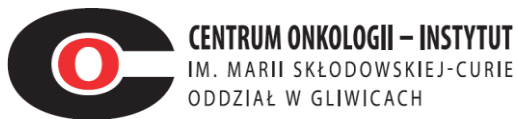


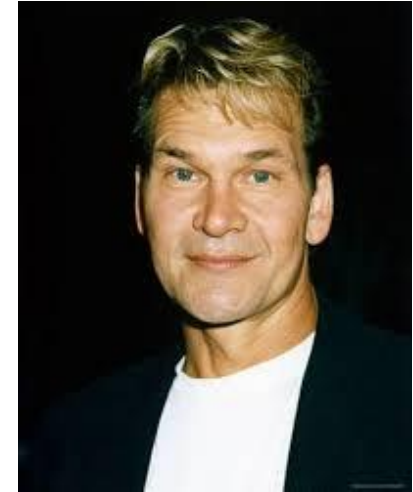
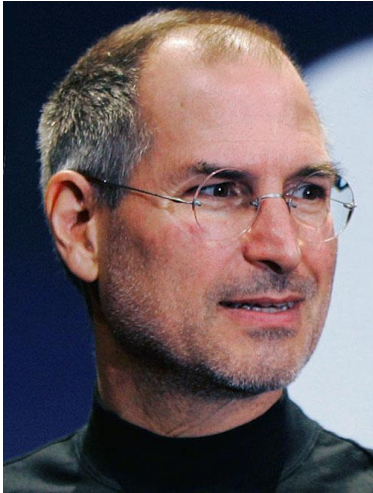
Radioterapia w raku trzustki:

wyniki badań klinicznych, praktyka kliniczna, miejsce SBRT

Rafał Suwiński



Rak trzustki



Rak trzustki: miejsce radioterapii

- **leczenie adjuwantowe**
- **leczenie neoadjuwantowe**
- **leczenie samodzielne (RT, RT-CT)**
- **leczenie paliatywne**

Further Evidence of Effective Adjuvant Combined Radiation
and Chemotherapy Following Curative
Resection of Pancreatic Cancer

GASTROINTESTINAL TUMOR STUDY GROUP

40 Gy d fx 2.0 (split course !) + 5 Fu

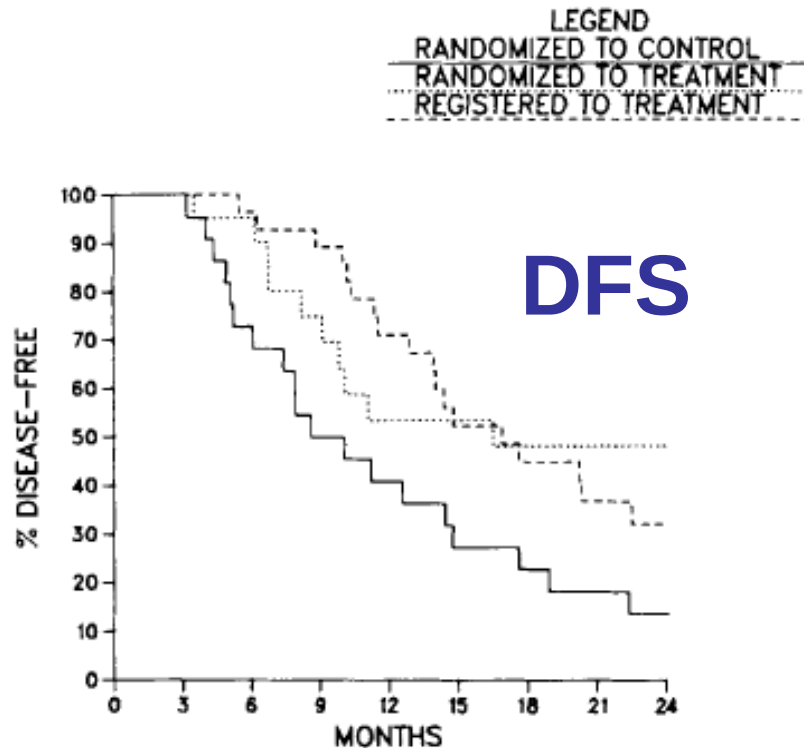


FIG. 1. Probability of disease-free survival by treatment.

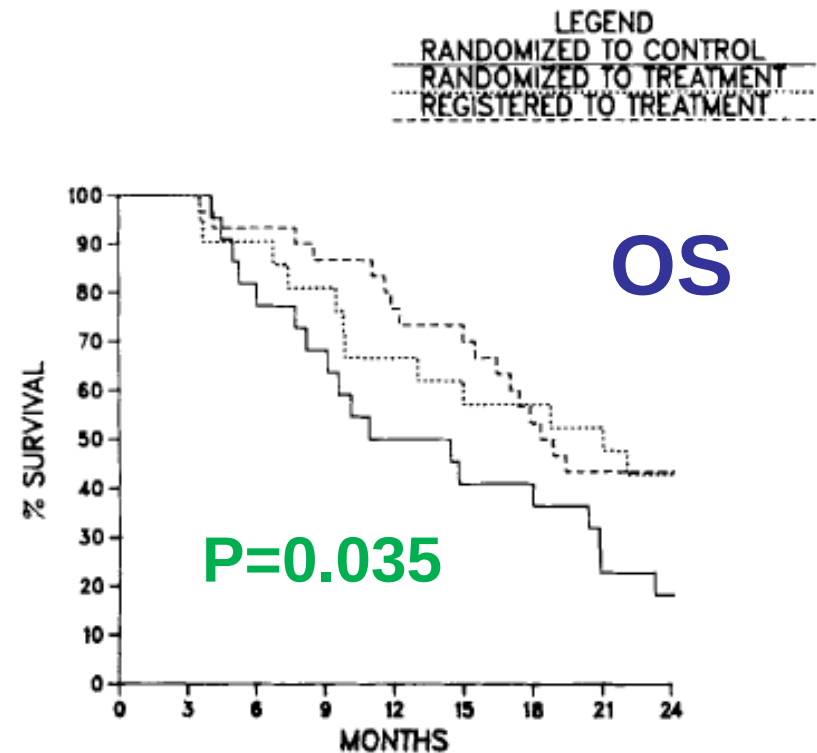
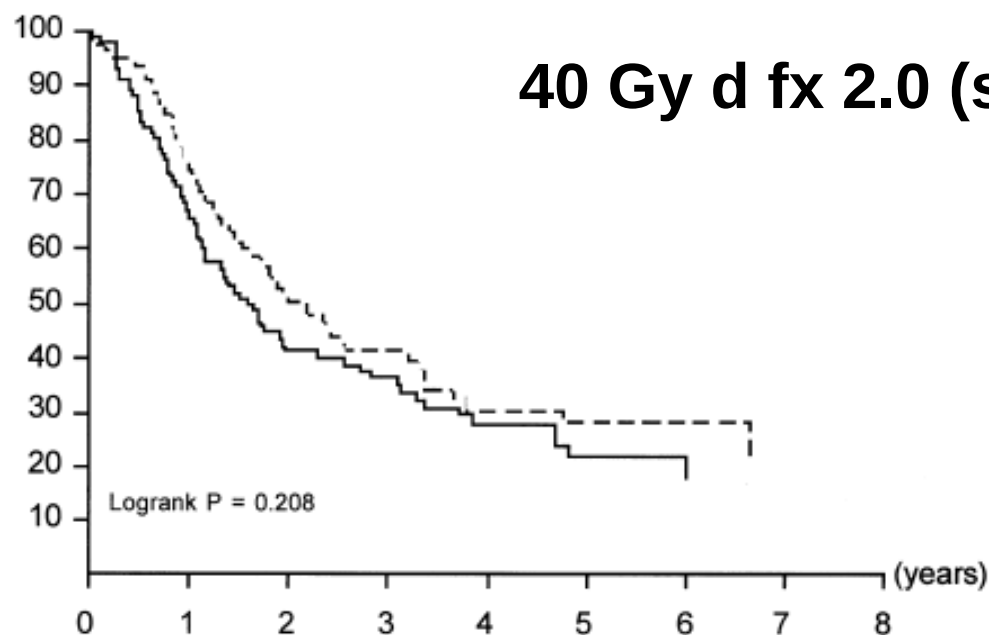


FIG. 2. Probability of survival by treatment.

Cancer 59:2006–2010, 1987.

Adjuvant Radiotherapy and 5-Fluorouracil After Curative Resection of Cancer of the Pancreas and Periapillary Region

Phase III Trial of the EORTC Gastrointestinal Tract Cancer Cooperative Group



40 Gy d fx 2.0 (split course !) + 5 Fu

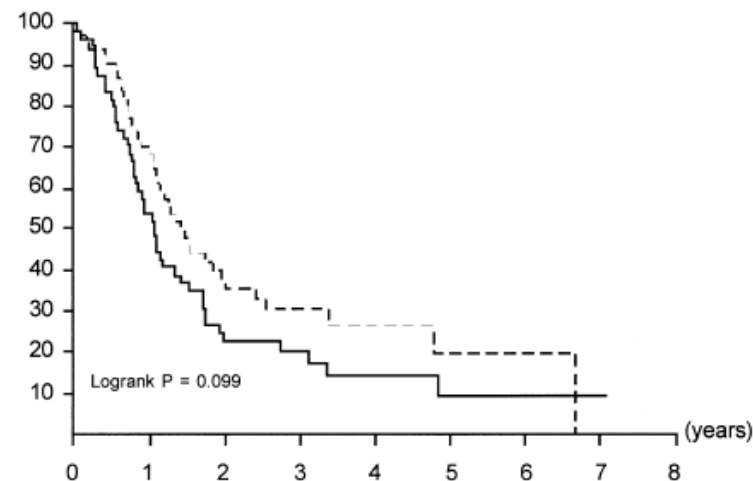
P=0.20

Ann. Surg. • December 1999

O	N	Number of patients at risk :								
72	103	67	37	27	17	8	5	2	Observ	
63	104	74	42	27	16	11	7	3	Rtx5FU	

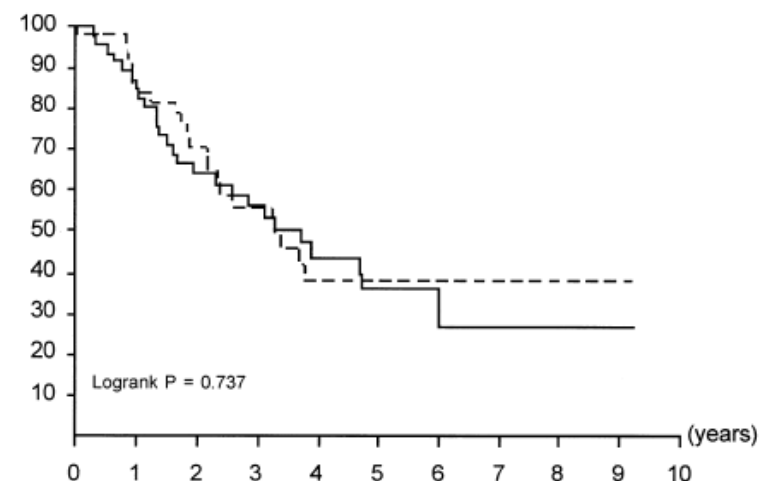
Adjuvant Radiotherapy and 5-Fluorouracil After Curative Resection of Cancer of the Pancreas and Periapillary Region

Phase III Trial of the EORTC Gastrointestinal Tract Cancer Cooperative Group



O	N	Number of patients at risk :								
45	54	29	11	7	5	1	1	1	—	Observ
41	60	39	17	9	6	3	1	0	- - -	Rtx5FU

