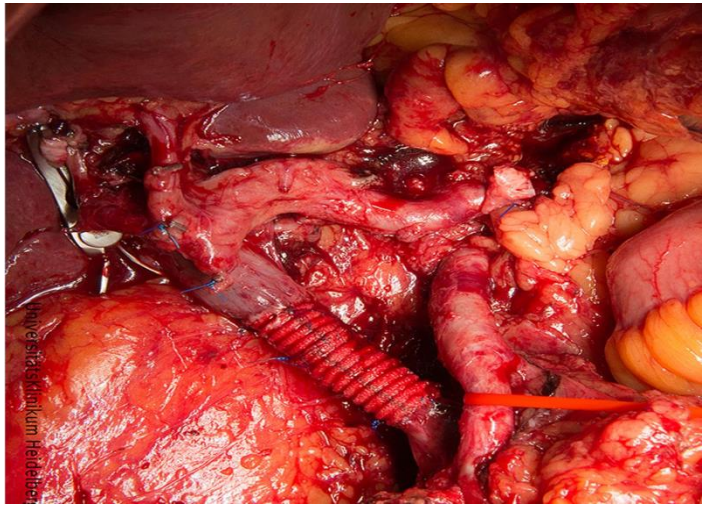
ΣΥΓΧΡΟΝΕΣ ΑΝΤΙΛΗΨΕΙΣ ΣΤΗ ΧΕΙΡΟΥΡΓΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΟΥ ΚΑΡΚΙΝΟΥ ΤΟΥ ΠΑΓΚΡΕΑΤΟΣ

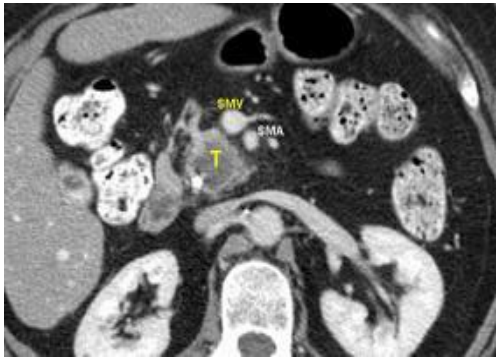
Οριακά Εξαιρέσιμος Καρκίνος Παγκρέατος: Σύγχρονη Αντιμετώπιση

Δημήτρης Π. Κορκολής
Χειρουργός
Διευθυντής Χειρουργικής Κλινικής
ΓΑΟΝΑ «Ο Άγιος Σάββας»

Pancreatic Cancer 2022

only chance for cure – radical surgery





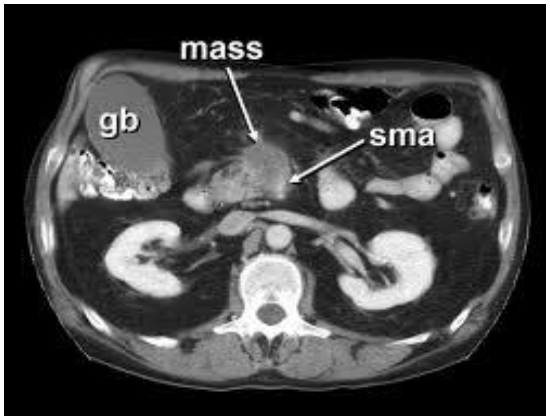
Pancreatic Cancer

20% operable

30% locally advanced

50% metastatic spread

Borderline Resectable



Borderline Resectable PDAC

1. Εξαιρέσιμος όγκος?
2. Δυσκολότερη επέμβαση?
3. Εκτεταμένοι χειρισμοί?
4. Αγγειακή εκτομή?
5. R0 αφαίρεση?
6. Μτχ νοσηρότης/θνητότης?
7. Συνολική έκβαση?

Critical Review

Management of Borderline Resectable Pancreatic Cancer

Different definitions of borderline resectable pancreatic cancer

Vessel	MDACC	AHPBA/SSO/SSAT	NCCN
CA	No contact	No contact	Pancreatic body/tail: solid tumor contact ≤180° or >180° without involvement of aorta or gastroduodenal artery
CHA	Short-segment encasement/abutment	Abutment or short segment encasement	Pancreatic head: solid tumor contact without extension to CA or hepatic artery bifurcation, allowing for safe and complete resection and reconstruction
SMA	Tumor abutment ≤180°	Tumor abutment ≤180°	Pancreatic head: solid tumor contact ≤180°
SMV/PV	Short-segment occlusion amenable to resection and reconstruction	Abutment with or without impingement; or encasement but without encasement of nearby arteries; or short-segment occlusion amenable to resection and reconstruction	Solid tumor contact >180° or ≤180° with contour irregularity or vein thrombosis but with suitable vessel proximally and distally to site of involvement, allowing for safe and complete resection and vein reconstruction*

Abbreviations: AHPBA/SSO/SSAT = Americas Hepato-Pancreato-Biliary Association/Society of Surgical Oncology/Society for Surgery of the Alimentary Tract; CA = celiac axis; CHA = common hepatic artery; MDACC = MD Anderson Cancer Center; NCCN = National Comprehensive Cancer Network; PV = portal vein; SMA = superior mesenteric artery; SMV = superior mesenteric vein.

* The most recent version of the NCCN resectability criteria also considers cases with solid tumor contact with the inferior vena cava as borderline resectable.

IJROBP 2018

Definitions of BR-PDAC

Pancreatology 2018

Definition	International Consensus 2017[5]	NCCN 2017[3]	MDACC 2008[16]
Anatomic			
SMV/PV	Tumor contact ≥ 180° or bilateral narrowing/occlusion, not exceeding inferior border of the duodenum	Tumor contact > 180° or ≤ 180° with contour irregularity or thrombosis—suitable vessel for reconstruction	Short segment occlusion suitable for reconstruction
SMA	Tumor contact < 180° without deformity/stenosis	Tumor contact ≤ 180°	Tumor contact ≤ 180°
CHA	Tumor contact, without contact with PHA and/or CA	Tumor contact without extension to CA/hepatic artery bifurcation allowing resection/-reconstruction	Any degree of contact for a short segment
CA	Tumor contact < 180° without deformity/stenosis	Tumor contact < 180° (head/uncinate); tumor contact ≥180 without the involvement of aorta and uninvolved GDA (body/tail)	Tumor contact ≤ 180°
Biologic	Clinical findings suspicious but not proven for distant metastasis, including CA 19-9 > 500 U/ml or diagnosed regional lymph nodes metastasis	None	Indeterminate lesions on imaging in the liver or suspicious distant lymph nodes; CA 19-9 ≥ 1000 U/ml (with normal bilirubin); biopsy-proven involvement of regional lymph nodes
Conditional	ECOG PS ≥ 2	None	Age ≥ 80 years old; severe reversible pre-existing comorbidities or ECOG PS ≥ 2

Πλεονεκτήματα ΝΤ στον BR-PDAC

- Αντιμετώπιση μη ορατών μεταστάσεων
- Καλύτερη δράση στο χειρουργικά παρθένο πεδίο
- Υποσταδιοποίηση – παθολ/κή υποστροφή
- Απομάκρυνση από μεγάλα αγγεία
- ↑ R0 εκτομών
- Αξιολόγηση ευαισθησίας θεραπευτικών σχημάτων
- Απομόνωση ασθενών (15-20%) με PD
- <60% κάνουν επικουρική θεραπεία
- Ευνοικότερη μτχ πορεία, ↓POPF

Μειονεκτήματα ΝΤ στον BR-PDAC

- Μικρή απεικονιστική ανταπόκριση
- Μικρή υποσταδιοποίηση
- Χρονική καθυστέρηση – Πρόοδος της νόσου
- Ανάγκη άμεσης αντιμετώπισης σε μονάδα παγκρέατος
- Μακροχρόνια αντιμετώπιση χολικής απόφραξης
- Απαίτηση ιστολογικής επιβεβαίωσης*

  **20-25% απαιτεί >2-3 FNABs υπό EUS*
- Δυσχερής παγκρεατεκτομή: αγγειακές εκτομές,↑χρόνου, ↑μεταγγίσεων
- Συναισθηματική επιβάρυνση ασθενούς

Επιλογή NT στον BR-PDAC

- Συστηματική Χημειοθεραπεία
    - α. Gemcitabine + nab-paclitaxel
    - β. FOLFIRINOX

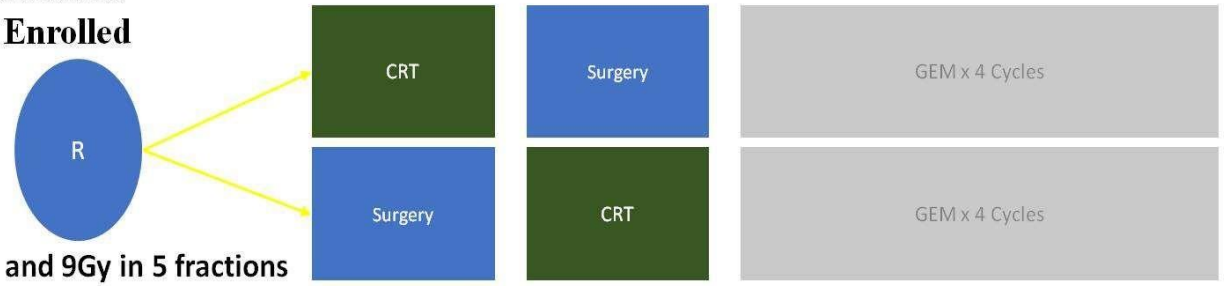
- Ακτινοθεραπεία
    - α. Hyper 5.5wks EBRT + Cap/Gem
    - β. Hypo 5days SBRT/IMRT

