A Case of Pathologic Complete Remission with FOLFIRINOX in Locally Advanced Pancreatic Cancer

Jong-chan Lee, Hyeong Woo Kim, Kyu-hyun Paik, Jingu Kang, Jaihwan Kim, Jin-Hyeok Hwang

Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Gyeonggi, Korea

서론: 진행성 췌장암은 조기 진단의 어려움, 빠른 암의 진행, 낮은 항암제 반응률, 높은 빈도의 전이로 인하여 매우 치료가 어려운 고형암 중 하나이며, 5년 생존율이 5% 미만으로 알려져 있다. 최근 다학제성 접근(multidisciplinary approach) 방법으로서 수술 전 항암화학요법(neoadjuvant chemotherapy)이 주목을 받고 있다. 본 증례는 국소진행성 췌장암 환자에서 항암화학요법 후 수술로 병리학적 완전 관해(complete remission)가 확인된 치험례이다.

증례: 49세 여자가 3개월 전부터 시작된 상복부 동통 및 등의 통증을 주소로 내원하였다. 환자는 상기 증상을 위염으로 판단하여 개인의원에서 경구약을 복용하였으나, 호전되지 않아 인근 종합병원에서 복부-골반 전산화 단층촬영(abdomen-pelvis computed tomography, APCT)을 시행 받았으며, 췌장암이 의심되어 추가 검사 위해 본원을 방문하였다. 과거력에서 당뇨병은 없었다. 혈액 검사 상 일반 혈액 검사는 정상 범위였으며, 혈청 아미노전이효소 17/28 U/L, 총빌리루빈 0.5 mg/dL, 알칼리성 인산분해 효소 93 U/L, 감마 글루타밀 전이효소 2 5U/L, C-반응성 단백질 0.01 mg/dL 등 일반화학 검사도 모두 정상 범위였다. CA19-9는 27.5 U/mL로 약간 증가되었다. APCT에서 췌장 경부를 침범하는 3.0×2.8 cm 크기의 종양이 발견되었으며, 병변은 상부 장간막 정맥 완전 폐쇄 및 우측 간동맥 침범 소견을 보이고 있었다. 원격 전이 소견은 발견되지 않았다. 복부 자기공명 영상에서도 동일한 소견을 보였으며, 전신의 양전자 방사단층촬영에서도 췌장의 동일 부위에 최대 표준 섭취값 3.6 정도의 고 대사성 병변이 관찰되었다. 이후 시행한 내시경 초음파 유도하 세침흡인 검사 결과 선암으로 진단되어 국소진행형 췌장암 진단 하에 FOLFIRINOX 치료(2013/11/19~2014/6/11)를 시행하였다. 2014년 6월 CT에서 절제 가능한(resectable) 췌장암으로 평가되어 PET-CT 후 유문 보존 췌십이지장 절제술을 시행하였다(2014/7/14). 병리검사 결과 종양세포가 발견되지 않아 병리학적 완전 관해로 최종 판단하였다. 퇴원 이후 환자는 특이 소견 없이 본원 외래에서 추적관찰 중이다.

결론: 본 증례는 국소진행성 췌장암 환자에서 항암화학요법만으로 병리학적 완전 관해를 보인 드문 사례이다.

Case Presentation

► F/49

► Chief Complaint

- **Upper abdominal pain with back pain** (O: 3 MA)

