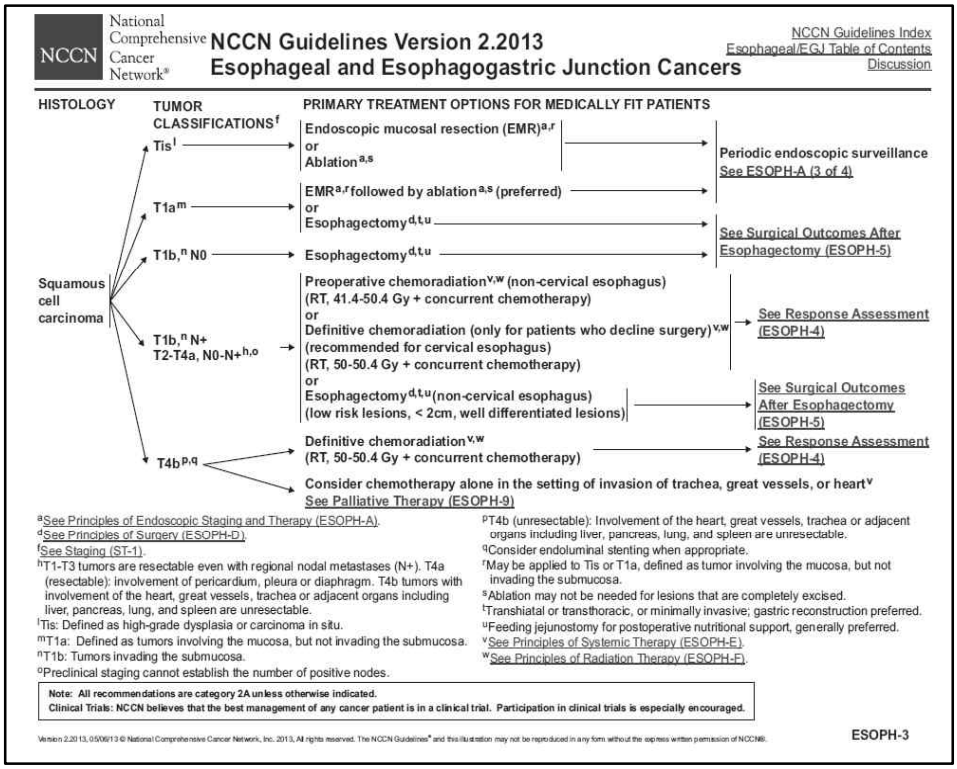
Courtesy of Fidias, P, El-Karak, FR.

Chemotherapy for locally advanced unresectable and metastatic esophageal and gastric cancer

2) Combination chemotherapy

- 몇몇 randomized trial에서는 Single agent therapy에 비해서 response rate는 높지만, 임상적인 survival benefit은 보이지 못했음.
- Metaanalysis에서는 survival benefit이 통계적으로 의미가 있었으며, Hazard ratio가 0.82.

- Cisplatin based regimen (cisplatin + 5-FU / Capecitabine)
- 5-FU + anthracycline regimen
  : FAM / FAMTX / EAP / ELF / ECF ...
- Taxane based combination
  : Paclitaxel regimen / Docetaxel regimen
- Oxaliplatin combination
- Irinotecan containing regimen (cisplatin / docetaxel / Fluropyridine)



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NCCN Guidelines Version 2.2013
Esophageal and Esophagogastric Junction Cancers