- Εισαγωγική χημειοθεραπεία + (χημειο)ακτινοθεραπεία

Dhir M, et al. World J Surg Oncol 2017

Neoadjuvant Versus Adjuvant – Chemoradiation

N = 110 BRPC Planned
N = 57 BRPC Enrolled



XRT 45Gy in 25 and 9Gy in 5 fractions
Gem 400mg/m2

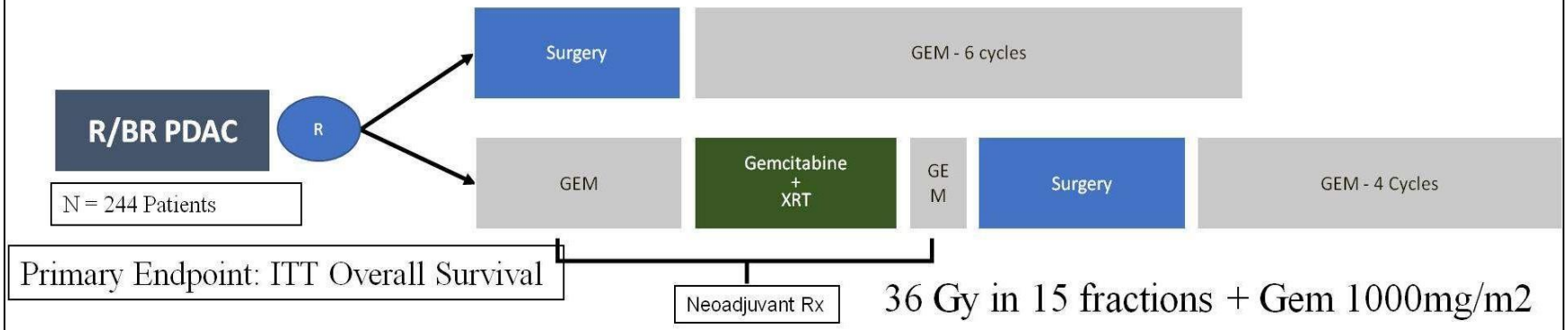
Primary Endpoint = 2-Yr Survival

	Neoadjuvant CRT	Adjuvant CRT	
2 year survival - ITT	**40%**	26%	p = 0.004
Median OS (months) – ITT	**21**	12	HR 1.97; p = 0.028
R0 Resection Rate - ITT	**51%**	26%	p = 0.004
R0 Resection Rate - Resected	**82%**	33%	p = 0.010
Positive Lymph Nodes	**29%**	83%	p = 0.004

Jang, J-Y et al, Annals of Surgery 2018

Jang JY, et al. Ann Surg 2018

Preoperative Radiochemotherapy Versus Immediate Surgery For (Borderline) Resectable Pancreatic Cancer: (PREOPANC)



	Immediate Surgery N=127	Neoadjuvant CRT N=119	P-value
Resection Rate (%)	72%	62%	.065
R0 Resection Rate PP (%)	31%	63%	<.001
Serious Adverse Events(%)	39	46	<.28

Van Tienhoven G, et al. ASCO 2018

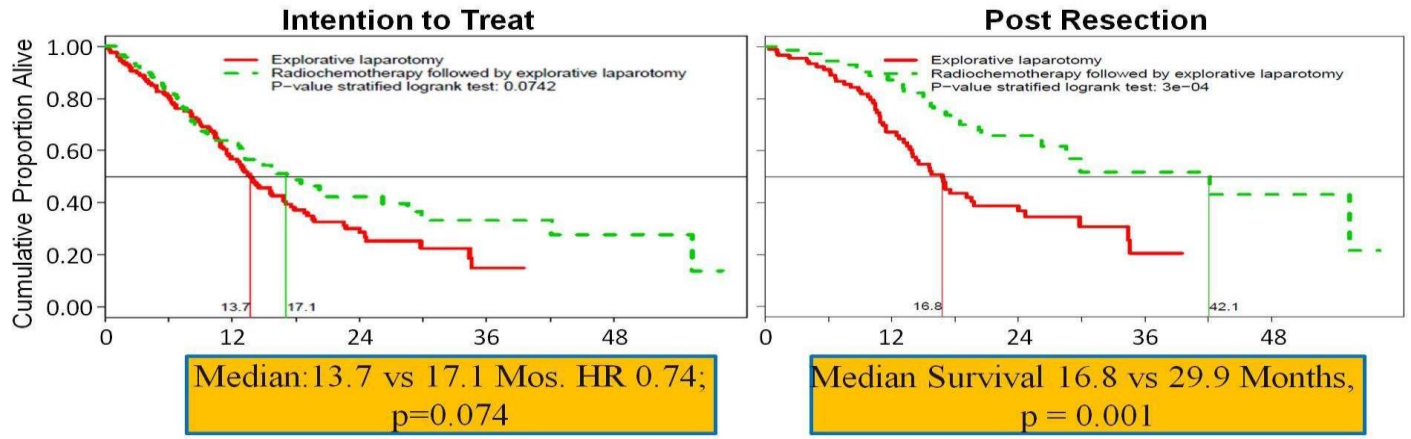
Van Tienhoven et al. JCO 2020

PREOPANC: OS

Median OS, Mos	Preoperative Radiochemotherapy (n = 119)	Immediate Surgery (n = 127)	HR	*P* Value
ITT*	17.1	13.7	0.74	.074
Subset with R0/R1 resection†	42.1	16.8	NR	< .001

*Preliminary analysis; only 149/176 events.
†Preoperative radiochemotherapy, n = 72; immediate surgery, n = 91.

Overall Survival Analyses



van Tienhove

PREOPANC: Secondary Endpoints

Outcome	Preoperative Radiochemotherapy (n = 119)	Immediate Surgery (n = 127)	HR	*P* Value
Resection rate, n (%)	72 (60)	91 (72)	--	.065
R0 resection rate, n/N (%)	45/72 (63)	28/91 (31)	--	< .001
Median DFS, mos	9.9	7.9	0.71	.023
Median distant metastases–free interval, mos	18.4	10.6	0.71	.013
Median locoregional recurrence-free interval, mos	Not reached	11.8	0.55	.002
Serious AEs, n (%)	55 (46)	49 (39)	--	.28

van Tienhoven G, et al. ASCO 2018. Abstract LBA4002.

2019

JAMA Oncology | Original Investigation

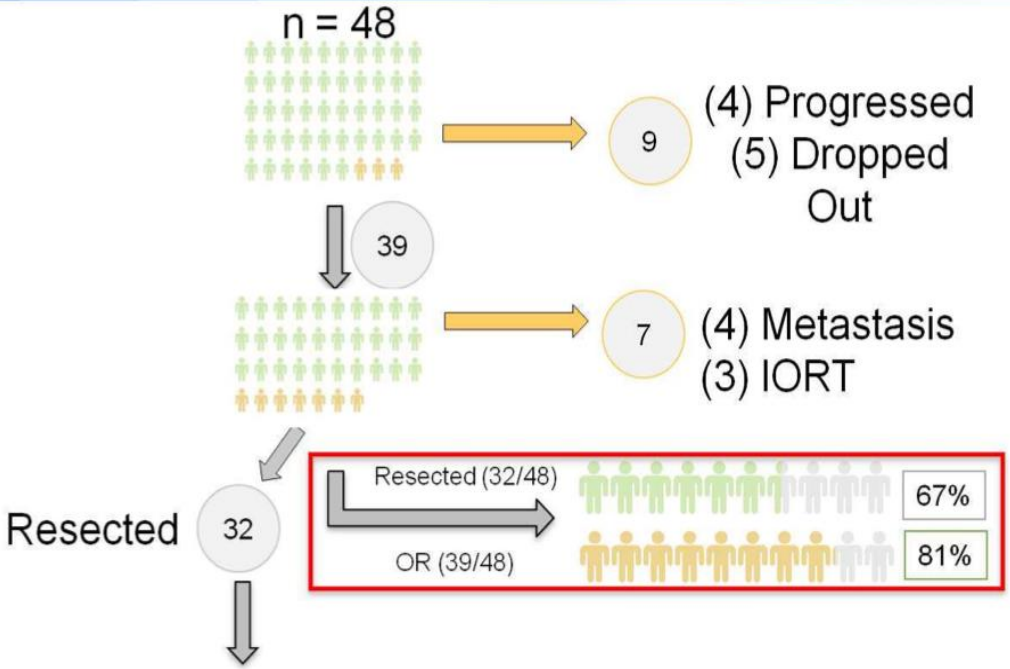
Total Neoadjuvant Therapy With FOLFIRINOX Followed by Individualized Chemoradiotherapy for Borderline Resectable Pancreatic Adenocarcinoma