Głowa trzustki



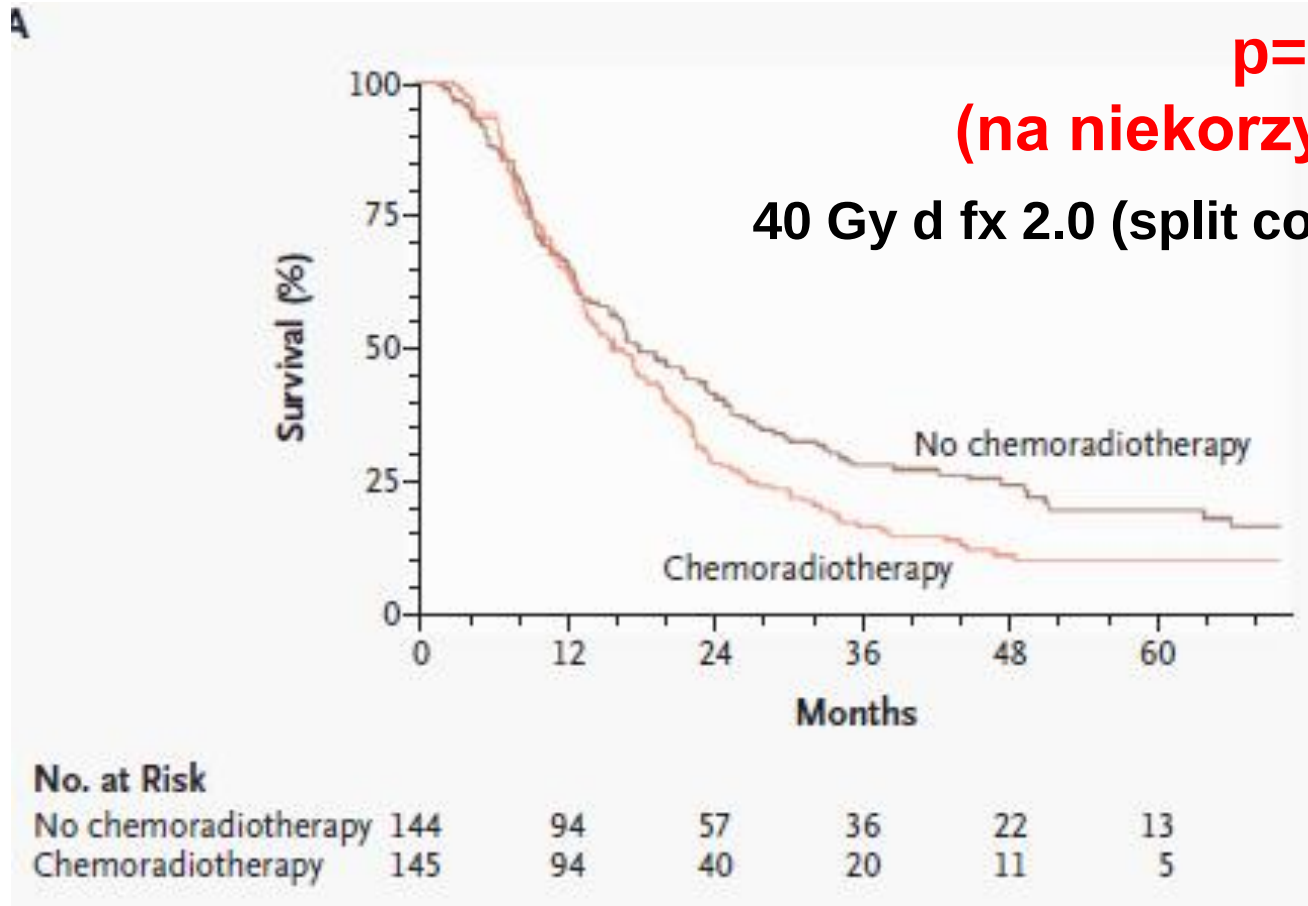
O	N	Number of patients at risk :										
26	48	38	26	20	12	7	4	1	1	1	—	Observ
22	44	35	25	18	10	8	6	3	3	1	- - -	Rtx5FU

Brodawka Vatera

Ann. Surg. • December 1999

A Randomized Trial of Chemoradiotherapy and Chemotherapy after Resection of Pancreatic Cancer

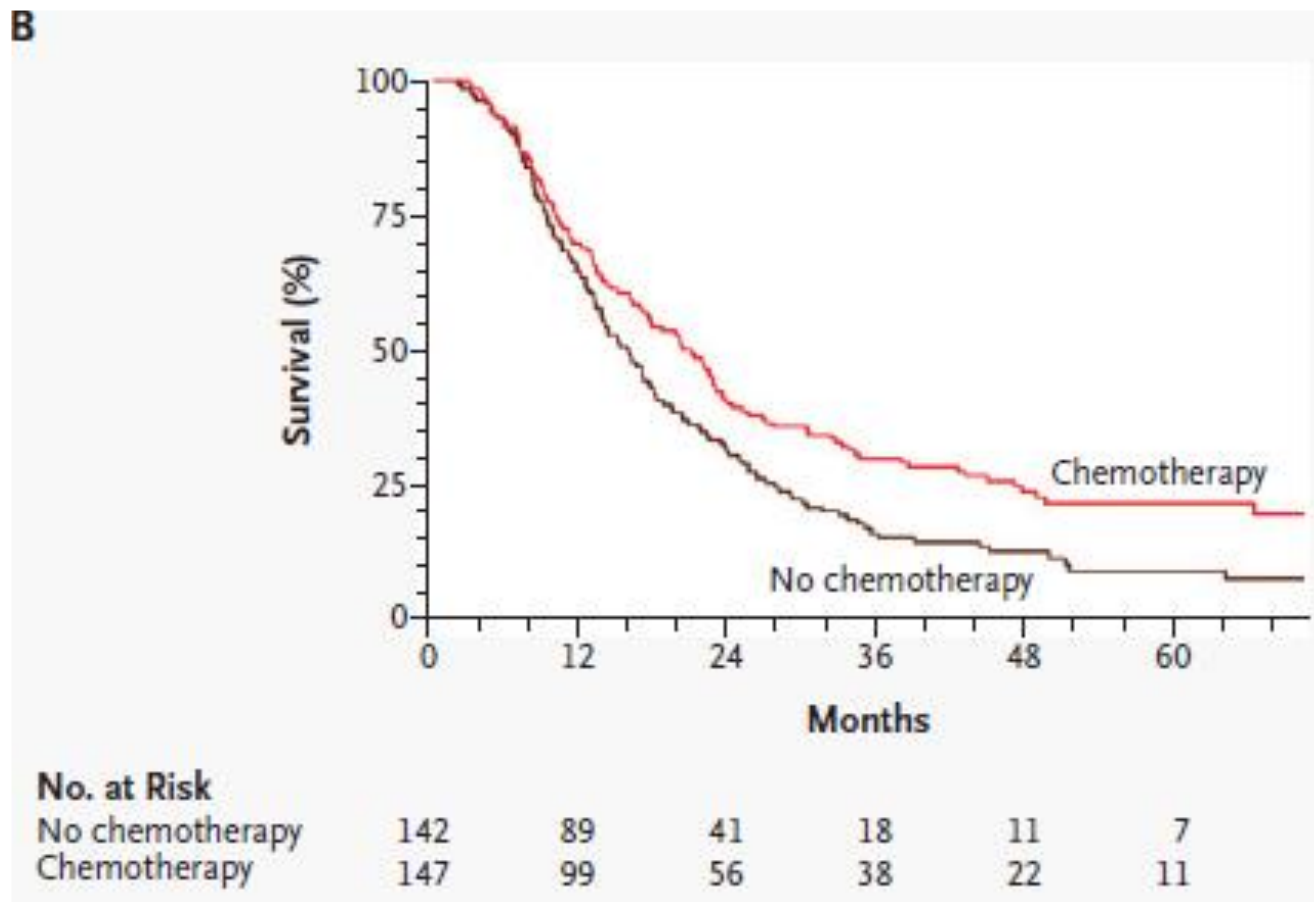
ESPAC-1 Trial



N ENGL J MED 350;12 WWW.NEJM.ORG MARCH 18, 2004

A Randomized Trial of Chemoradiotherapy and Chemotherapy after Resection of Pancreatic Cancer

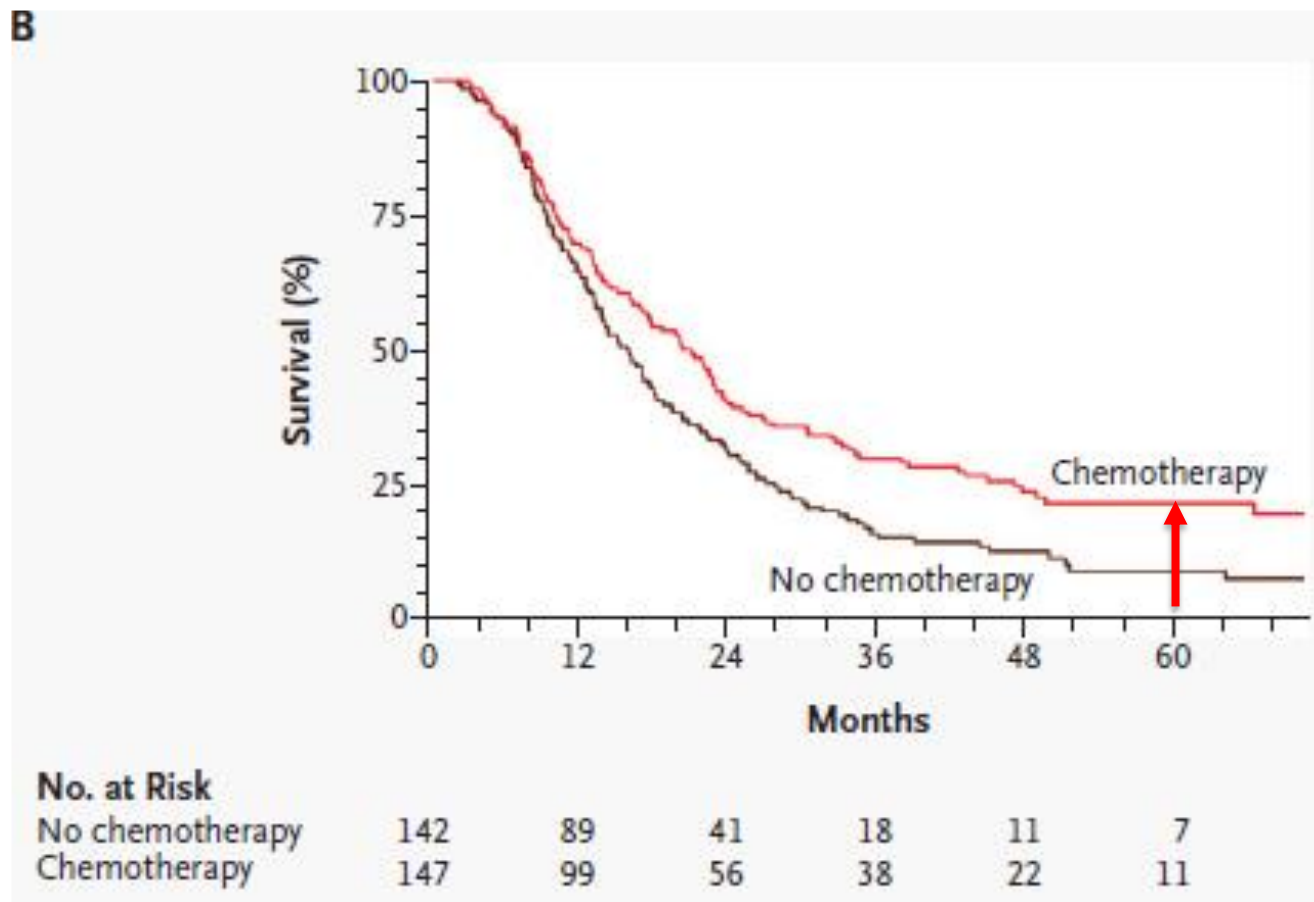
ESPAC-1 Trial



p=0.009
(na korzyść CT)