► Present Illness

- 3 MA: upper abdominal pain & back pain

  → local clinic: r/o gastritis, medication

  → abdomen USG at other clinic : abnormal finding on pancreas

- 1 WA: (**outside hospital APCT**) r/o pancreatic cancer

  → visit SNUBH for further evaluation

Case Presentation

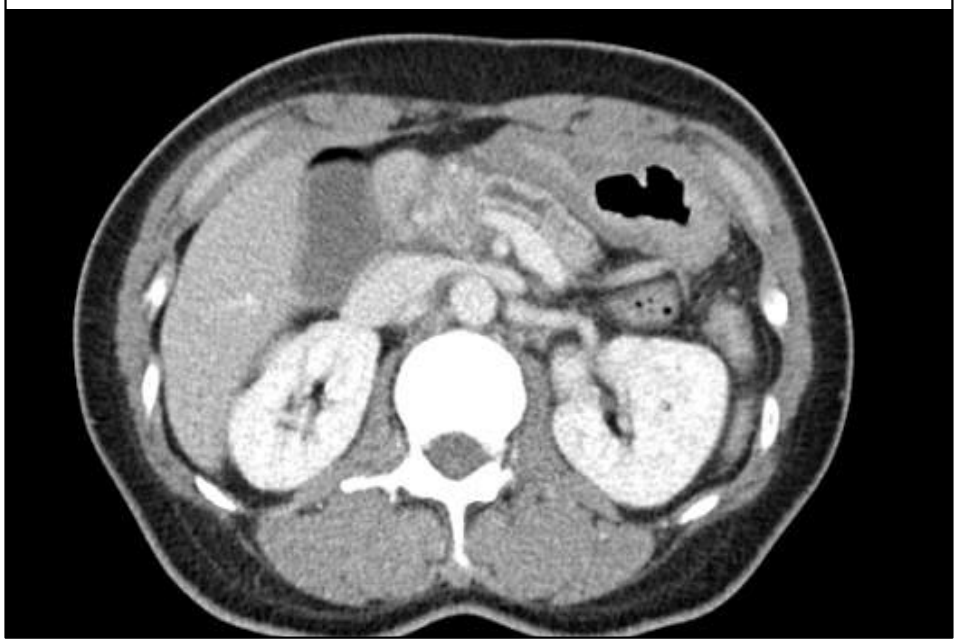
► Initial V/S
- 134/88 – 36.7 – 90 – 20 (SpO2 100%)

► PMHx & SHx
- DM/ HTN/TB/CLD (-/+/-/-) on medication
- Cesarean section at 1998, 2002
- alcohol(-), smoking(-)

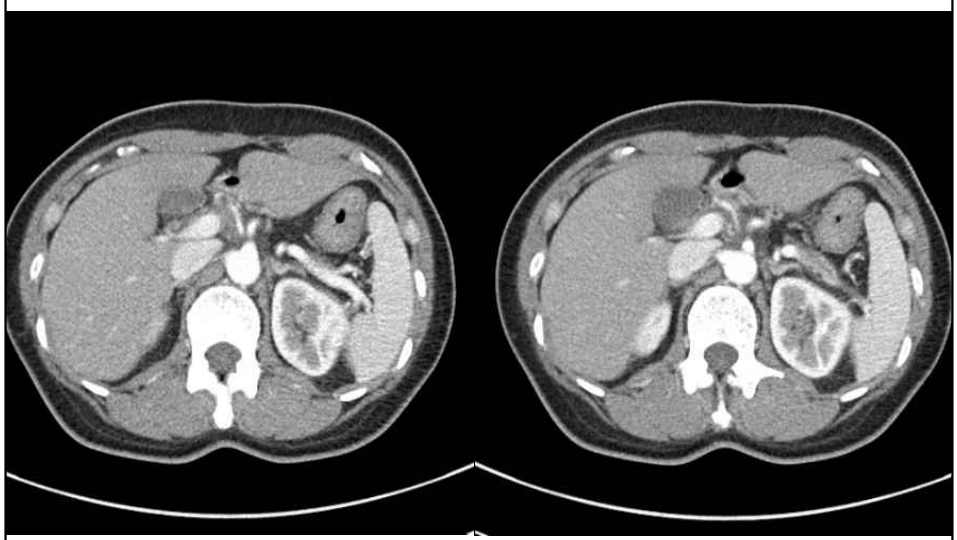
► ROS & P/E
- GW(-) F/C (-/-) Wt loss(-) night sweat(-) A/N/V/D/C (-/-/-/-/-) H/M/H (-/-/-)
- Upper abdominal pain (+), back pain (+), dyspepsia (+)
- alert and oriented, soft & flat Abd, normoactive BS, T/RT(-/-) L/K/S (-/-/-) shifting dullness (-) CVAT (-/-)

► Lab
- CBC 7,090 – 14.3 – 191k (seg 70.2%) CRP 0.01
- LFT T-C 167 T-P/ Alb 7.4/ 4.3 T-B 0.5 AST/ALT 17/ 28 ALP 93 γ-GT 25 PT(INR) 1.12
- CA 19-9 **27.5** U/mL CEA 2.6