A Phase 2 Clinical Trial

Janet E. Murphy, MD, MPH; Jennifer Y. Wo, MD; David P. Ryan, MD; Wenqing Jiang, MS; Beow Y. Yeap, ScD; Lorraine C. Drapek, NP, PhD; Lawrence S. Blaszkowsky, MD; Eunice L. Kwak, MD, PhD; Jill N. Allen, MD; Jeffrey W. Clark, MD; Jason E. Faris, MD; Andrew X. Zhu, MD, PhD; Lipika Goyal, MD, MPhil; Keith D. Lillemoe, MD; Thomas F. DeLaney, MD; Carlos Fernández-del Castillo, MD; Cristina R. Ferrone, MD*; Theodore S. Hong, MD* *Co-senior authors

- 8 cycles of FOLFIRINOX + Individualized SBRT → Operation
- Single-arm Phase 2 trial of 48 patients
- Primary endpoint: R0 Resection Rate
- MGH

Borderline Resectable (11-328)



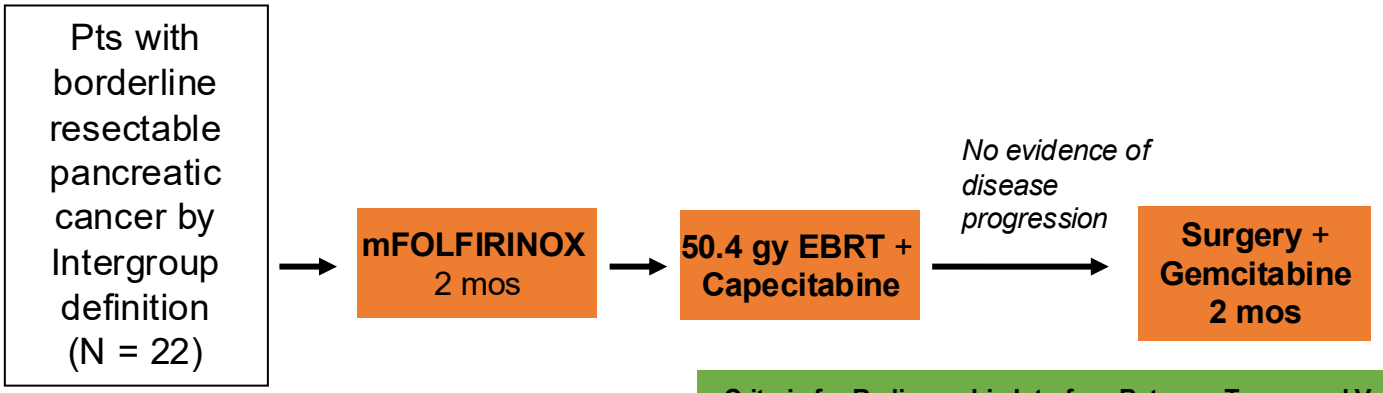
R0 31/32 (97%)

Progression or Mets at Exploration 17%

DFS: 48.6 mo

Alliance A021101: Study Design

- Multicenter pilot study[1]



- Primary endpoints
  - Accrual
  - Rate of preoperative treatment-related toxicity or delay
  - Rate of completion of all planned preoperative and operative therapy

Criteria for Radiographic Interface Between Tumor and Vessel for Borderline Resectable[2]	
Portal vein	TVI ≥ 180° and/or reconstructable occlusion
Superior mesenteric artery	TVI < 180°
Hepatic artery	Reconstructable short-segment TVI of any degree
Celiac trunk	TVI < 180°

1. Katz MHG, et al. ASCO 2015. Abstract 4008. 2. Katz MHG, et al. Ann Surg Onc. 2013;20:2197-2203.

Alliance A021101: Surgery, Pathology, and AEs

- Among 15 pts undergoing surgery
  - 80% (n = 12) with portal vein resection
  - 27% (n = 4) with hepatic artery resection
  - R0 resection in 93%
  - OS 21.7 mo
  - N0 status in 67% of pathologic specimens
  - < 5% residual tumor cells in 47%
  - Complete pathologic response in 13%
  - 1 death occurred within 90 days of surgery

Surgery Grade ≥ 3 AEs, %	**Pts (N = 15)**
Anemia	38
Infection with unknown ANC	23
Infection with normal or grade 1/2 ANC	15
Surgical or postoperative hemorrhage	15
Anorexia	15

Katz MHG, et al. ASCO 2015. Abstract 4008.

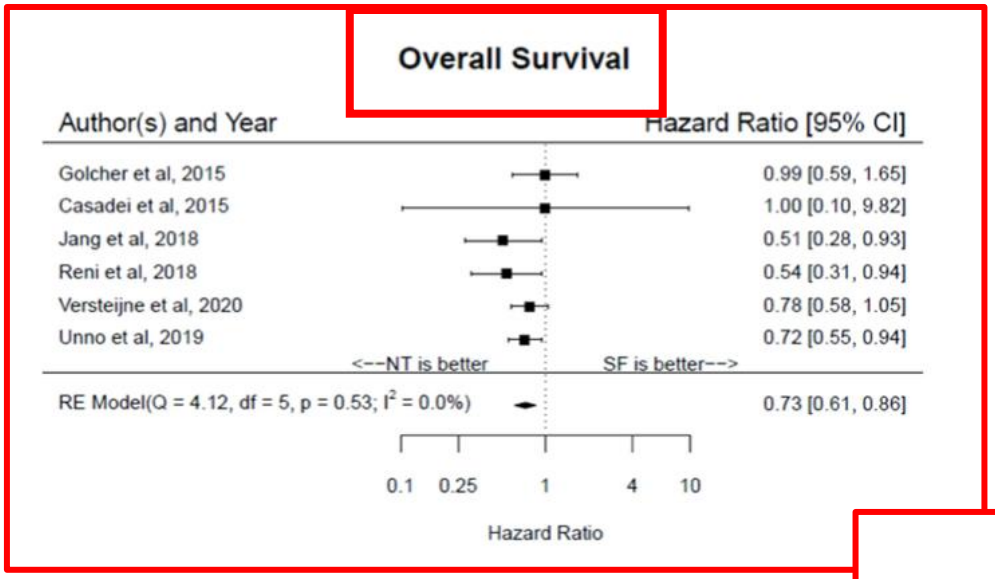
Article

Neoadjuvant Therapy for Resectable and Borderline Resectable Pancreatic Cancer: A Meta-Analysis of Randomized Controlled Trials

Jordan M. Cloyd [1,*], Victor Heh [1], Timothy M. Pawlik [1], Aslam Ejaz [1], Mary Dillhoff [1], Allan Tsung [1], Terence Williams [2], Laith Abushahin [3], John F. P. Bridges [4] and Heena Santry [1]

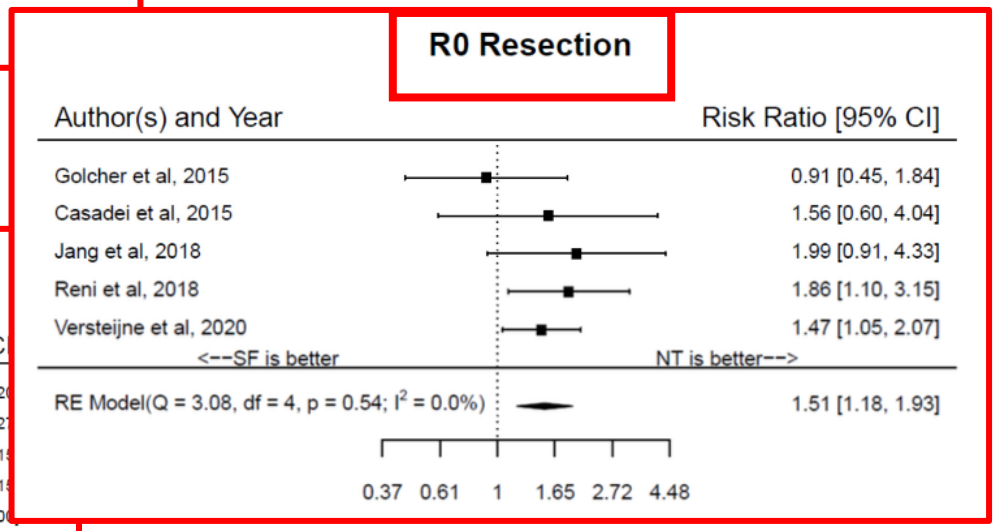
Author	Institution	Origin	Setting	PR/BR Definition	Sample Size	Neoadjuvant Therapy	Regimen	Adjuvant Therapy
Golcher	Multi-	Germany	PR	≤180 "peripancreatic vessels"	66	CRT	Gemcitabine/Cisplatin; 56Gy	Gemcitabine
Casadei	Single-	Italy	PR	<180 SMV/PV; No contact to CA/HA/SMA	38	CRT	Gemcitabine; 54Gy	Gemcitabine
Jang	Multi-	Korea	BR	2012 NCCN criteria	50	CRT	Gemcitabine; 54Gy	CRT, Gemcitabine
Reni	Multi-	Italy	PR	No invasion of SMA/SMV/PV/CA/HA	88	Chemo	Cisplatin, Epirubicin, Gemcitabine, Capecitabine	Cisplatin, Epirubicin, Gemcitabine, Capecitabine or Gemcitabine
Versteijne	Multi-	Netherlands	PR/BR	PR: <90 SMV/PV; no CA/HA/SMA contact BR: <90 CA/HA/SMA; 90–270 PV/SMV without occlusion	246	CRT	Gemcitabine; 36Gy	Gemcitabine
Unno	Multi-	Japan	PR	No CA/HA/SMA abutment	362	Chemo	Gemcitabine, S-1	S1