A Randomized Trial of Chemoradiotherapy and Chemotherapy after Resection of Pancreatic Cancer

ESPAC-1 Trial

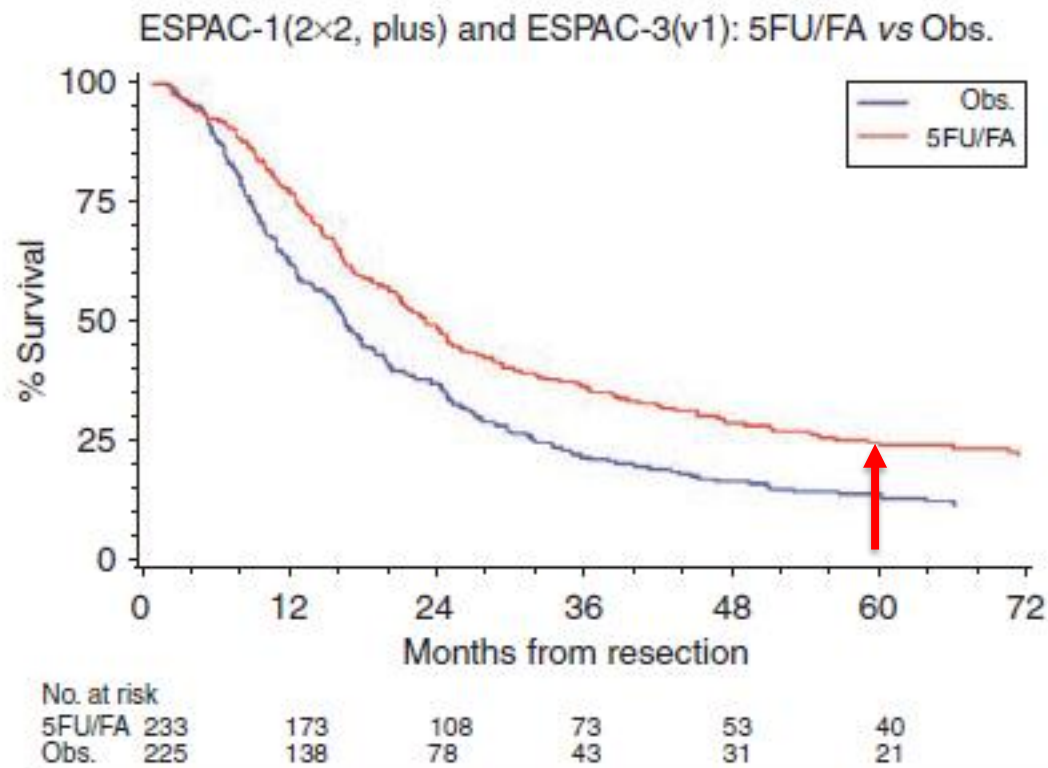


p=0.009
(na korzyść CT)

5-year OS
~20%

Adjuvant 5-fluorouracil and folinic acid vs observation for pancreatic cancer: composite data from the ESPAC-1 and -3(v1) trials

ESPAC-1 + ESPAC-3



5-Fu+Lv

**5-year OS
~25%**

Figure 4 Kaplan-Meier overall survival curves non-stratified by trial.

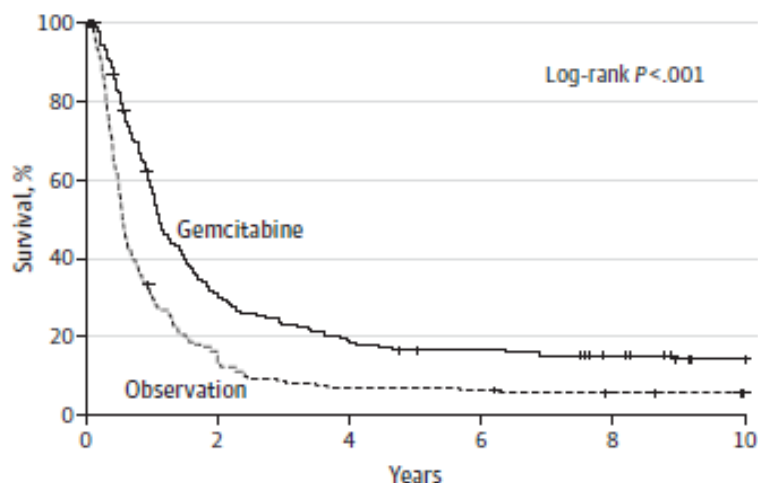
British Journal of Cancer (2009) 100, 246–250

Adjuvant Chemotherapy With Gemcitabine and Long-term Outcomes Among Patients With Resected Pancreatic Cancer

The CONKO-001 Randomized Trial

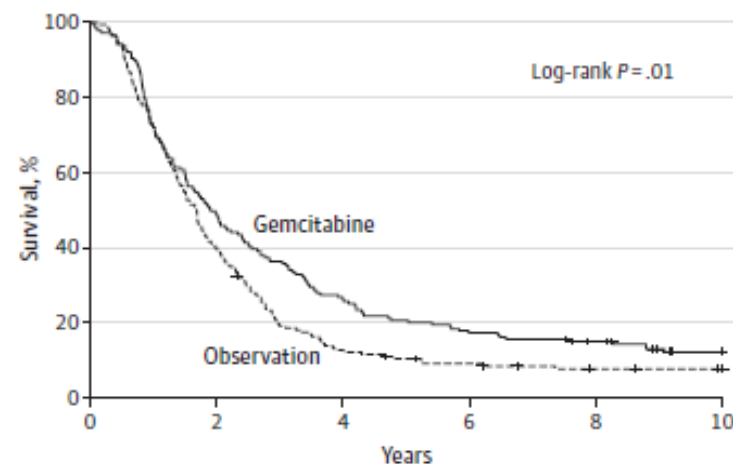
CONKO-001

A Disease-free survival



No. at risk	0	2	4	6	8	10
Gemcitabine	179	52	32	26	20	12
Observation	175	26	12	11	8	6

B Overall survival

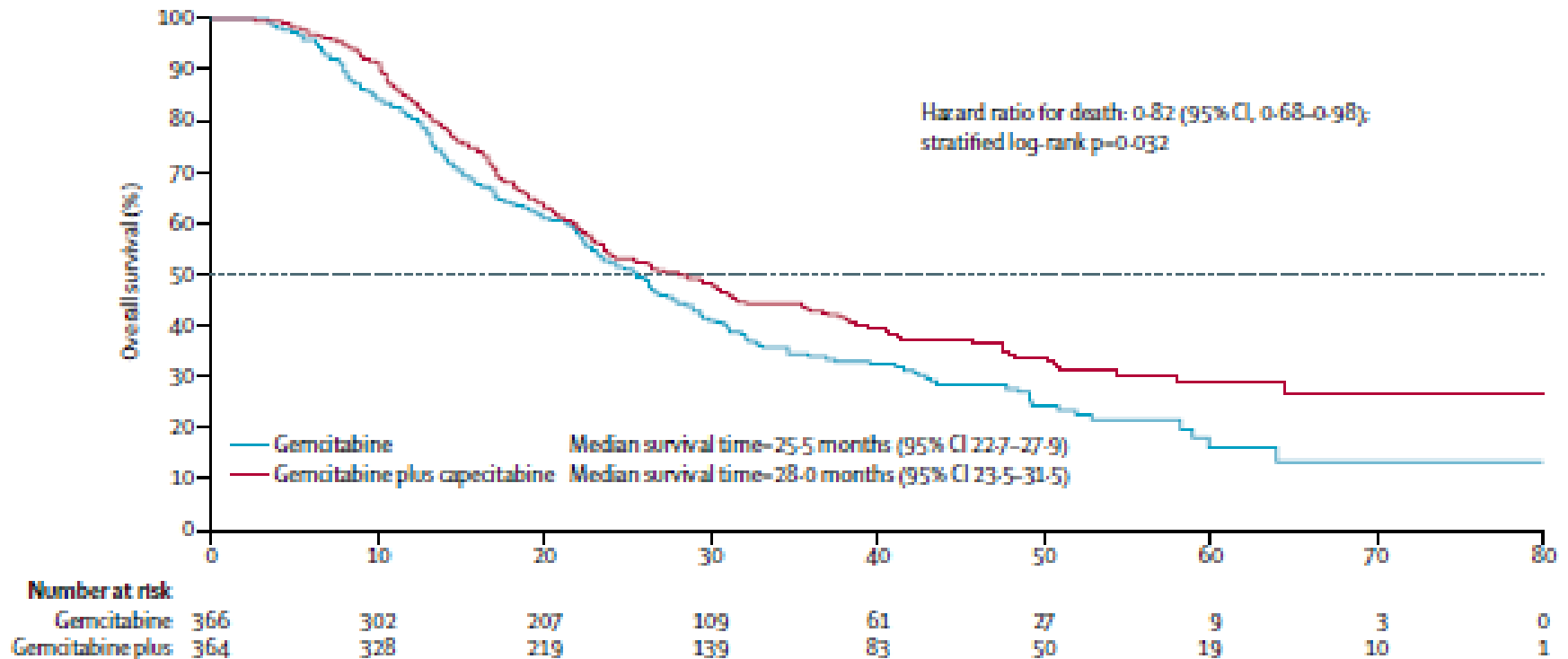


No. at risk	0	2	4	6	8	10
Gemcitabine	179	87	47	31	24	14
Observation	175	70	22	14	9	7

JAMA. 2013;310(14):1473-1481.