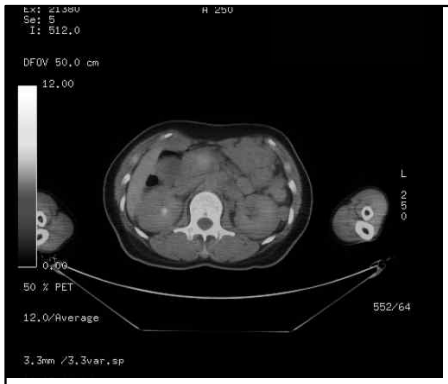
Initial Outside CT



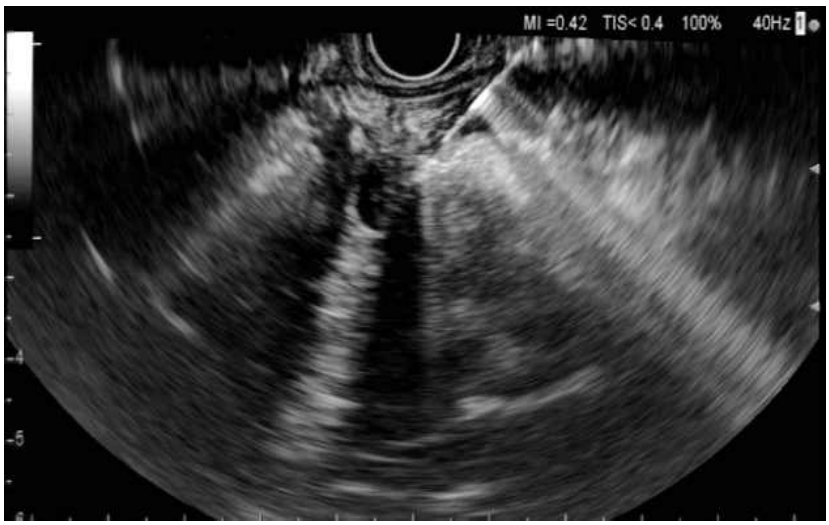
Initial Outside CT



PET & MRCP MRI



EUS-FNA



► **Biopsy report**

– satisfactory for evaluation

– diagnostic of **adenocarcinoma**

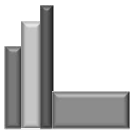
Initial Assessment and Plan

► Initial Assessment

- **Pancreatic Cancer**, unresectable
- Known HTN

► Initial Plan

- Start FOLFIRINOX



Standard FOFIRINOX

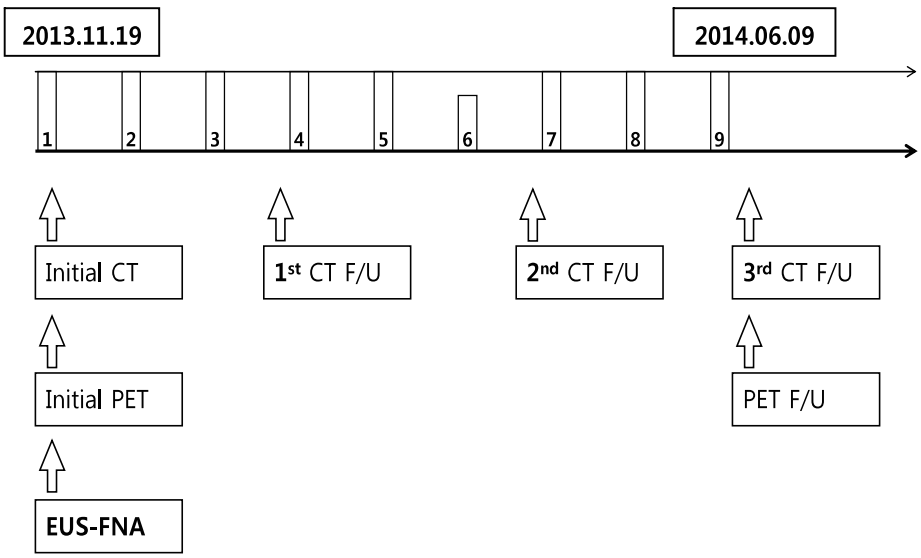
: oxaliplatin **85** mg/m^2

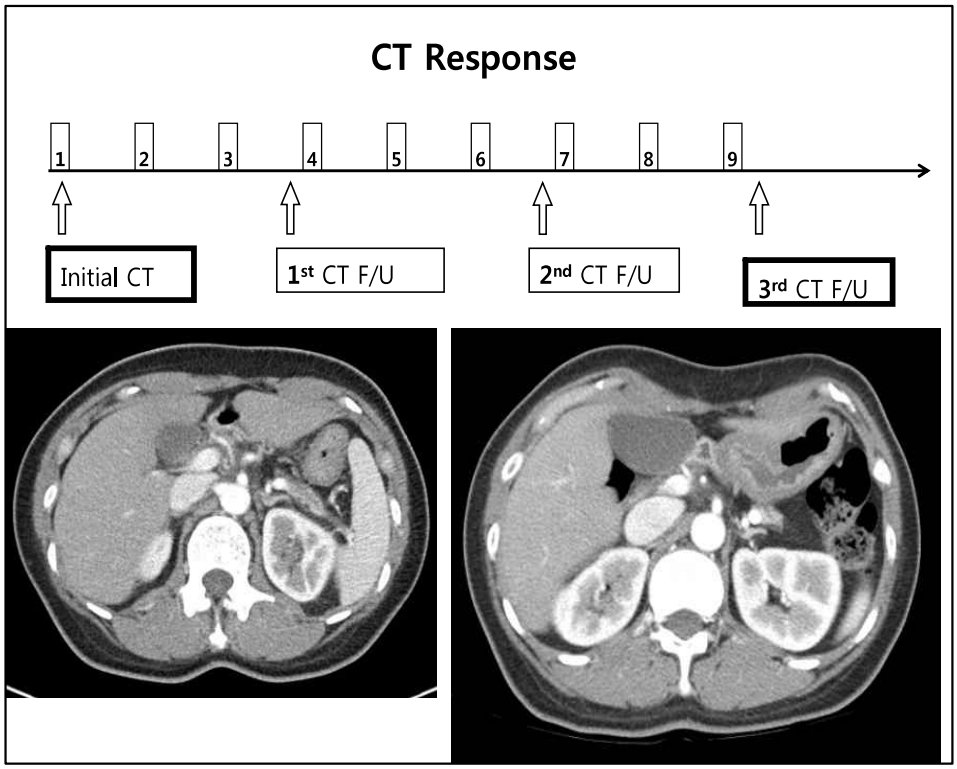
irinotecan **180** mg/m^2

