

WEBAPPENDIX FOR: “A patient-level meta-analysis of FOLFIRINOX for locally advanced pancreatic cancer.”

Detailed search strategy

Embase.com

((('folinic acid'/exp AND fluorouracil/exp AND irinotecan/exp AND oxaliplatin/exp AND 'drug combination'/exp AND ('pancreas cancer'/de OR 'pancreas tumor'/de OR 'pancreas adenoma'/de OR 'pancreas adenocarcinoma'/de OR 'pancreas carcinoma'/de OR 'pancreas islet cell carcinoma'/de OR (pancrea* NEAR/3 (cancer* OR neoplas* OR tumo* OR adenocarcinom* OR carcinom* OR adenom*)):ab,ti)) OR (Folfinrox):ab,ti)

Medline (OvidSP)

((Leucovorin/ AND fluorouracil/ AND irinotecan.mp. AND oxaliplatin.mp. AND Drug Combinations/ AND (expPancreatic Neoplasms/ OR (pancrea* ADJ3 (cancer* OR neoplas* OR tumo* OR adenocarcinom* OR carcinom* OR adenom*)):ab,ti.)) OR (Folfinrox).ab,ti.)

Cochrane

(Folfinrox):ab,ti

Web-of-science

TS=(Folfinrox)

Scopus

TITLE-ABS-KEY(Folfinrox)

PubMed publisher

Folfinrox[tiab] AND publisher[sb]

Google scholar

Folfinrox

Excluded studies after full text assessment

1. Paniccia A, Edil BH, Schulick RD, et al: Neoadjuvant FOLFIRINOX application in borderline resectable pancreatic adenocarcinoma. *Medicine* 93, 2014
2. Conroy T, Gavaille C, Samalin E, et al: The role of the FOLFIRINOX regimen for advanced pancreatic cancer. *Curr Oncol Rep* 15:182-189, 2013
3. Nakai Y, Isayama H, Sasaki T, et al: A retrospective analysis of early CA19-9 change in salvage chemotherapy for refractory pancreatic cancer. *Cancer Chemother Pharmacol* 72:1291-1297, 2013
4. Shitara K, Munakata M, Kasai M, et al: Prolongation of survival and improvement in performance status following palliative chemotherapy in gastrointestinal cancer patients with a poor performance status. *Oncology (Switzerland)* 74:135-142, 2008
5. Kobayashi N, Shimamura T, Tokuhisa M, et al: Second-line chemotherapy by folfinorox with unresectable pancreatic cancer (phase I, II study). *Ann Oncol* 24:ix47, 2013
6. Tinchon C, Hubmann E, Pichler A, et al: Safety and efficacy of neoadjuvant FOLFIRINOX treatment in a series of patients with borderline resectable pancreatic ductal adenocarcinoma. *Acta Oncol* 52:1231-1234, 2013
7. Edil BH, Schulick RD, Byers JT, et al: Neoadjuvant FOLFIRINOX Application in Borderline Resectable Pancreatic Adenocarcinoma: A Retrospective Cohort Study. *Medicine (Baltimore)* 93:e198, 2014
8. Christians KK, Tsai S, Mahmoud A, et al: Neoadjuvant FOLFIRINOX for borderline resectable pancreas cancer: A new treatment paradigm? *Oncologist* 19:266-274, 2014
9. Taieb J, Lecomte T, Aparicio T, et al: FOLFIRI.3, a new regimen combining 5-fluorouracil, folinic acid and irinotecan, for advanced pancreatic cancer: Results of an Association des Gastro-Enterologues Oncologues (Gastroenterologist Oncologist Association) multicenter phase II study. *Ann Oncol* 18:498-503, 2007
10. Oh SY, Kim HJ, Kim TH, et al: Pilot study of irinotecan/oxaliplatin (IROX) combination chemotherapy for patients with gemcitabine- and 5-fluorouracil- refractory pancreatic cancer. *Invest New Drugs* 28:343-349, 2010
11. Mazard T, Ychou M, Thezenas S, et al: Feasibility of biweekly combination chemotherapy with capecitabine, irinotecan, and oxaliplatin in patients with metastatic solid tumors: results of a two-step phase I trial: XELIRI and XELIRINOX. *Cancer Chemother. Pharmacol.* 69:807-814, 2012