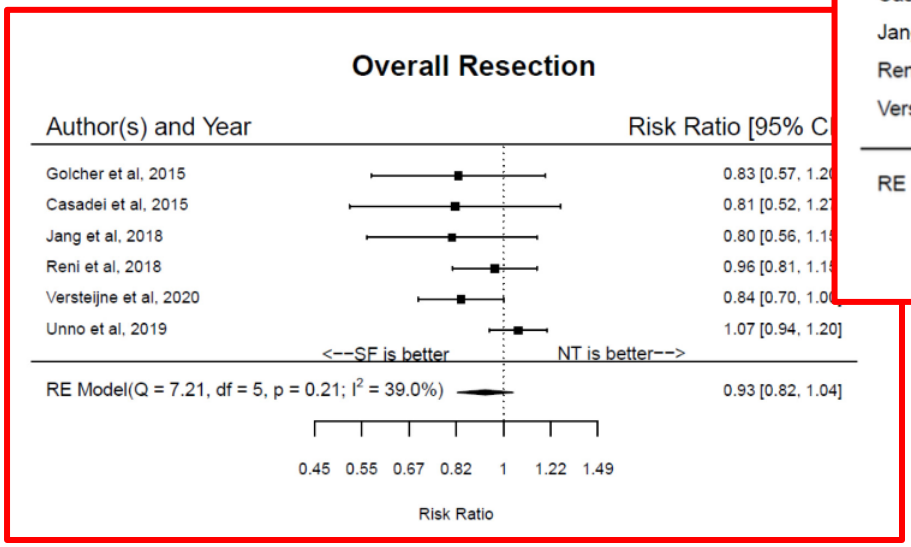
J Clin Medicine 2020



6 RCTs
850 pts R/BR-PDAC

411 (48.3%) NAT
439 pts (51.7%) SF





J Clin Medicine 2020

Systematic review

Meta-analysis comparing upfront surgery with neoadjuvant treatment in patients with resectable or borderline resectable pancreatic cancer

E. Versteijne[1], J. A. Vogel[2], M. G. Besselink[2], O. R. C. Busch[2], J. W. Wilmink[3], J. G. Daams[4], C. H. J. van Eijck[5], B. Groot Koerkamp[5], C. R. N. Rasch[1] and G. van Tienhoven[1], on behalf of the Dutch Pancreatic Cancer Group

- 38 studies were included with 3484 patients, of whom 1738 (49.9%) had neoadjuvant treatment
- The weighted median overall survival by intention to treat was 18.8 months for neoadjuvant treatment and 14.8 months for upfront surgery. The difference was larger among patients whose tumours were resected (26.1 versus 15 months respectively).
- The overall resection rate was lower with neoadjuvant treatment than with upfront surgery (66% versus 81.3% P < 0·001), but the R0 rate was higher (86.8% versus 66.9 P < 0·001).
- The pathological lymph node rate was 43.8% after neoadjuvant therapy and 64.8% in the upfront surgery group (P < 0·001).
- Toxicity of at least grade III was reported in up to 64 per cent of the patients.

J Clin Oncol 2020

Gemcitabine-Based Neoadjuvant Treatment in Borderline Resectable Pancreatic Ductal Adenocarcinoma: A Meta-Analysis of Individual Patient Data

Francesco Giovinazzo[1], Fiammetta Soggiu[2], Jin-Young Jang[3], Eva Versteijne[4], Geertjan van Tienhoven[4], Casper H. van Eijck[5], Youngmin Han[3], Seong Ho Choi[6], Chang Moo Kang[7], Mark Zalupski[8], Hasham Ahmad[9], Sarah Yentz[8], Scott Helton[10], J. Bart Rose[11], Chie Takishita[12], Yuichi Nagakawa[12] and Mohammad Abu Hilal[1,13]**

Frontiers in Oncology 2021

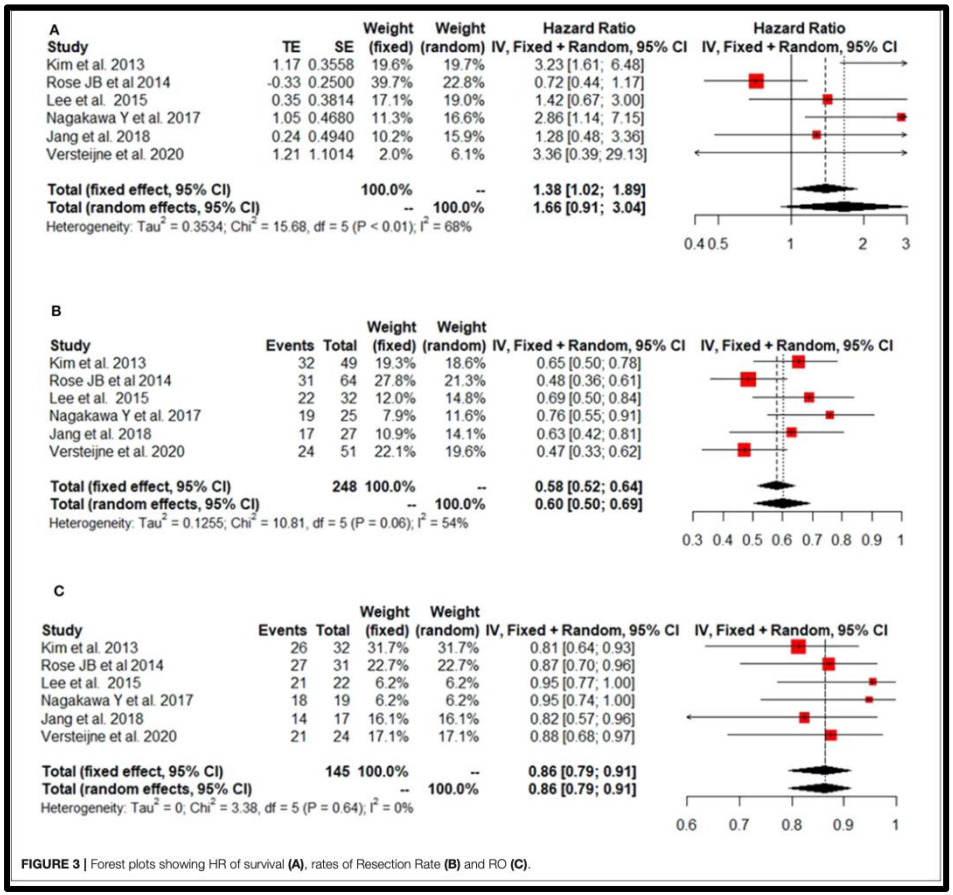
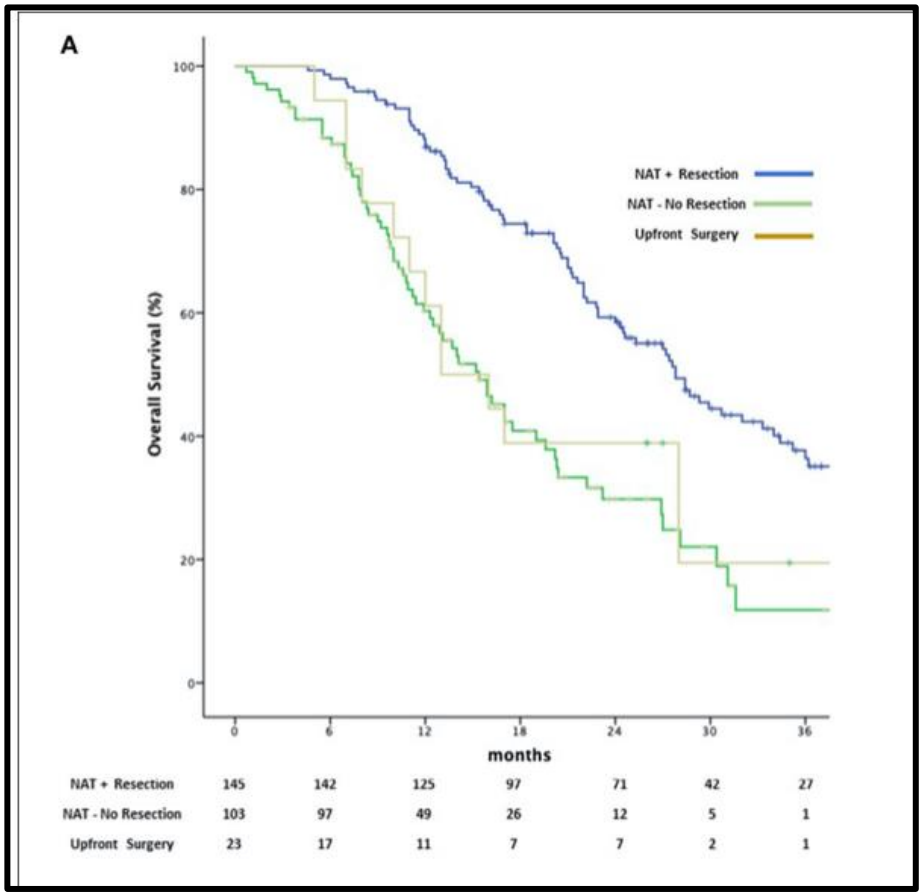
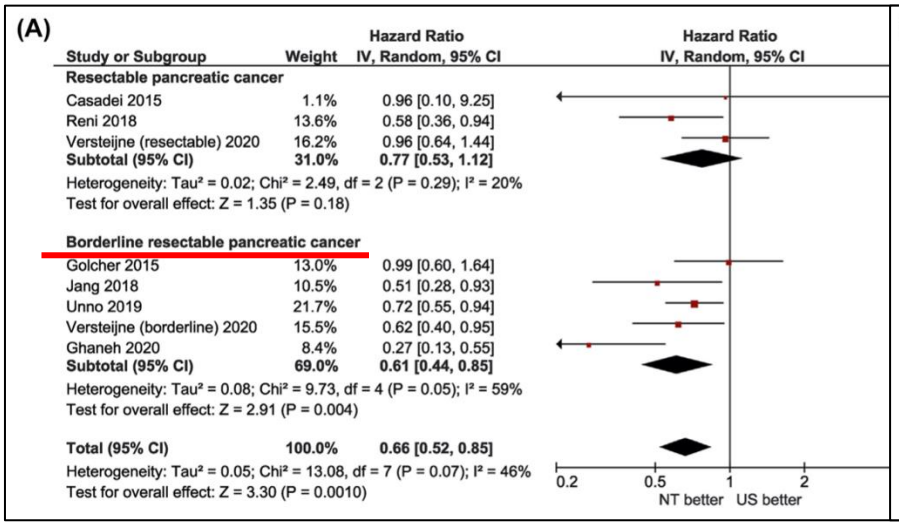
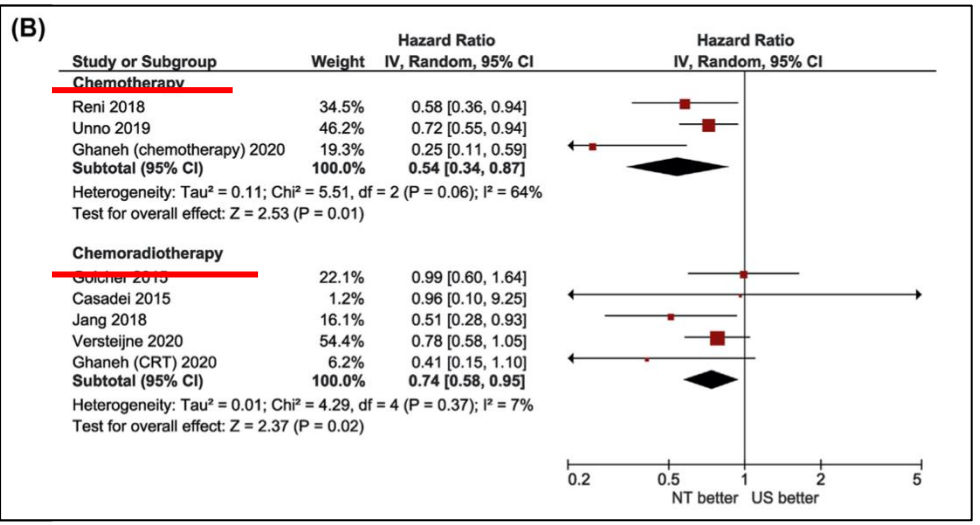