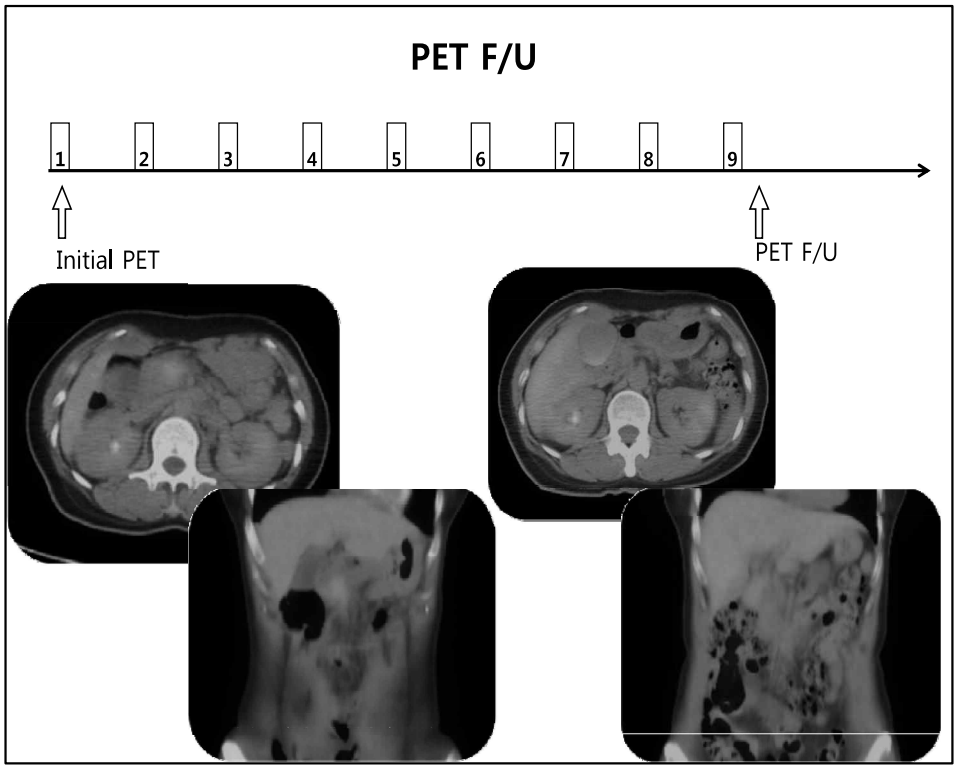
5-FU bolus **400** mg/m^2

5-FU infusion **2,400** mg/m^2

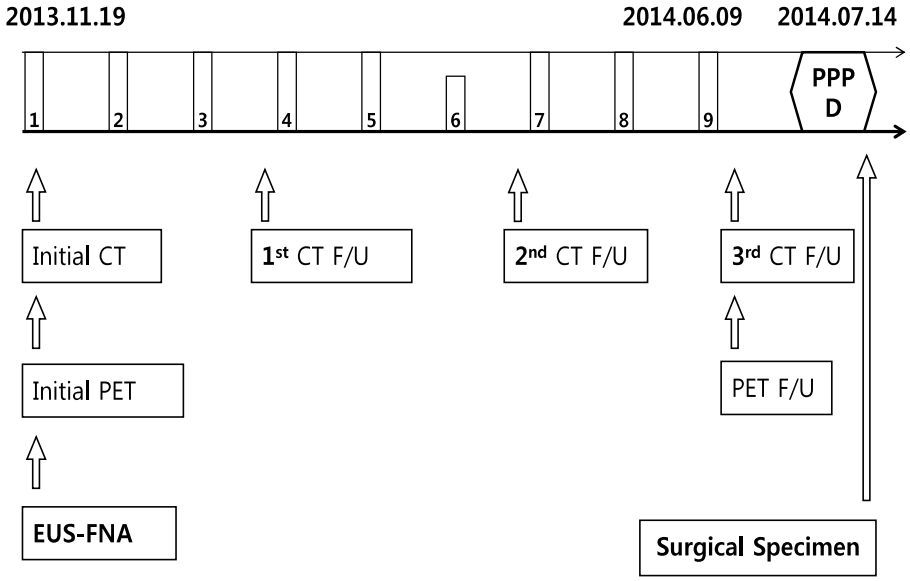
Schedule of FOLFIRINOX



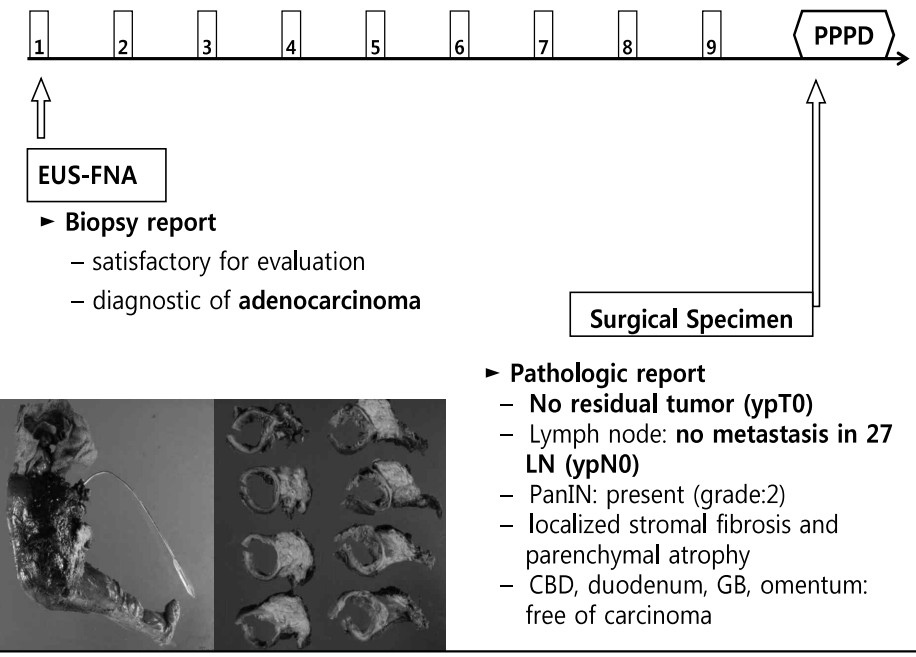

CT Response
1
2
3
4
5
6
7
8
9
Initial CT
1st CT F/U
2nd CT F/U
3rd CT F/U


PET F/U
1
2
3
4
5
6
7
8
9
Initial PET
PET F/U

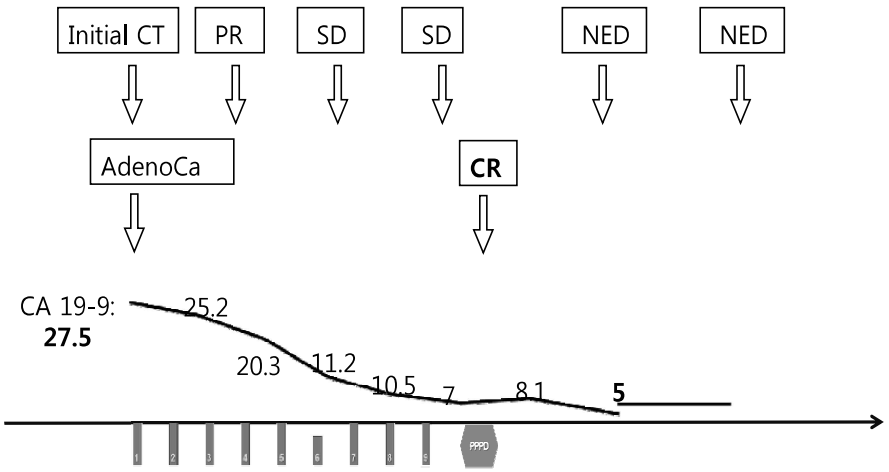
Neoadjuvant FOLFIRINOX + Surgery



Biopsy and Surgical Specimen

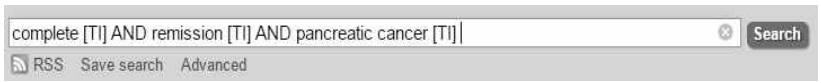


Summary of Time Course



Complete Remission in Pancreatic Cancer

(2015.03.01) PUBMED search