12. Lee MG, Lee SH, Hwang JH, et al: FOLFIRINOX as second-line chemotherapy in patients with advanced pancreatic cancer who have progressed on gemcitabine-based therapy. *Eur J Intern Med* 24:e140, 2013
13. Lee MG, Lee SH, Lee SJ, et al: 5-fluorouracil/leucovorin combined with irinotecan and oxaliplatin (FOLFIRINOX) as second-line chemotherapy in patients with advanced pancreatic cancer who have progressed on gemcitabine-based therapy. *Chemotherapy* 59:273-279, 2014
14. Abendroth A, Nourredine R, Abramczyk M, et al: Prognostic factors in patients with pancreatic cancer receiving sequential chemotherapies (CTX) at the West German Cancer Center (WTZ), one of the 12 Oncology Centers of Excellence in Germany. *Oncol Res Treat* 37:123-124, 2014
15. Anota A, Mouillet G, Trouilloud I, et al: Sequential FOLFIRI.3+Gemcitabine Improves Health-Related Quality of Life Deterioration-Free Survival of Patients with Metastatic Pancreatic Adenocarcinoma: A Randomized Phase II Trial. *PLoS One* 10, 2015
16. Nanda RH, El-Rayes B, Maithel SK, et al: Neoadjuvant modified FOLFIRINOX and chemoradiation therapy for locally advanced pancreatic cancer improves resectability. *J Surg Oncol* 111:1028-1034, 2015
17. Yao X, Cong X, Thumar JR, et al: FOLFIRINOX for locally advanced and metastatic pancreatic cancer: single institution retrospective review of efficacy and toxicity Review. *Med Oncol* 30:361, 2013

Webappendix tables and figures

Table 1. Articles retrieved from different electronic databases.

Electronic database	Retrieved	Unique studies
Embase.com	741	730
Medline (OvidSP)	163	14
Web-of-science	199	43
Scopus	194	12
PubMed publisher	7	3
Cochrane central	12	0
Google scholar	100	38
Total	1416	840

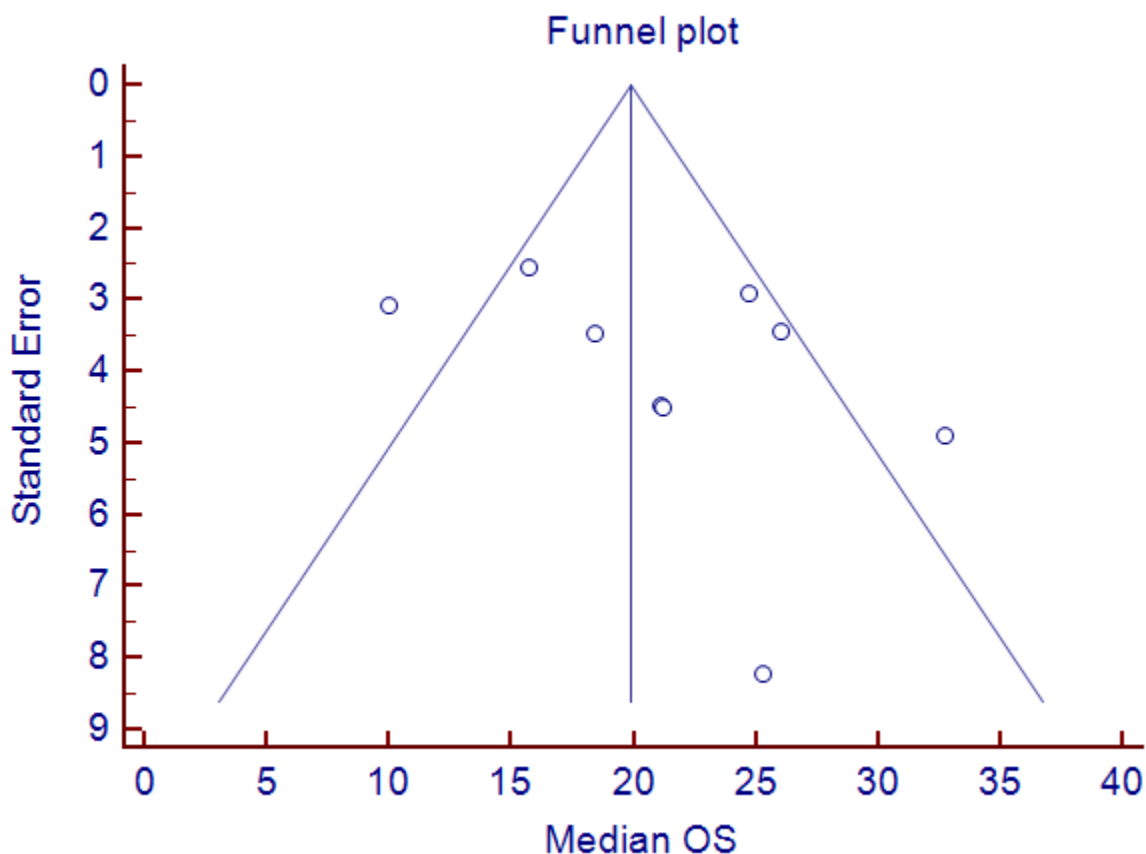
Last search in electronic databases performed on the 2nd of July 2015