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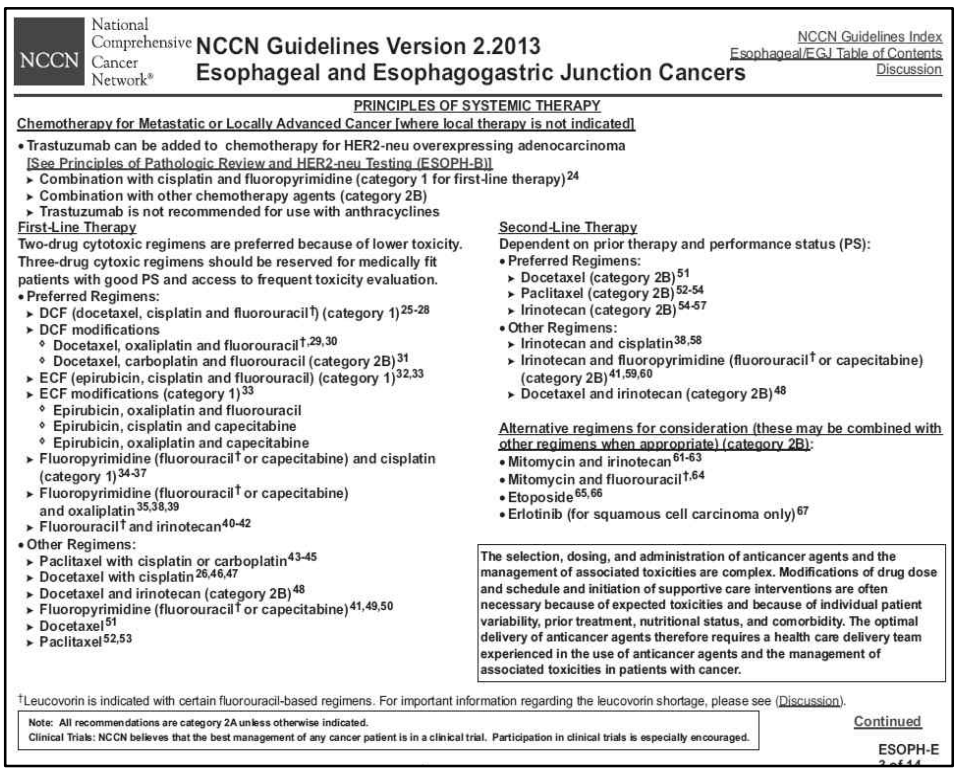
HISTOLOGY	TUMOR CLASSIFICATIONS[f]	PRIMARY TREATMENT OPTIONS FOR MEDICALLY FIT PATIENTS
Squamous cell carcinoma	Tis[l]	Endoscopic mucosal resection (EMR)[a,r] or Ablation[a,s] → Periodic endoscopic surveillance See ESOPH-A (3 of 4)
	T1a[m]	EMR[a,r] followed by ablation[a,s] (preferred) or Esophagectomy[d,t,u] → See Surgical Outcomes After Esophagectomy (ESOPH-5)
	T1b,[n] N0	Esophagectomy[d,t,u] → See Surgical Outcomes After Esophagectomy (ESOPH-5)
	T1b,[n] N+ T2-T4a, N0-N+[h,o]	Preoperative chemoradiation[v,w] (non-cervical esophagus) (RT, 41.4-50.4 Gy + concurrent chemotherapy) or Definitive chemoradiation (only for patients who decline surgery)[v,w] (recommended for cervical esophagus) (RT, 50-50.4 Gy + concurrent chemotherapy) → See Response Assessment (ESOPH-4) or Esophagectomy[d,t,u] (non-cervical esophagus) (low risk lesions, < 2cm, well differentiated lesions) → See Surgical Outcomes After Esophagectomy (ESOPH-5)
	T4b[p,q]	Definitive chemoradiation[v,w] (RT, 50-50.4 Gy + concurrent chemotherapy) → See Response Assessment (ESOPH-4) Consider chemotherapy alone in the setting of invasion of trachea, great vessels, or heart[v] See Palliative Therapy (ESOPH-9)