Results: 7

3

1. **Complete** pathological **remission** of locally advanced, unresectable **pancreatic cancer** (LAPC) after intensified neoadjuvant chemotherapy.
Hartlapp I, Müller J, Kenn W, Steger U, Isbert C, Scheurlen M, Germer CT, Einsele H, Kunzmann V.
Onkologie. 2013;36(3):123-5. doi: 10.1159/000348527. Epub 2013 Feb 25.
PMID: 23486001 [PubMed - indexed for MEDLINE]

4. **Complete remission** of metastatic **pancreatic cancer** with cardiac involvement after gemcitabine, oxaliplatin and 46-h infusion of 5-fluorouracil/leucovorin.
Wu WC, Chen SC, Su YC, Chuang WL, Chen LT.
J Gastroenterol Hepatol. 2004 Jun;19(6):716-7. No abstract available.
PMID: 15151634 [PubMed - indexed for MEDLINE]

7. **Complete** clinical **remission** in a patient with advanced **pancreatic cancer** using mitomycin C-based chemotherapy: the role of adjunctive heparin.
Sadoff L, Latino F.
Am J Clin Oncol. 1999 Apr;22(2):187-90.
PMID: 10199458 [PubMed - indexed for MEDLINE]

Complete Remission in Pancreatic Cancer

(2015.03.01) PUBMED search

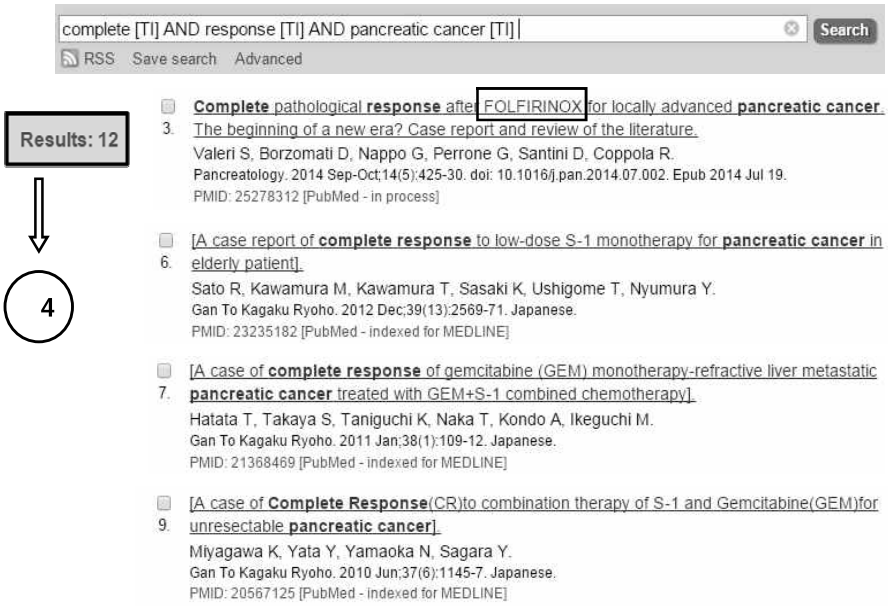


Table 1
The role of FOLFIRINOX in locally advanced pancreatic cancer.