FIGURE 3 | Forest plots showing HR of survival **(A)**, rates of Resection Rate **(B)** and RO **(C)**.



Neoadjuvant therapy or upfront surgery for resectable and borderline resectable pancreatic cancer: A meta-analysis of randomised controlled trials



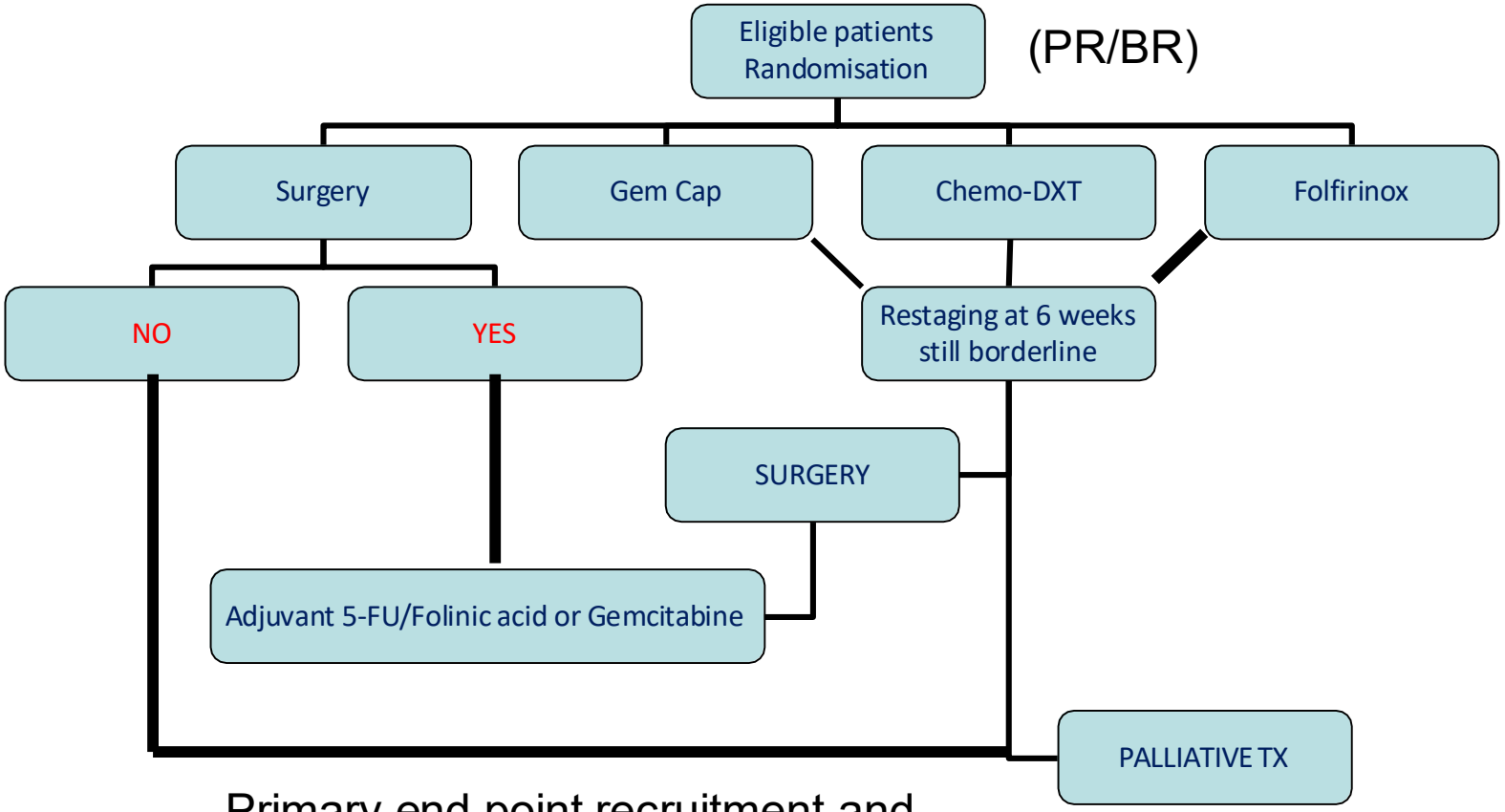


GRADE summary of findings.