Gemcytabine

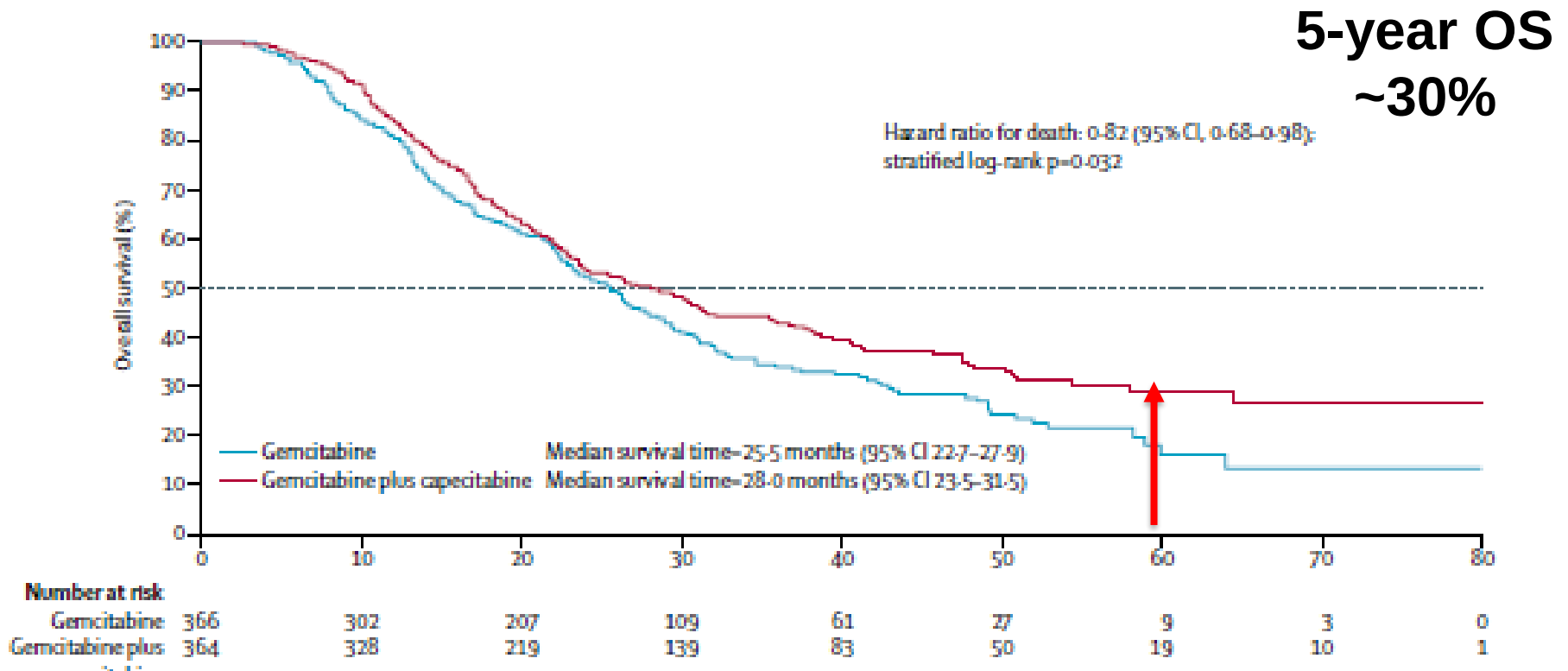
Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial



Gem+Cape

Lancet 2017; 389: 1011-24

Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial



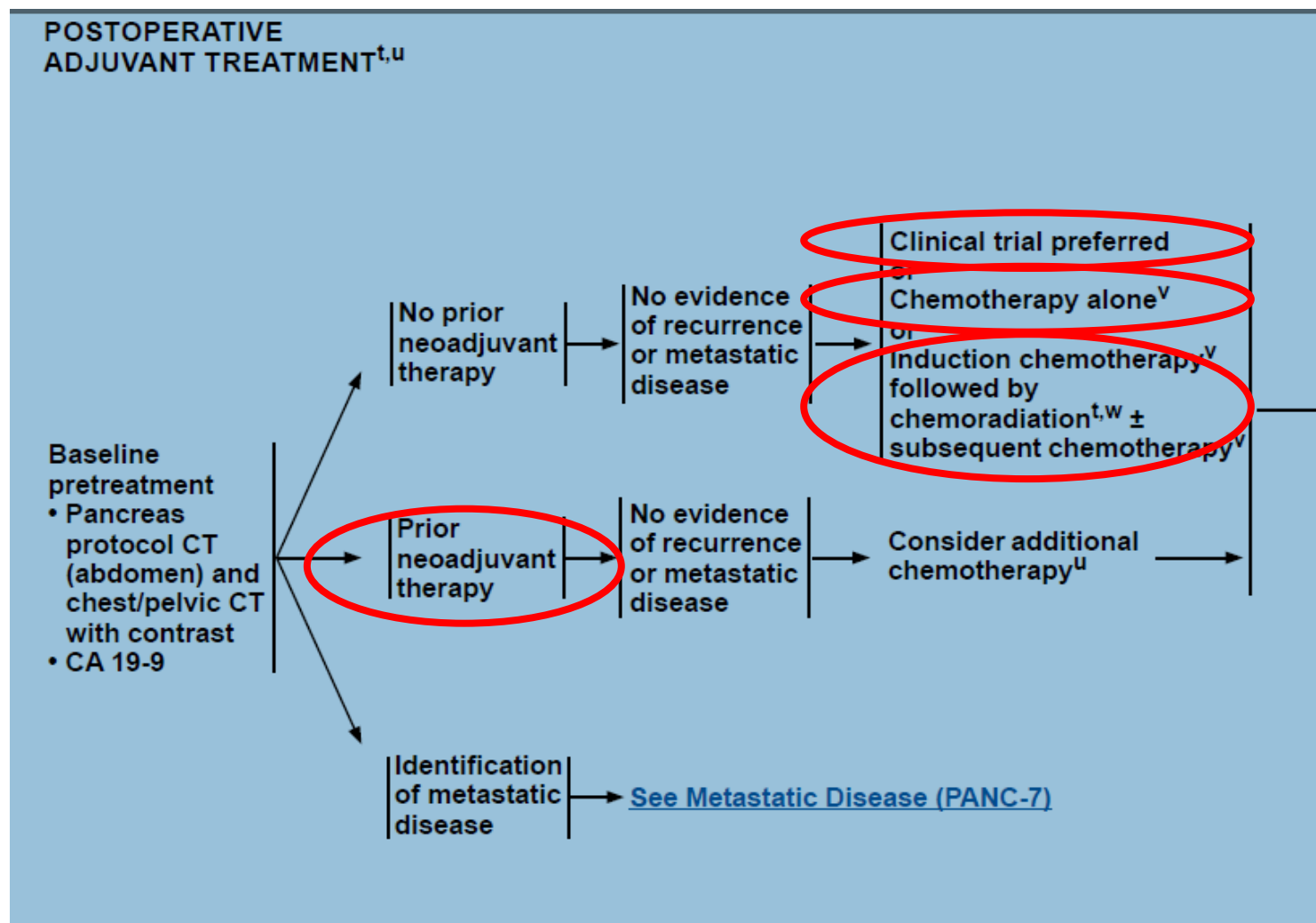
Gem+Cape

Lancet 2017; 389: 1011–24

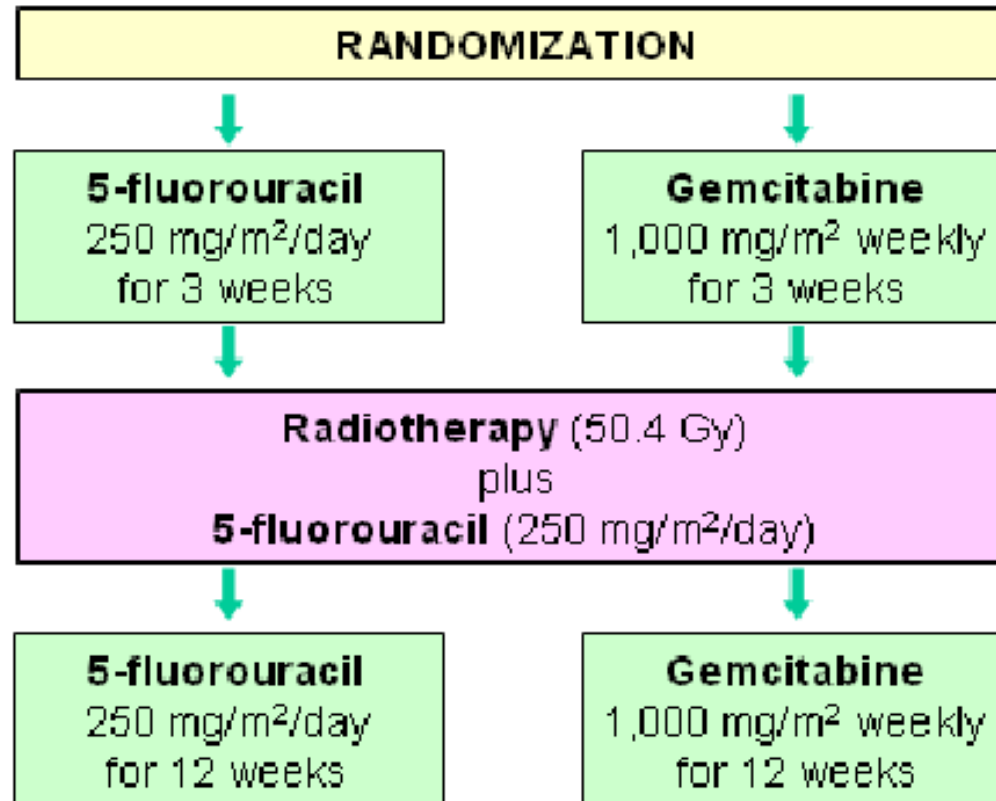
Rak trzustki: leczenie uzupełniające

ESMO / PTOK: Chemioterapia

Rak trzustki: zalecenia NCCN

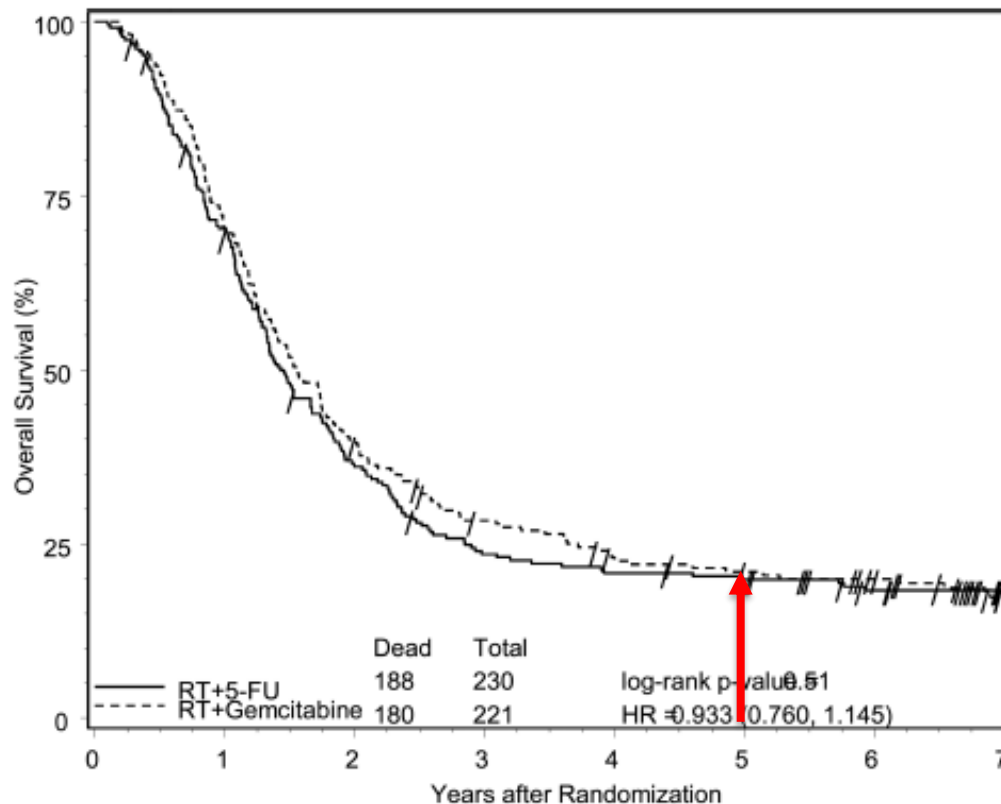


Fluorouracil Based Chemoradiation with Either Gemcitabine or Fluorouracil Chemotherapy Following Resection of Pancreatic Adenocarcinoma: 5-Year Analysis of the US Intergroup/RTOG 9704 Phase III Trial



Ann Surg Oncol. 2011 May ; 18(5): 1319–1326.