Authors	Journal, year	Total number of patients/n. of patients with locally advanced disease	Toxicity	Disease control rate	Resection rate	Complete pathological response	Median overall survival (OS)	Median Progression free survival (PFS)	1-year survival rate	1-year progression free survival rate
Conroy et al.	J Clin Oncol, 2005	46/11	No toxic death. Grade 3 to 4 neutropenia in 52% of patients. Grade 3 to 4 nausea in 20%, vomiting in 17%, diarrhea (17%) and grade 3 neuropathy (15%)	Response rate (26%) Complete response (4%)	Not reported	Not reported	10.2 months	5.6 months	43%	Not reported
Mahaseth et al.	J Clin Oncol, 2012	28/28	Grade 3 to 4 nausea/vomiting (11%), diarrhea (11%), fatigue (11%), neuropathy (4%), neutropenia (4%), trombocitopenya (4%), sepsis-not related to neutropenia (4%)	Disease control rate (71%): complete response (7.1%), partial response (14.2%), stability disease (50%)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Peddi et al.	JOP, 2012	61/19	No toxic death. Grade 3 to 4 neutropenia (19.7%), thrombocytopenia (3.3%), diarrhea (3.3%), fatigue (4.9%)	Disease control rate (72.5%): complete response (2.5%), partial response (22.5%), stability disease (47.5%)	13.1%	0%	13.5 months	7.5 months	55.6%	35.3%
Marthey et al.	Ann Oncol, 2012	53/53	No toxic death. Grade 3 to 4 neutropenia (15%), nausea (13%), diarrhea (8%), anemia (2%), thrombocytopenia (2%). Grade 2–3 neuropathy (19%).	Disease control rate (83%): partial response rate (30%), stability disease (53%)	32%	0%	Not reported	Not reported	80%	54%
Vasile et al.	Ann Oncol, 2012	15/15	Not reported	Disease control rate (100%): partial response (40%), stability disease (60%)	55.5%	0%	30.1 months	24.5 months	Not reported	Not reported
Lowery et al.	J Clin Oncol, 2012	80/19	Not reported	Disease control rate (87.5%): partial response (31.2%), stability disease (45%)	1.25%	0%	Not reported	Not reported	Not reported	Not reported
Gunturu et al.	J Clin Oncol, 2012	35/16	Not reported	Disease control rate (48.6%)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Hosein et al.	BMC Cancer, 2012	18/14	Grade 3 to 4 neutropenia (22%), thrombocytopenia (11%), fatigue (11%), diarrhea (11%)	Disease control rate (94.4%): partial response (38.9%), stability disease (55.5%)	50%	0%	Not reported	Not reported	100%	83%
Gunturu et al.	Med Oncol, 2013	33/16	Grade 3 to 4 neutropenia (11.4%), thrombocytopenia (2.9%), fatigue (5.7%), diarrhea (2.9%), vomiting (2.9%)	Disease control rate (88%): complete response (3%), partial response (45%), stability disease (39%)	6.1%	0%	Not reported	16.1 months	Not reported	Not reported
Faris et al.	The Oncologist, 2013	22/22	Grade 3 to 4 neutropenia (18.2%), thrombocytopenia (4.5%)	Disease control rate (100%): partial response (27.3%, stability disease (72.7%)	22.7%	4.5%	Not reported	11.7 months	Not reported	Not reported
Boone et al.	J Surg Oncol, 2013	25/13	Grade 3 to 4 neutropenia (12%), hypoalbuminemia (5%), weight loss (5%), diarrhea (5%), neuropathy (5%), leukopenia (8%), thrombocytopenia (10%)	Not reported	43%	0%	Not reported	Not reported	Not reported	Not reported
Hartlapp et al.	Onkologie, 2013	1	Absent	Not reported	/	100%	Not reported	Not reported	100%	100%

S. Valeri et al. Pancreatology 14 (2014) 425-430