Table 2. Quality assessment according to Critical Appraisal Skill Program.

CASP factors	Boone	Conroy	Faris	Ferrone	Gunturu	Hohla	Hosein	Mahaseth	Marthey	Mellon	Moorcraft	Peddi	Sadot
Clearly focused question	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Appropriate design	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Appropriate recruitment	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Operation clearly defined	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Appropriate outcomes used	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Confounding factors identified	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Confounding factors accounted	Yes	Yes	NR	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Follow-up complete enough	No	Yes	No	Yes	NR	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Suitable duration of follow-up	No	Yes	No	No	No	NR	No	NR	Yes	Yes	Yes	No	Yes
Precise statistical results presented	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Appropriate interpretation	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Possible bias acknowledged	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ability to generalise results	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Interpretation related to the existing evidence	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

NR = Not Reported

Figure 1. Funnel plot of the survival studies.



Two studies are not shown in this funnel plot as Peddi et al. did not reach the median OS and Mellon et al. did not have a sufficient number of events to calculate the standard error. Therefore the median OS in this funnel plot differs slightly from the pooled analysis.

Figure 3. Percentage of (chemo)radiation and median OS across studies ($p=0.12$).

Figure 2 Median number of FOLFIRINOX cycles and median OS across studies (p=0.95).

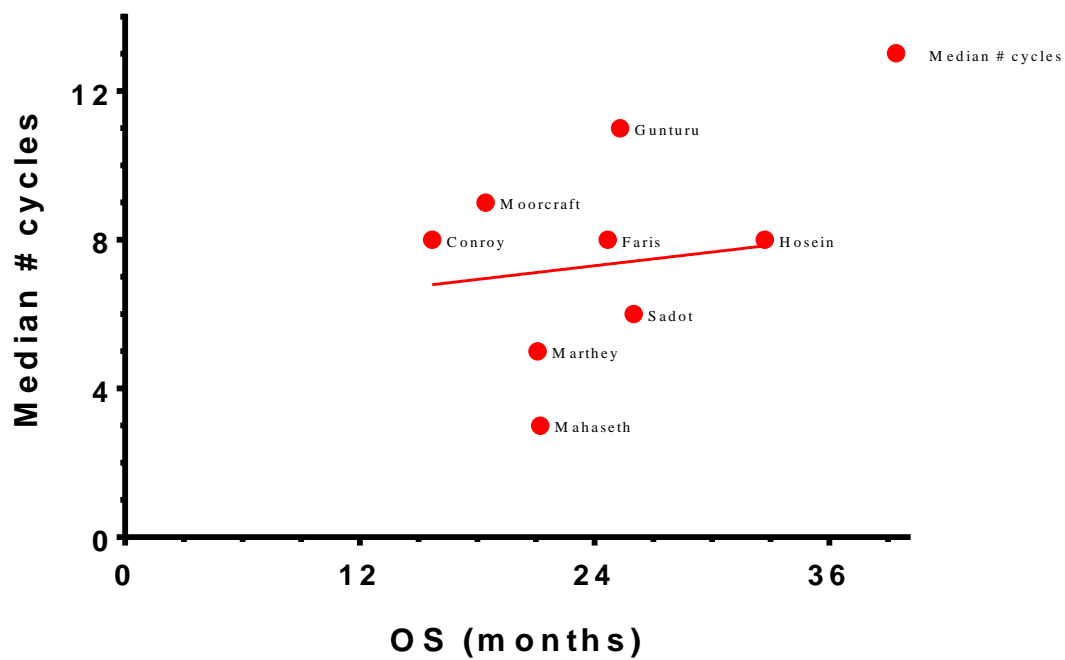


Figure 3. Percentage of (chemo)radiation and median OS across studies (p=0.12).

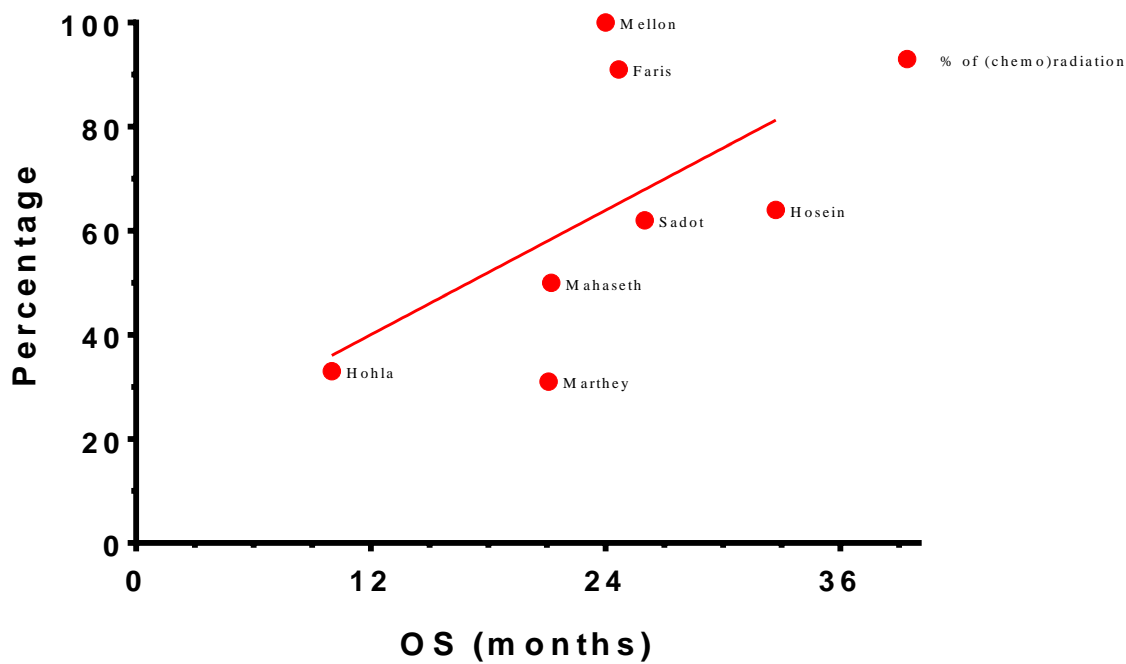


Figure 4 Percentage of resection and median OS across studies (p=0.39).