Fluorouracil Based Chemoradiation with Either Gemcitabine or Fluorouracil Chemotherapy Following Resection of Pancreatic Adenocarcinoma: 5-Year Analysis of the US Intergroup/RTOG 9704 Phase III Trial

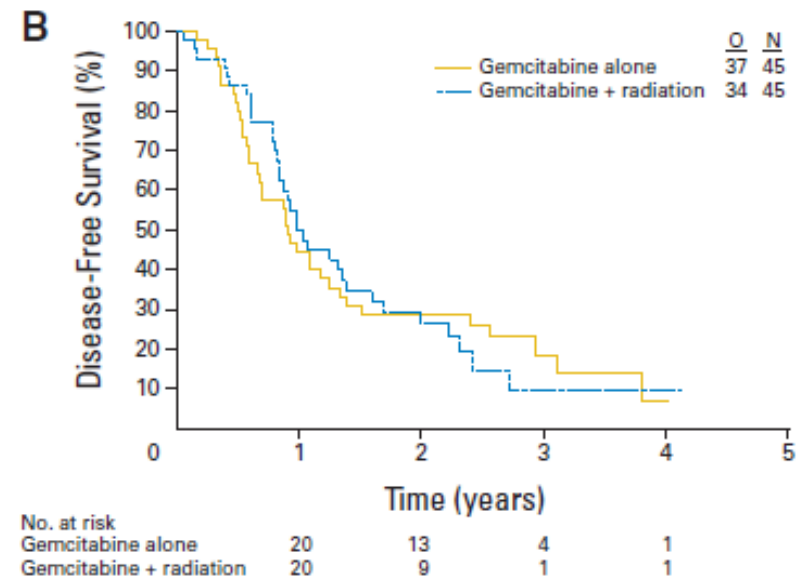
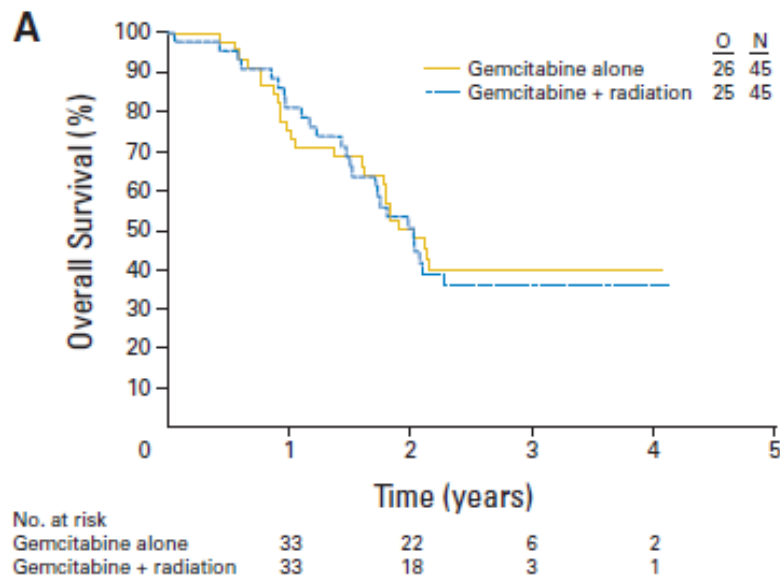


**5-year OS
~20%**

Patients at Risk

RT + 5-FU	230	160	81	52	46	43	33	20
RT + Gemcitabine	221	155	88	59	45	41	34	22

Adjuvant Gemcitabine Alone Versus Gemcitabine-Based Chemoradiotherapy After Curative Resection for Pancreatic Cancer: A Randomized EORTC-40013-22012/FFCD-9203/GERCOR Phase II Study



Conclusion

Adjuvant gemcitabine-based CRT is feasible, well-tolerated, and not deleterious; adding this treatment to full-dose adjuvant gemcitabine after resection of pancreatic cancer should be evaluated in a phase III trial.

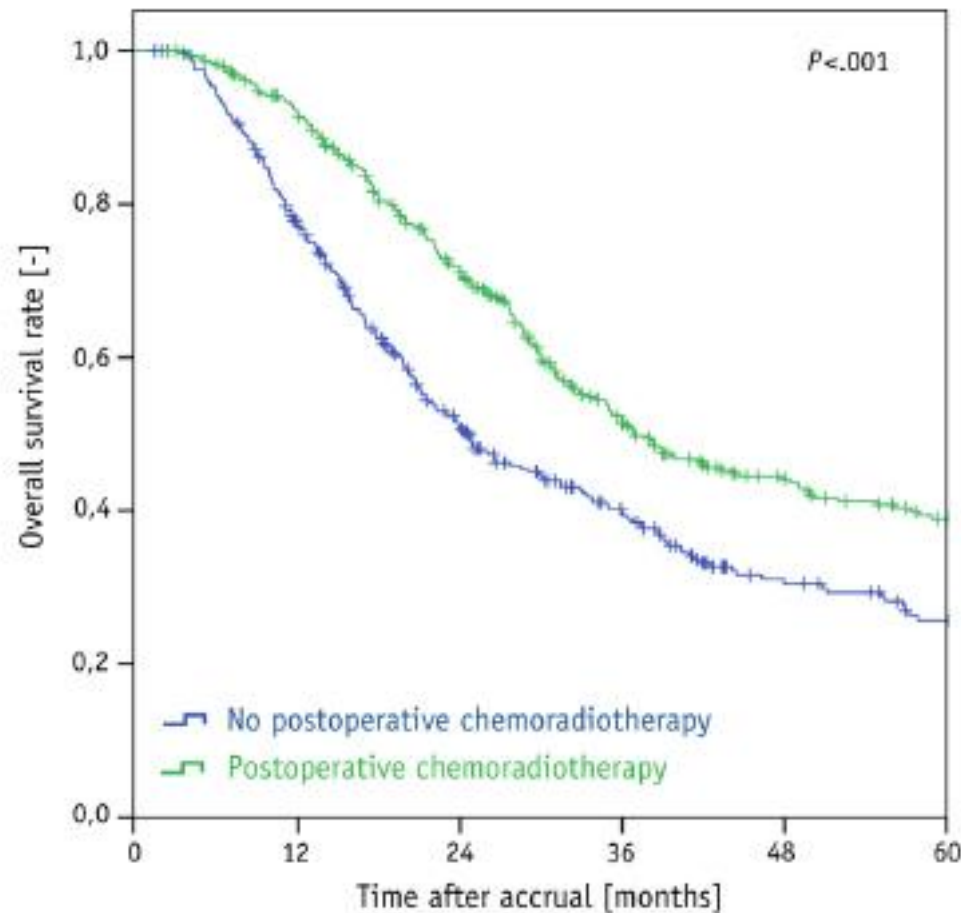
RT (50.4 Gy)+Gem vs Gem

VOLUME 28 · NUMBER 29 · OCTOBER 10 2010

JOURNAL OF CLINICAL ONCOLOGY

Warszawa 2018

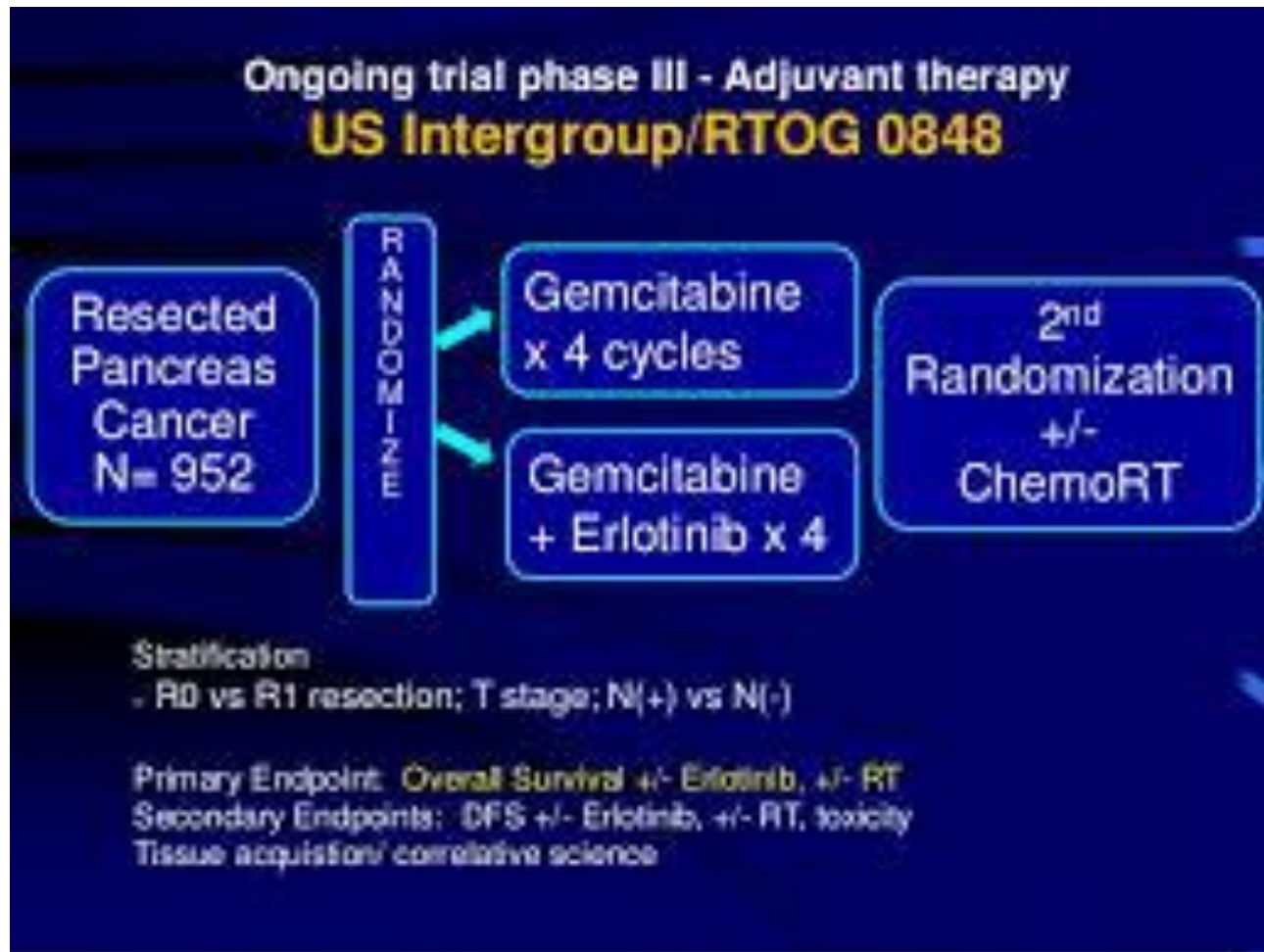
Multi-institutional Pooled Analysis on Adjuvant Chemoradiation in Pancreatic Cancer