Outcomes	Anticipated absolute effects (95% CI)[a]		Relative effect (95% CI)	No. of participants (studies)	Certainty of evidence (GRADE)
	Upfront surgery	Neoadjuvant therapy			
Median overall survival	19 months[b]	**29 months** (22–37)	**HR 0.66** (0.52–0.85)	938 (7 RCTs)	⊕⊕⊕⊕ HIGH
Resection	80 per 100	**75 per 100** (71–80)	**RR 0.94** (0.89–1.01)	938 (7 RCTs)	⊕⊕⊕◯[c] MODERATE
R0 resection	29 per 100	**42 per 100** (33–52)	**RR 1.47** (1.17–1.84)	576 (6 RCTs)	⊕⊕⊕◯[d] MODERATE
N0 resection	17 per 100	**36 per 100** (28–46)	**RR 2.15** (1.69–272)	938 (7 RCTs)	⊕⊕⊕◯[d] MODERATE
Major surgical complications	31 per 100	**19 per 100** (11–33)	**RR 0.60** (0.34–1.05)	153 (3 RCTs)	⊕⊕◯◯[c,e] LOW

Eur J Cancer 2022

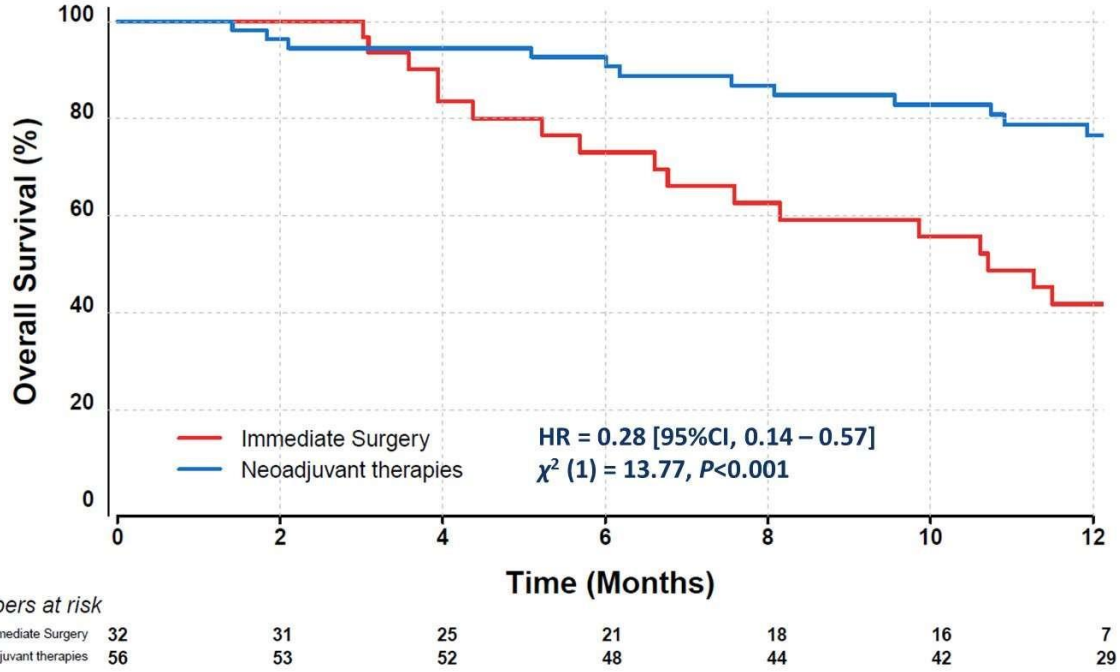
ESPAC – 5F



Primary end point recruitment and resection rate (R0 & R1)

J Clin Oncol. 2020;38:4505–4505. ASCO 2020

Secondary outcomes - overall survival (I)

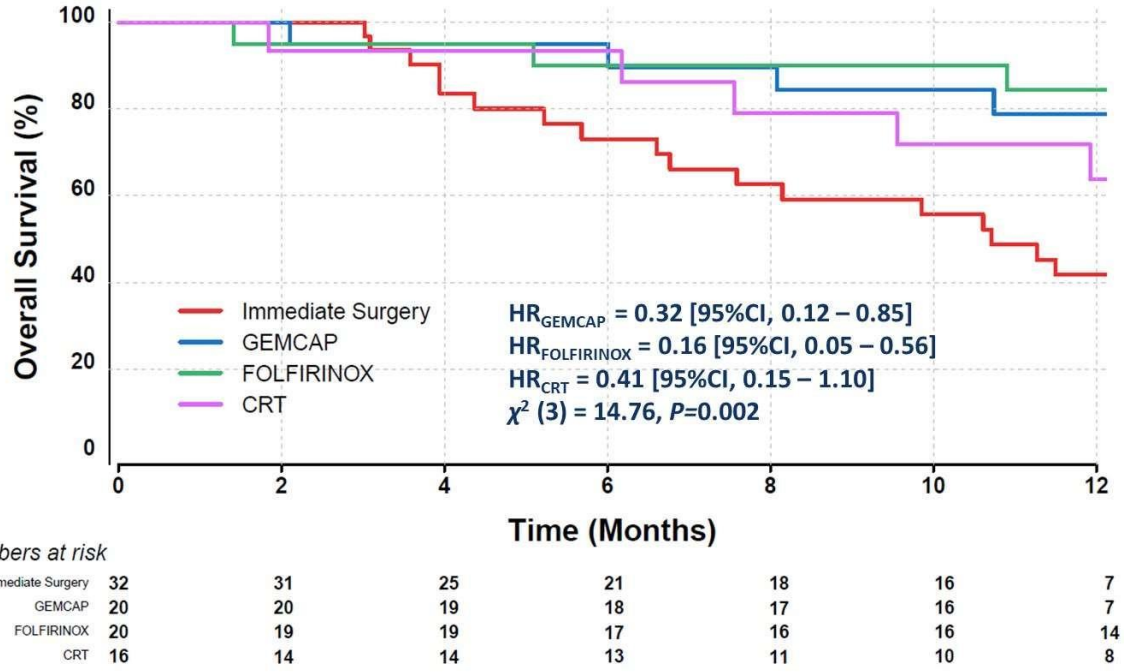


12-months survival estimate (95% CI)

Immediate Surgery	42% (27% , 64%)
Neoadjuvant therapy	77% (66% , 89%)

J Clin Oncol. 2020;38:4505–4505.

Secondary outcomes - overall survival (II)



Numbers at risk

Immediate Surgery	32	31	25	21	18	16	7
GEMCAP	20	20	19	18	17	16	7
FOLFIRINOX	20	19	19	17	16	16	14
CRT	16	14	14	13	11	10	8

12-months survival estimate (95% CI)

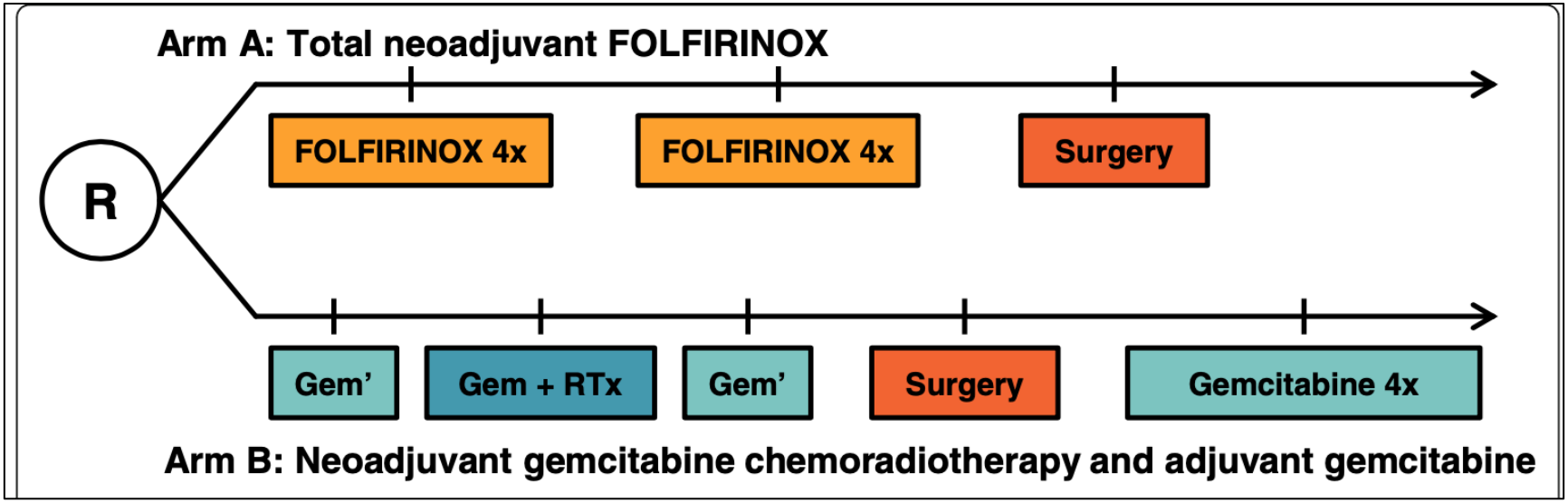
Immediate Surgery	42% (27% , 64%)
GEMCAP	79% (62% , 100%)
FOLFIRINOX	84% (70% , 100%)
CRT	64% (43% , 95%)

J Clin Oncol. 2020;38:4505–4505.