[a] See Principles of Endoscopic Staging and Therapy (ESOPH-A).
[d] See Principles of Surgery (ESOPH-D).
[f] See Staging (ST-1).
[h] T1-T3 tumors are resectable even with regional nodal metastases (N+). T4a (resectable): involvement of pericardium, pleura or diaphragm. T4b tumors with involvement of the heart, great vessels, trachea or adjacent organs including liver, pancreas, lung, and spleen are unresectable.
[l] Tis: Defined as high-grade dysplasia or carcinoma in situ.
[m] T1a: Defined as tumors involving the mucosa, but not invading the submucosa.
[n] T1b: Tumors invading the submucosa.
[o] Preclinical staging cannot establish the number of positive nodes.
[p] T4b (unresectable): Involvement of the heart, great vessels, trachea or adjacent organs including liver, pancreas, lung, and spleen are unresectable.
[q] Consider endoluminal stenting when appropriate.
[r] May be applied to Tis or T1a, defined as tumor involving the mucosa, but not invading the submucosa.
[s] Ablation may not be needed for lesions that are completely excised.
[t] Transhiatal or transthoracic, or minimally invasive; gastric reconstruction preferred.
[u] Feeding jejunostomy for postoperative nutritional support, generally preferred.
[v] See Principles of Systemic Therapy (ESOPH-E).
[w] See Principles of Radiation Therapy (ESOPH-F).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

ESOPH-3



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Esophageal and Esophagogastric Junction Cancers

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PRINCIPLES OF SYSTEMIC THERAPY

Chemotherapy for Metastatic or Locally Advanced Cancer [where local therapy is not indicated]

- Trastuzumab can be added to chemotherapy for HER2-neu overexpressing adenocarcinoma
  [See Principles of Pathologic Review and HER2-neu Testing (ESOPH-B)]
  - Combination with cisplatin and fluoropyrimidine (category 1 for first-line therapy)[24]
  - Combination with other chemotherapy agents (category 2B)
  - Trastuzumab is not recommended for use with anthracyclines

First-Line Therapy

Two-drug cytotoxic regimens are preferred because of lower toxicity. Three-drug cytoxic regimens should be reserved for medically fit patients with good PS and access to frequent toxicity evaluation.

- Preferred Regimens:
  - DCF (docetaxel, cisplatin and fluorouracil†) (category 1)[25-28]
  - DCF modifications
    - Docetaxel, oxaliplatin and fluorouracil†,[29,30]
    - Docetaxel, carboplatin and fluorouracil (category 2B)[31]
  - ECF (epirubicin, cisplatin and fluorouracil) (category 1)[32,33]
  - ECF modifications (category 1)[33]
    - Epirubicin, oxaliplatin and fluorouracil
    - Epirubicin, cisplatin and capecitabine
    - Epirubicin, oxaliplatin and capecitabine
  - Fluoropyrimidine (fluorouracil† or capecitabine) and cisplatin (category 1)[34-37]
  - Fluoropyrimidine (fluorouracil† or capecitabine) and oxaliplatin[35,38,39]
  - Fluorouracil† and irinotecan[40-42]
- Other Regimens:
  - Paclitaxel with cisplatin or carboplatin[43-45]
  - Docetaxel with cisplatin[26,46,47]
  - Docetaxel and irinotecan (category 2B)[48]
  - Fluoropyrimidine (fluorouracil† or capecitabine)[41,49,50]
  - Docetaxel[51]
  - Paclitaxel[52,53]

Second-Line Therapy

Dependent on prior therapy and performance status (PS):

- Preferred Regimens:
  - Docetaxel (category 2B)[51]
  - Paclitaxel (category 2B)[52-54]
  - Irinotecan (category 2B)[54-57]
- Other Regimens:
  - Irinotecan and cisplatin[38,58]
  - Irinotecan and fluoropyrimidine (fluorouracil† or capecitabine) (category 2B)[41,59,60]
  - Docetaxel and irinotecan (category 2B)[48]

Alternative regimens for consideration (these may be combined with other regimens when appropriate) (category 2B):

- Mitomycin and irinotecan[61-63]
- Mitomycin and fluorouracil†,[64]
- Etoposide[65,66]
- Erlotinib (for squamous cell carcinoma only)[67]

The selection, dosing, and administration of anticancer agents and the management of associated toxicities are complex. Modifications of drug dose and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, nutritional status, and comorbidity. The optimal delivery of anticancer agents therefore requires a health care delivery team experienced in the use of anticancer agents and the management of associated toxicities in patients with cancer.

† Leucovorin is indicated with certain fluorouracil-based regimens. For important information regarding the leucovorin shortage, please see (Discussion).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Continued

ESOPH-E