**Badanie
retrospektywne !**

Int J Radiation Oncol Biol Phys, Vol. 90, No. 4, pp. 911–917, 2014

Badanie w toku: RTOG 0848



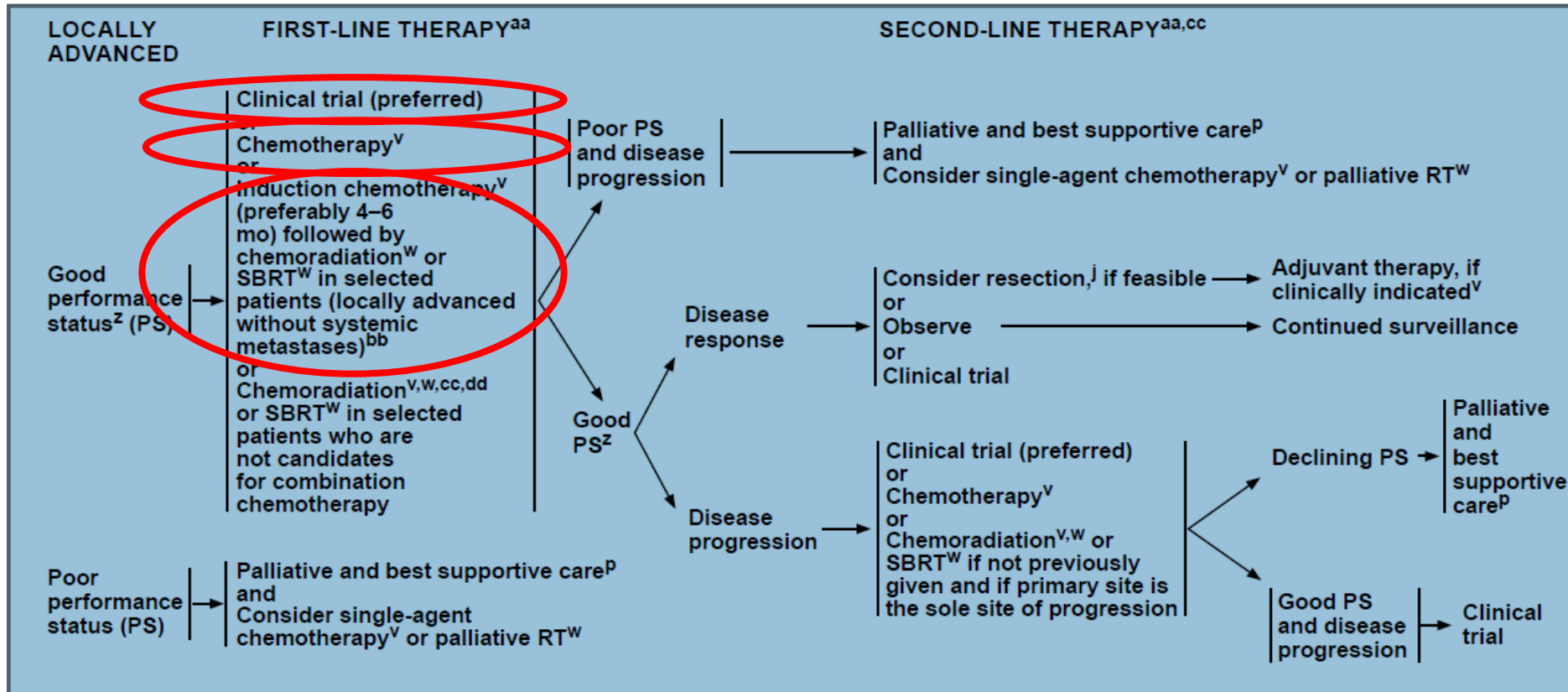
Neoadjuwantowa RT-CT

TABLE IV. Selected Studies on Neoadjuvant Radiation Therapy for Borderline Resectable Pancreatic Cancer

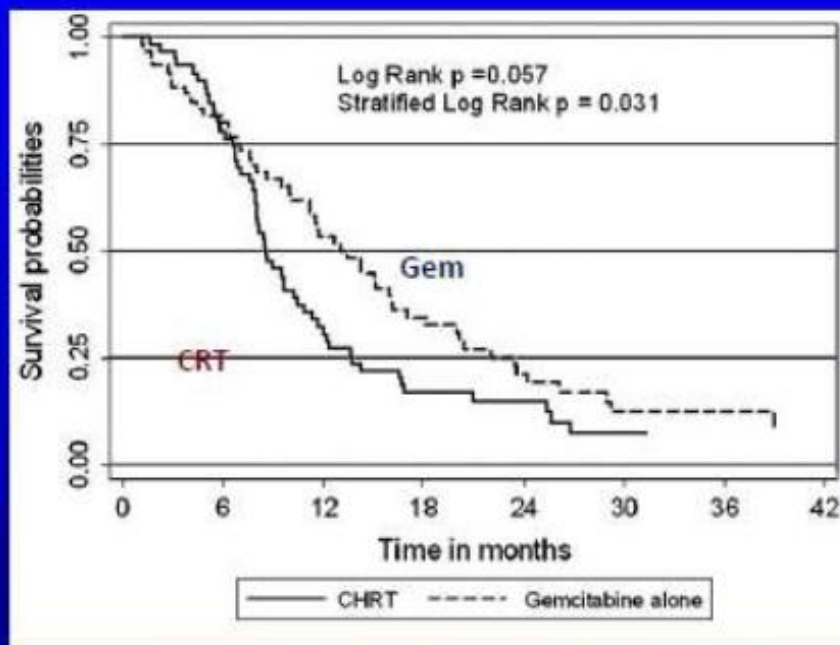
Study	Patients, n	Chemotherapy	Radiotherapy	Patients amenable to surgery (%)
Mehta et al. [24]	15 borderline	5-fluorouracil	50.4–56 Gy	60
Massucco et al. [25]	18 borderline 10 unresectable	Gemcitabine	45–Gy	39
Small et al. [26]	16 resectable 9 borderline 14 unresectable	Gemcitabine	36–Gy in 2.4–Gy/fraction	39
Patel et al. [27]	17 borderline	Gemcitabine	IMRT 50–Gy to gross disease and 45–Gy to microscopic disease	64
Stokes et al. [28]	40 borderline	Capecitabine	50.4 Gy	40

Journal of Surgical Oncology 2013;107:86–96

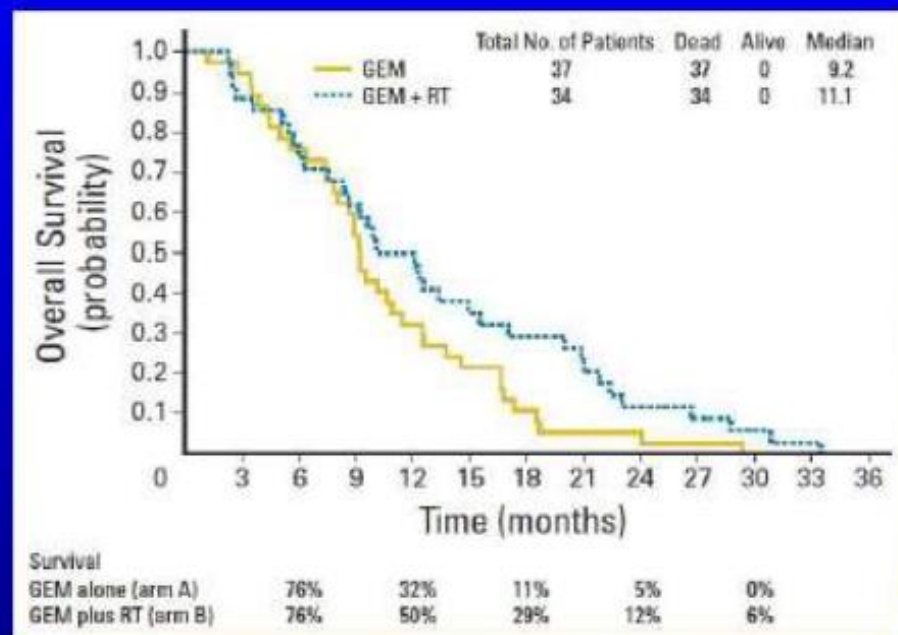
Miejscowo zaawansowany rak trzustki: zalecenia NCCN



Rak trzustki miejscowo zaawansowany

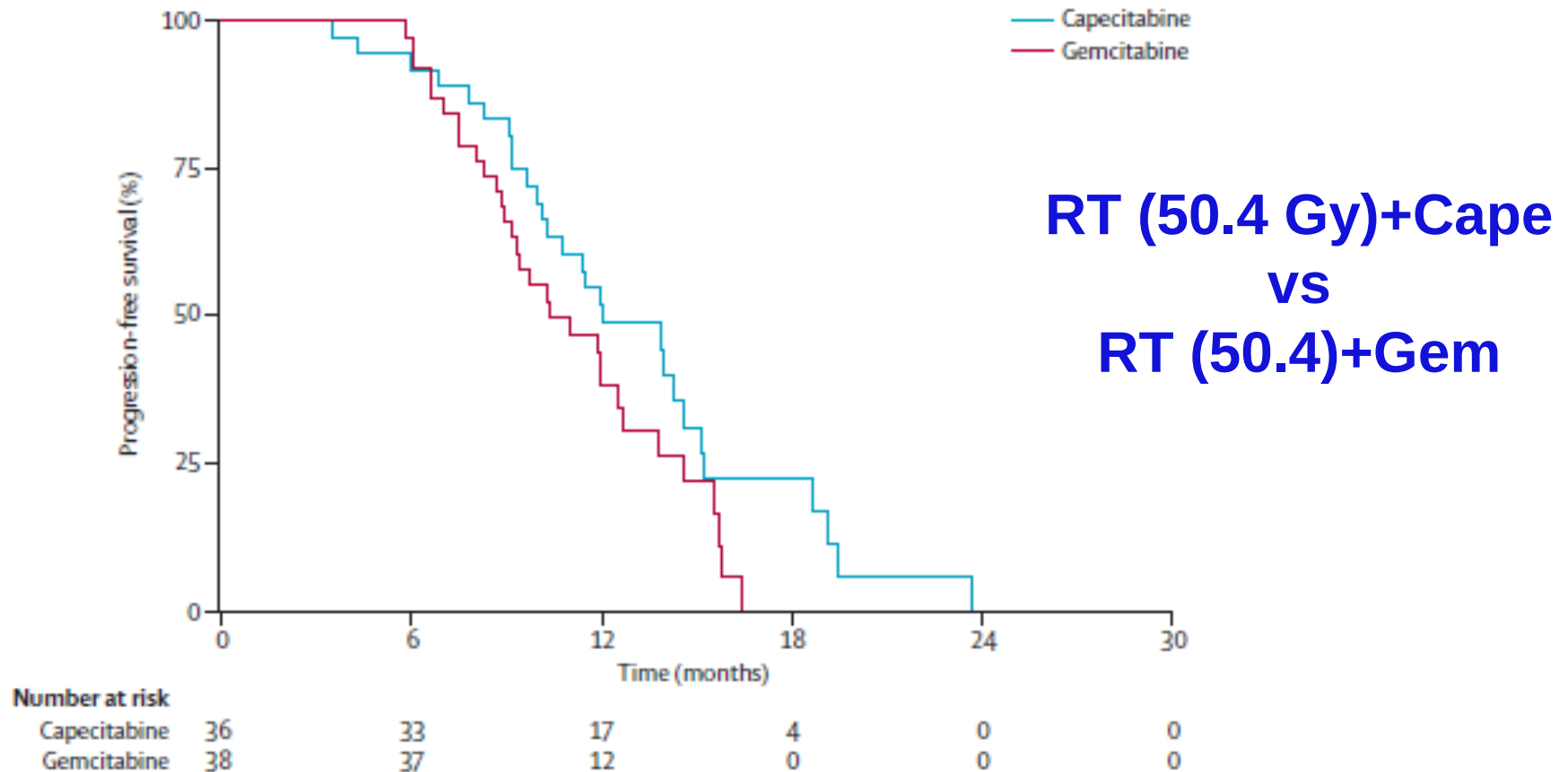


Chauffert B et al. Ann Oncol 2008



Loehrer P et al. J Clin Oncol 2011

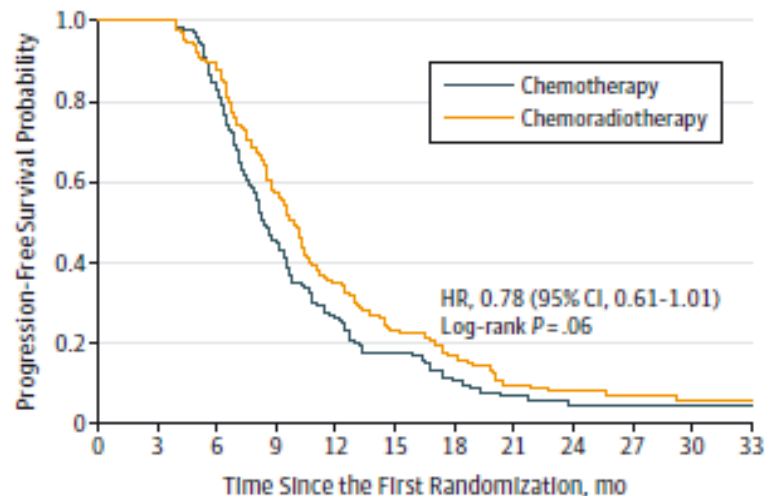
Gemcitabine-based or capecitabine-based chemoradiotherapy for locally advanced pancreatic cancer (SCALOP): a multicentre, randomised, phase 2 trial