STUDY PROTOCOL Open Access

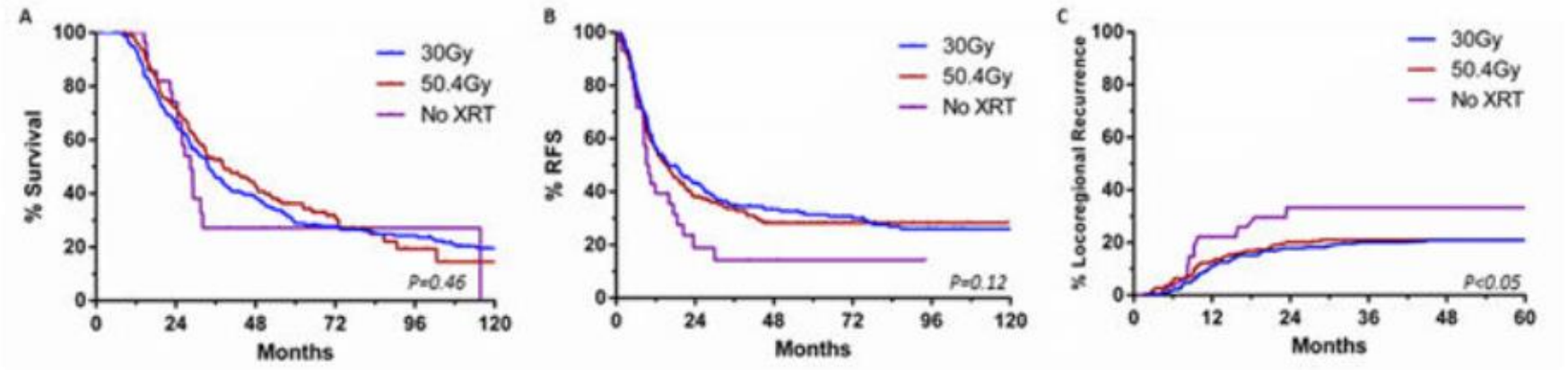
Total neoadjuvant FOLFIRINOX versus neoadjuvant gemcitabine-based chemoradiotherapy and adjuvant gemcitabine for resectable and borderline resectable pancreatic cancer (PREOPANC-2 trial): study protocol for a nationwide multicenter randomized controlled trial

Q. P. Janssen[1], J. L. van Dam[1], B. A. Bonsing[2], H. Bos[3], K. P. Bosscha[4], P. P. L. O. Coene[5], C. H. J. van Eijck[1], I. H. J. T. de Hingh[6], T. M. Karsten[7], M. B. van der Kolk[8], G. A. Patijn[9], M. S. L. Liem[10], H. C. van Santvoort[11], O. J. L. Loosveld[12], J. de Vos-Geelen[13], B. M. Zonderhuis[14], M. Y. V. Homs[15†], G. van Tienhoven[16†], M. G. Besselink[17†], J. W. Wilmink[18†], B. Groot Koerkamp[1*] and for the Dutch Pancreatic Cancer Group



Impact of Hypofractionated and Standard Fractionated Chemoradiation Prior to Pancreatoduodenectomy for Pancreatic Ductal Adenocarcinoma

Jordan M Cloyd, MD[1], Christopher H Crane, MD[2], Eugene J Koay, MD, PhD[2], Prajnan Das, MD, MS, MPH[2], Sunil Krishnan, MD[2], Laura Prakash, MD[1], Rebecca A Snyder, MD, MPH[1], Gauri R Varadhachary, MD[3], Robert A Wolff, MD[3], Milind Javle, MD[3], Rachna T Shroff, MD[3], David Fogelman, MD[3], Michael Overman, MD[3], Huamin Wang, MD, PhD[4], Anirban Maitra, MD[4], Jeffrey E Lee, MD[1], Jason B Fleming, MD[1], and **Matthew HG Katz, MD[1]**



500pts

30Gy ≠ 50.4Gy

R0 resection
LN ratio
OS
RFS

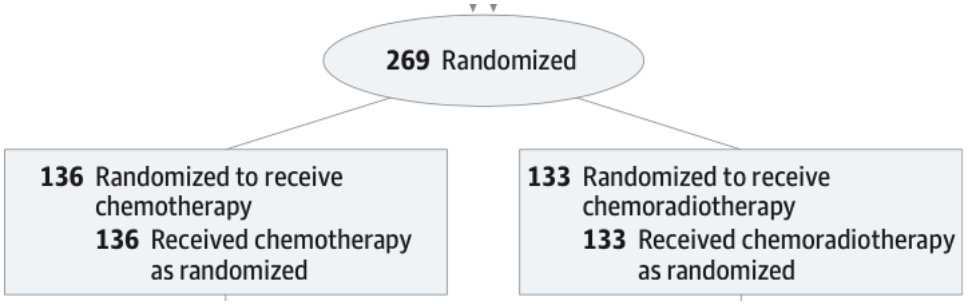
Radio vs Chemo alone

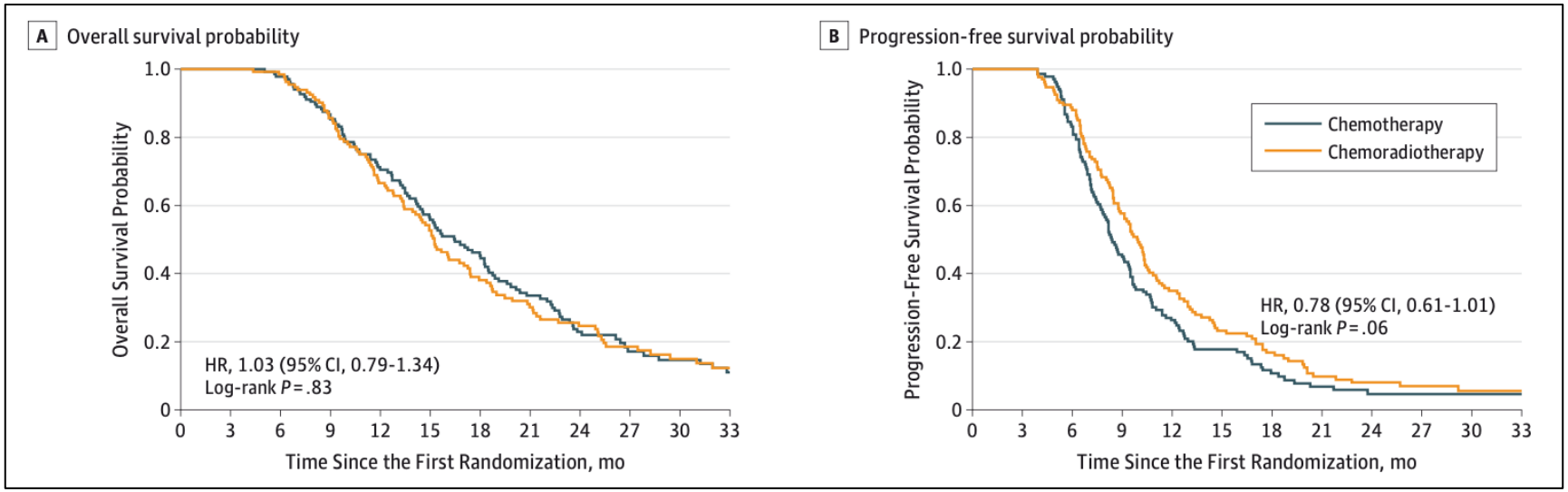
↑ Locoregional Control

Cancer 2016

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

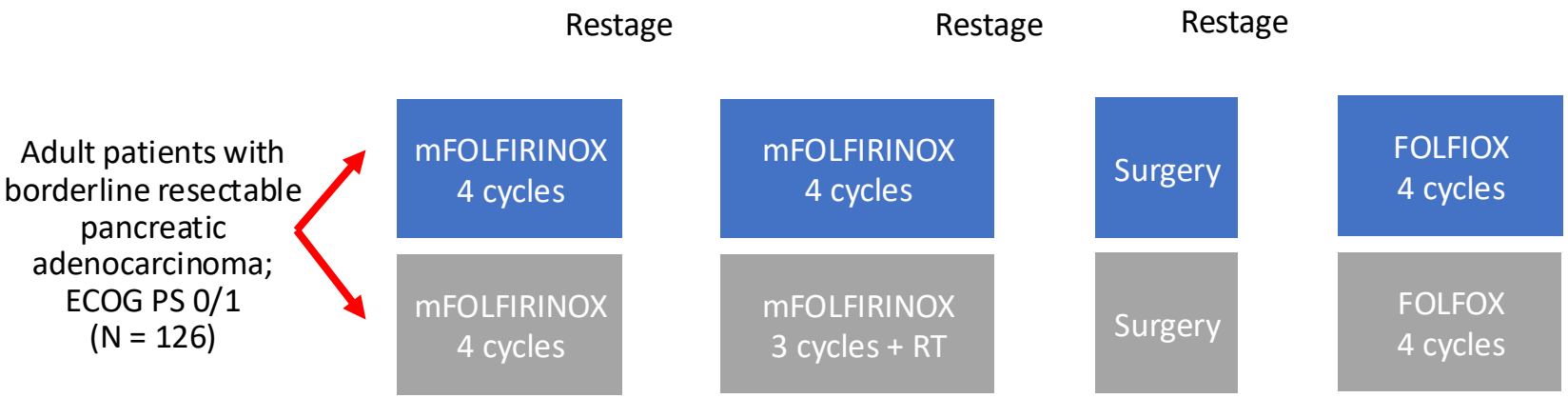




JAMA Surg 2016

Alliance A021501: Neoadjuvant mFOLFIRINOX With or Without RT in Borderline Resectable Pancreatic Cancer

- Multicenter, randomized phase II trial



- Primary endpoint: binary 18-month OS rate
- Key secondary endpoints: EFS, safety, R0 resection rate, pCR rate

Katz. ASCO GI 2021. Abstr 377.