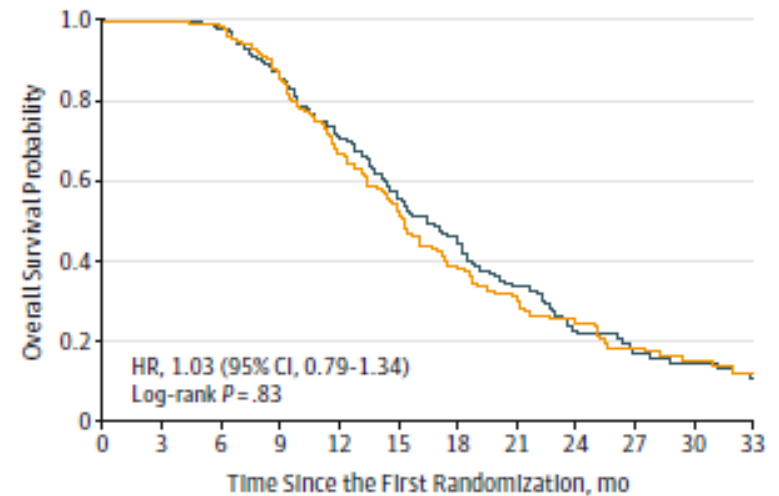
Lancet Oncol 2013; 14: 317-26

Effect of Chemoradiotherapy vs Chemotherapy on Survival in Patients With Locally Advanced Pancreatic Cancer Controlled After 4 Months of Gemcitabine With or Without Erlotinib The LAP07 Randomized Clinical Trial

B Progression-free survival probability



A Overall survival probability



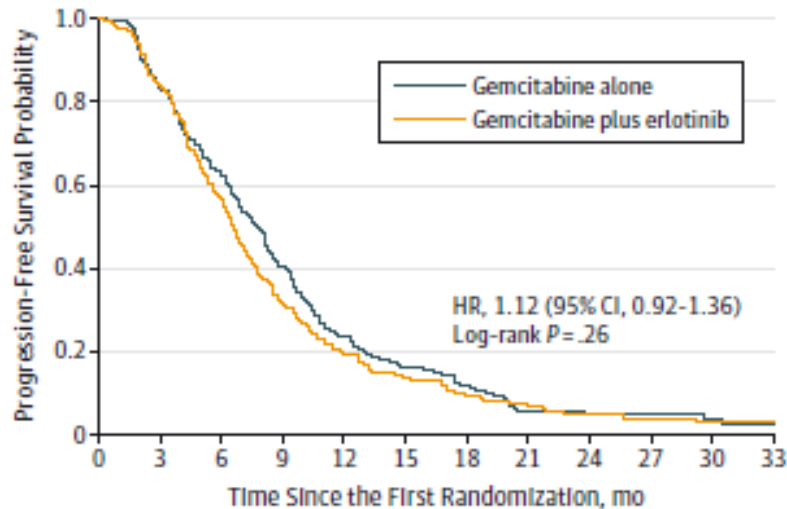
**RT (54 Gy) + Gem
vs Gem**

JAMA May 3, 2016 Volume 315, Number 17

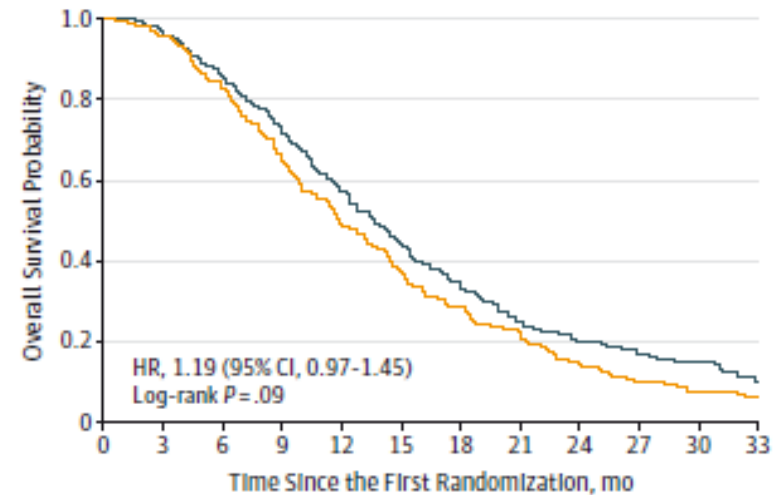
Effect of Chemoradiotherapy vs Chemotherapy on Survival in Patients With Locally Advanced Pancreatic Cancer Controlled After 4 Months of Gemcitabine With or Without Erlotinib

The LAP07 Randomized Clinical Trial

B Progression-free survival probability



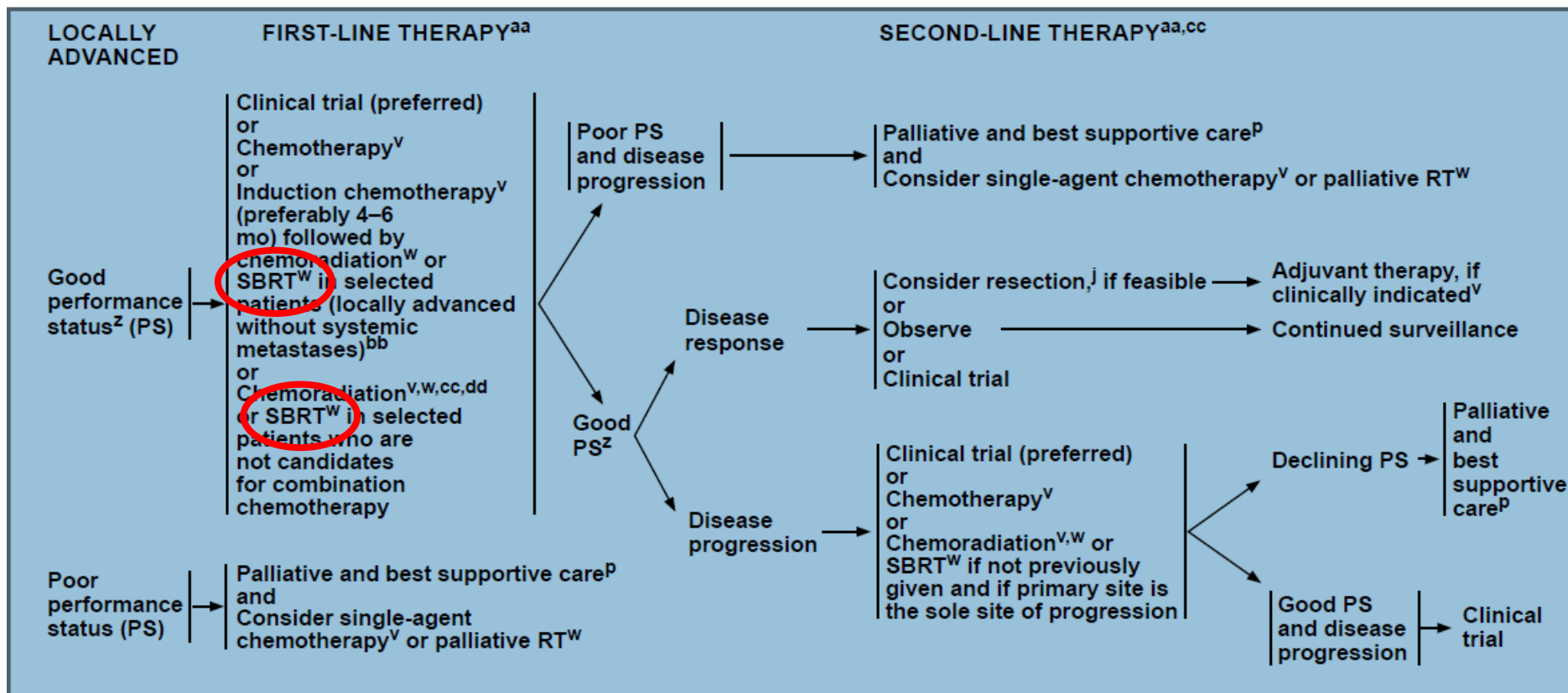
A Overall survival probability



JAMA May 3, 2016 Volume 315, Number 17

**Gem vs Gem + Erlotinib
(± RT)**

Rak trzustki: miejsce SBRT



Rak trzustki: miejsce SBRT

Study	N	Regimen	Median OS Months	Local control (1 year)	Grade ≥3 Toxicity * Acute	Late
Mahadevan (2010) GEM	36	8-12 Gy x 3	14.3	78%	8% G3	6% G3
Polistina (2010) GEM	23	10 Gy x 3	10.6	50%	0	0
Lominska (2011) 5-FU/GEM	28	4-8 Gy x 3-5	5.9	86%	0	7.1% G3
Chuong (2012) GTX	16	5-10 Gy X 5	15	81%*	0	5.3% G3
Tozzi (2013) GEM	30	8 Gy x 5	11.0	86%	0	0
Gurka (2013) GEM	10	5 Gy x 5	12.2	40%	0	0
Herman, (2013, Multi-center)	49	6.6 Gy x 5	13.9	83%	12.2%	10.6%

Pagkretasos K 2014

Mediana OS: 6-14 msc
1-year LC 40-86%

Rak trzustki: miejsce SBRT

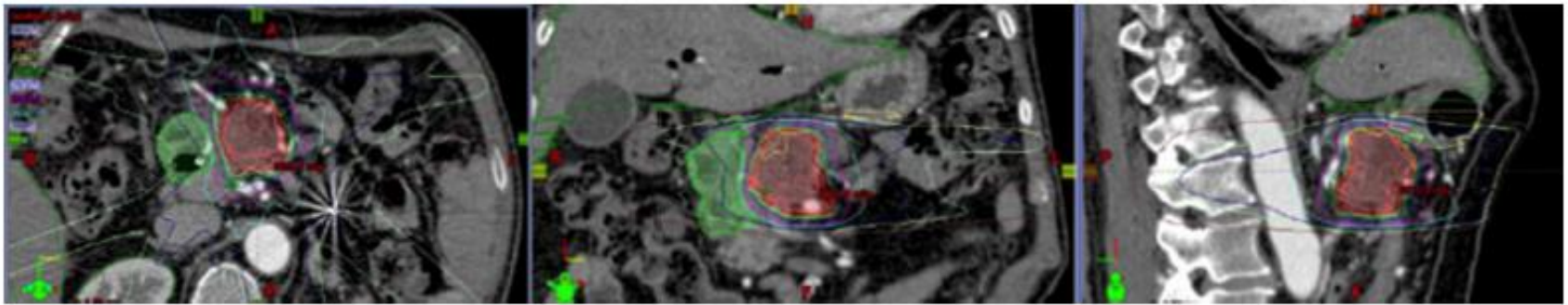


Fig. 1. SBRT treatment plan for locally advanced pancreatic adenocarcinoma. Stereotactic body radiotherapy (SBRT) using an 11 field plan to deliver a total dose of 3,300 cGy delivered in five fractions of 660 cGy each to the pancreas tumor. Note highly conformal isodose lines around the primary tumor.

6,6 Gy x 5 fx (33 Gy)

Journal of Surgical Oncology 2013;107:86–96

Rak trzustki: BT/IORT



Figure 1. EUS-guided iodine-125 seed implantation in pancreatic cancer

Endoscope-assisted brachytherapy for pancreatic cancer: From tumor killing to pain relief and drainage

J Interv Gastroenterol 1:1, 23-27; January/February/March 2011;

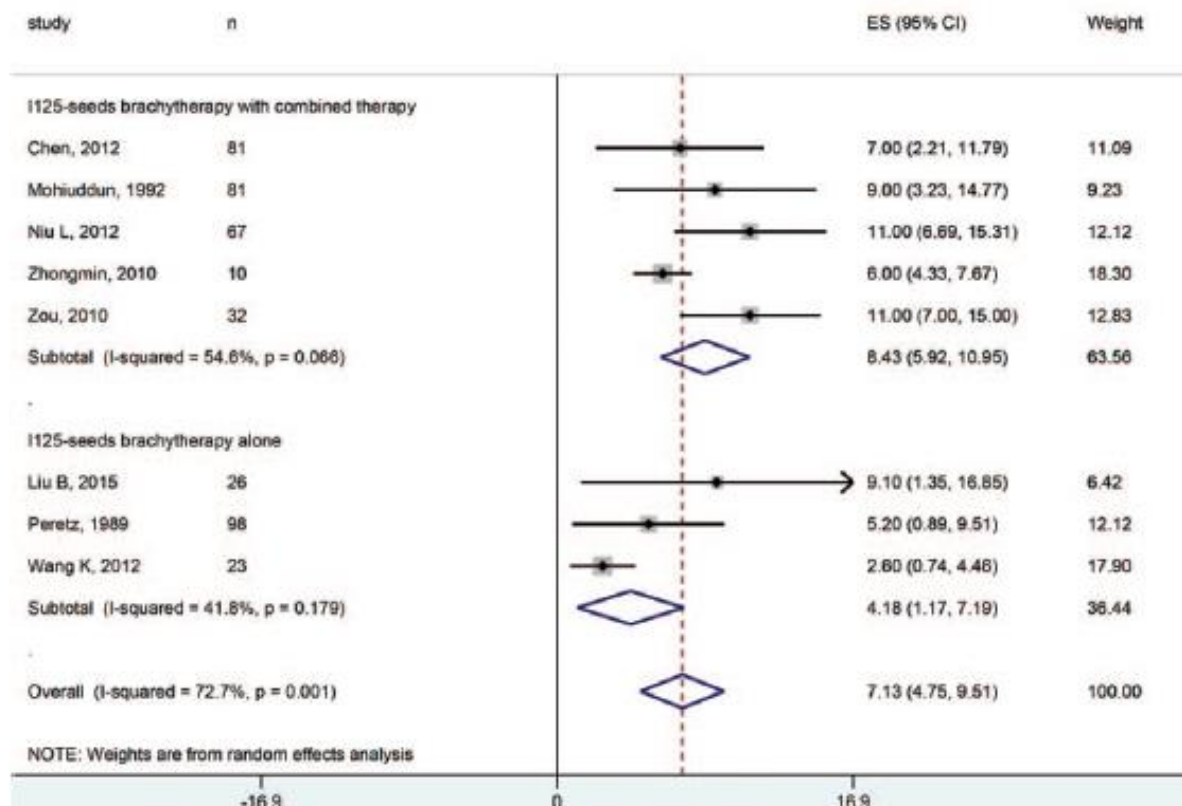


Intraoperative radiation therapy (IORT) in pancreatic cancer

Krempien and Roeder *Radiation Oncology* (2017) 12:8

Survival of patients with advanced pancreatic cancer after iodine¹²⁵ seeds implantation brachytherapy

A meta-analysis

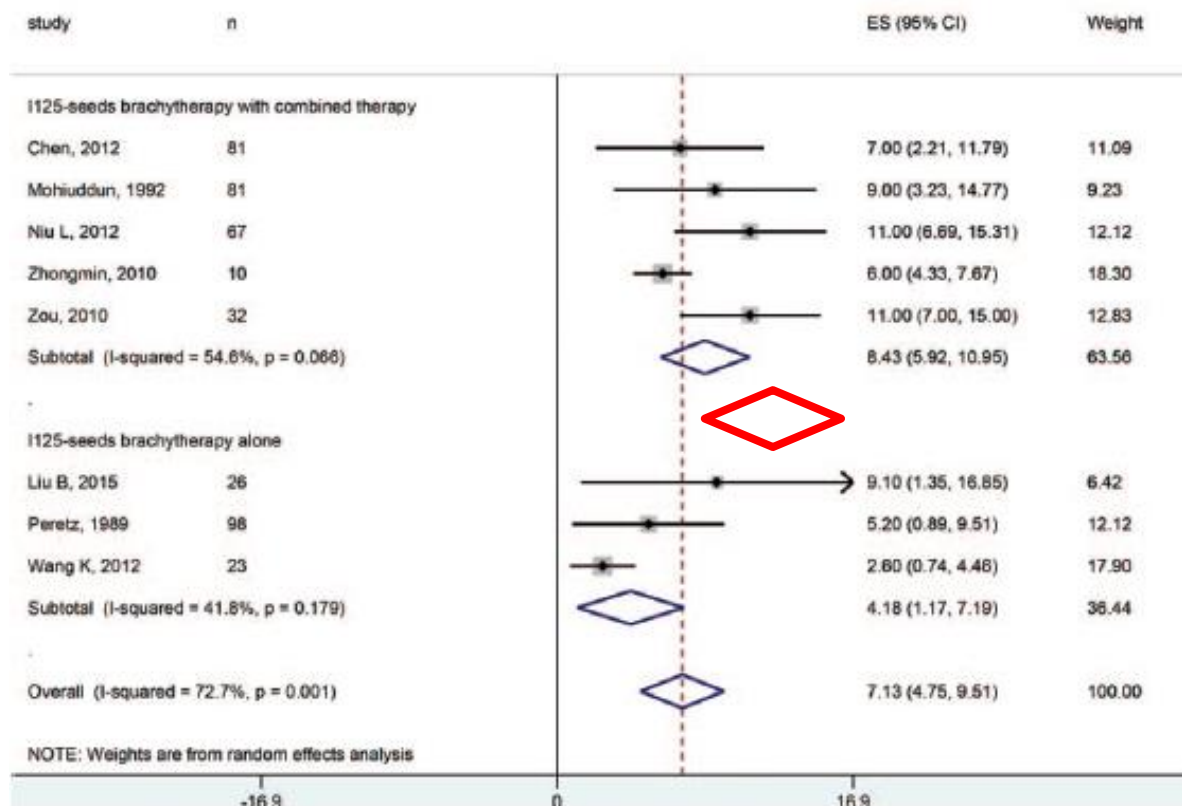


**Median OS
(IV stopień):**

**6 msc (BT)
7 msc (BT+CT)**

Survival of patients with advanced pancreatic cancer after iodine¹²⁵ seeds implantation brachytherapy

A meta-analysis



**Median OS
(IV stopień):**

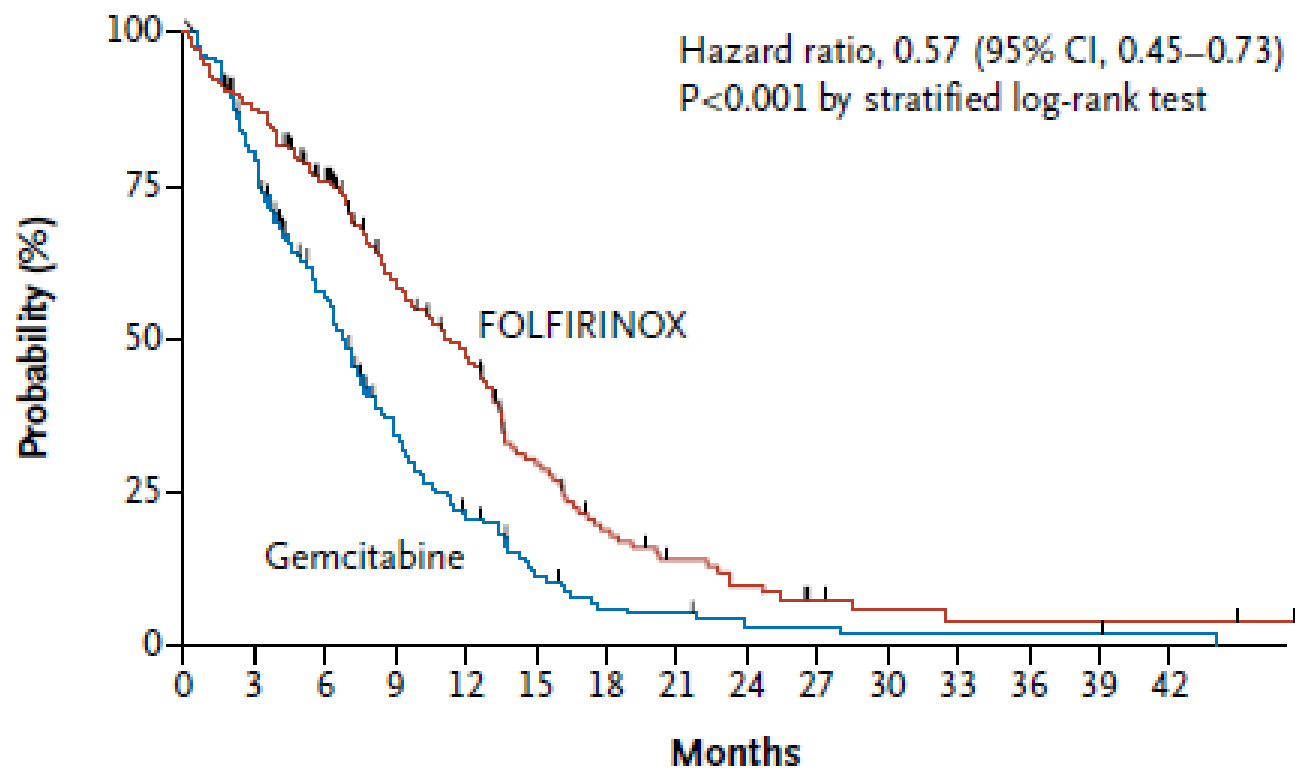
6 msc (BT)

7 msc (BT+CT)

Folfirinox: 11.1 msc

FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer

A Overall Survival



No. at Risk

Gemcitabine	171	134	89	48	28	14	7	6	3	3	2	2	2	2	1
FOLFIRINOX	171	146	116	81	62	34	20	13	9	5	3	2	2	2	2

N Engl J Med 2011;364:1817-25.

Rak trzustki: BT/IORT

**VERY LIMITED INDICATIONS IN THE ERA OF HIGH-DOSE
CONFORMAL STEREOTACTIC BODY RT AND IG-IMRT!**

Pagkretasos K 2014

Podsumowanie