Slide credit: clinicaloptions.com

Alliance A021501: OS and EFS

Outcome	mFOLFIRINOX (n = 65)	mFOLFIRINOX + RT (n = 55)
R0	**25**	**11**
▪ Events	35	40
▪ Median OS, mos	29.8	17.1
▪ 18-mo OS rate, %	66.4	47.3
EFS		
▪ Events	45	44
▪ Median EFS, mos	15.0	10.2

Katz. ASCO GI 2021. Abstr 377.

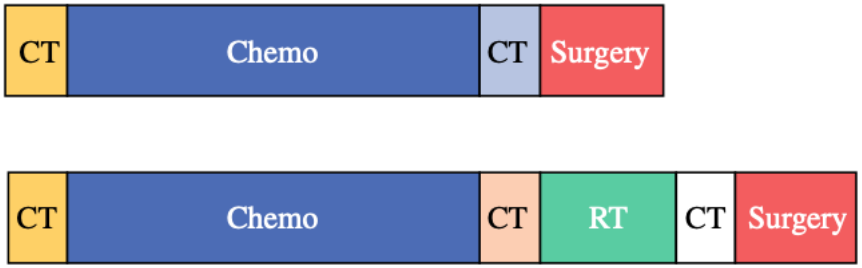
Slide credit: clinicaloptions.com

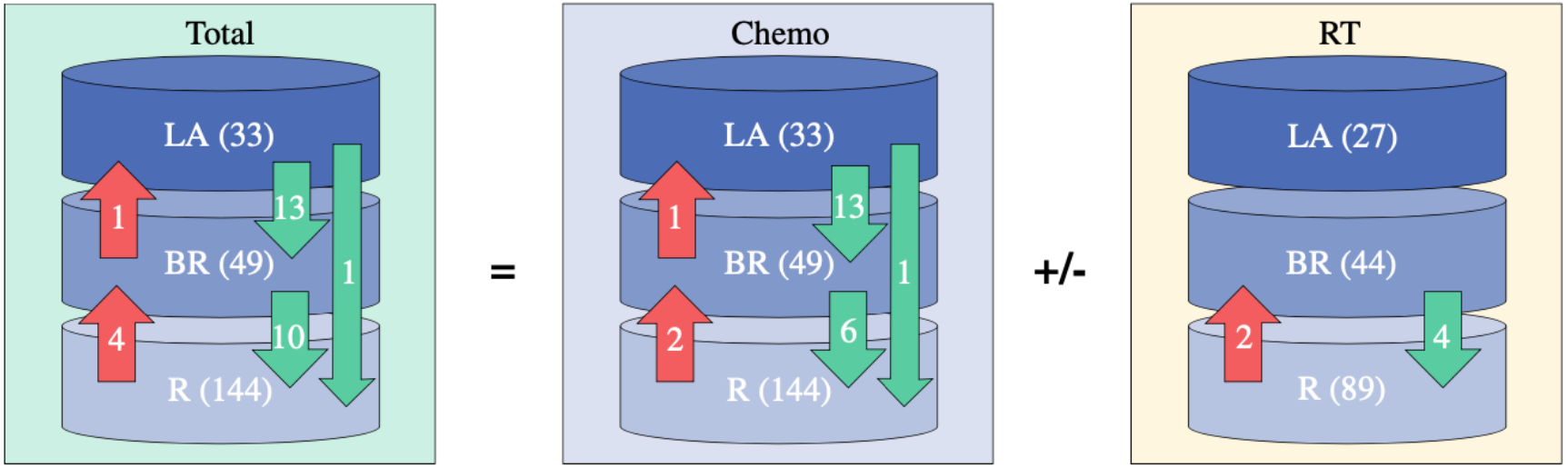
The Sequential Radiographic Effects of Preoperative Chemotherapy and (Chemo)Radiation on Tumor Anatomy in Patients with Localized Pancreatic Cancer

Giampaolo Perri, MD[1], Laura Prakash, MD[1], Giuseppe Malleo, MD[2], Andrea Caravati, MD[2], Gauri R. Varadhachary, MD[3], David Fogelman, MD[3], Shubham Pant, MD[3], Eugene J. Koay, MD[4], Joseph Herman, MD[4], Laura Maggino, MD[2], Michele Milella, MD[5], Michael Kim, MD[1], Naruhiko Ikoma, MD[1], Ching-Wei Tzeng, MD[1], Roberto Salvia, MD[2], Jeffrey E. Lee, MD[1], Claudio Bassi, MD[2], and Matthew H. G. Katz, MD[1]

Ann Surg Oncol 2020

226 pts
BRPC/LA





Αξιολόγηση-Ανταπόκριση NT στον BR-PDAC

- Αδυναμία διάκρισης Tu από φλεγμονή/ίνωση
- Μικρή υποσταδιοποίηση με RECIST criteria
- CA 19.9↓↓↓
- PET scan?
- Νεότεροι βιοδείκτες

  circulating tumor cells (CTCs)

  circulating cell-free tumor DNA

  other proteins

Radiological and Surgical Implications of Neoadjuvant Treatment With FOLFIRINOX for Locally Advanced and Borderline Resectable Pancreatic Cancer

	Pre-FOLFIRINOX Treatment (n = 40)		Post-FOLFIRINOX Treatment (n = 40)
CA 19.9, median (range)[1]	169 (1–4754)		0.17 (0.01–9.81)
CA 19.9 > 40 U[1]	26 (70.3%)		11 (28.9%)
Tumor diameter at CT, median (range), cm	3.6 (0–6.0)		2.1 (0–5.4)
Gastrointestinal consensus group	LAPC = 25 (62.5%) Borderline = 15 (37.5%)		Complete = 6 (15%) Partial = 30 (75%) Stable = 4 (10%) Progression = 0
Blinded review by senior pancreatic surgeon (A.L.W.)	Resectable—0		Resectable—12 (30%)
	Borderline—14 (35%) LA—26 (65%)	70%	Borderline—9 (22%) LA—19 (48%)

	No Neoadjuvant (N = 87)	FOLFIRINOX (N = 40)	*P*
Stage			<0.001
I	4 (5%)	10 (25%)	0.006
IIa	15 (17%)	16 (40%)	
IIb	68 (78%)	14 (35%)	
Median size of tumor on pathology (cm)	3.2 (1.5–10.7)	2.5 (0.1–5.5)	
N+	69 (79%)	14 (35%)	<0.001
R0	75 (86%)	35 (92%)	0.550
Lymphatic invasion	61 (70%)	14 (35%)	<0.001
Perineural invasion	83 (95.4%)	29 (72.5%)	<0.001

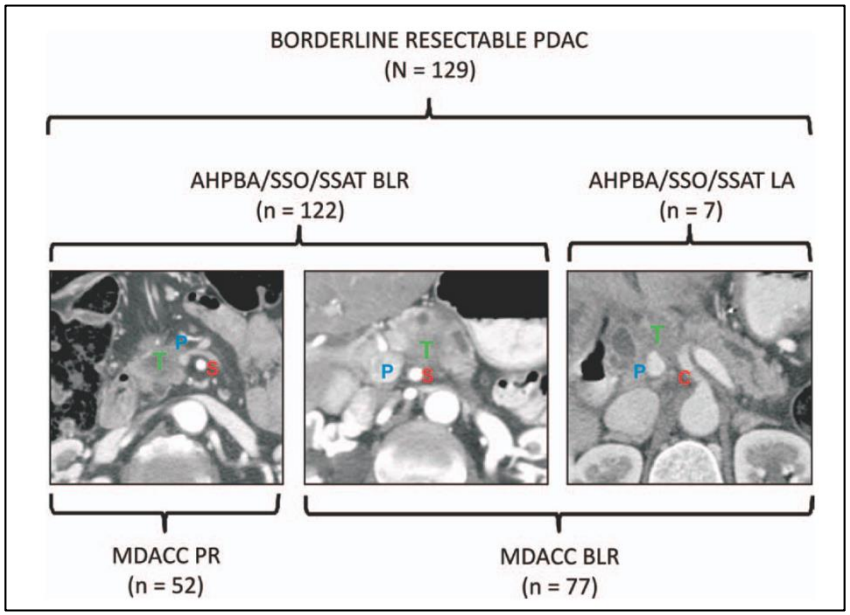
Resectability: 100% R0: 92%

Ferrone et al. Ann Surg 2015

Response of Borderline Resectable Pancreatic Cancer to Neoadjuvant Therapy Is Not Reflected by Radiographic Indicators

Matthew H. G. Katz, MD[1]; Jason B. Fleming, MD[1]; Priya Bhosale, MD[2]; Gauri Varadhachary, MD[3]; Jeffrey E. Lee, MD[1]; Robert Wolff, MD[3]; Huamin Wang, MD[4]; James Abbruzzese, MD[3]; Peter W. T. Pisters, MD[1]; Jean-Nicolas Vauthey, MD[1]; Chusilp Charnsangavej, MD[2]; Eric Tamm, MD[2]; Christopher H. Crane, MD[5]; and Aparna Balachandran, MD[2]

Cancer 2012



122 pts BR-PDAC

ST	69%
PR	12%
PD	19%
R	0.8%

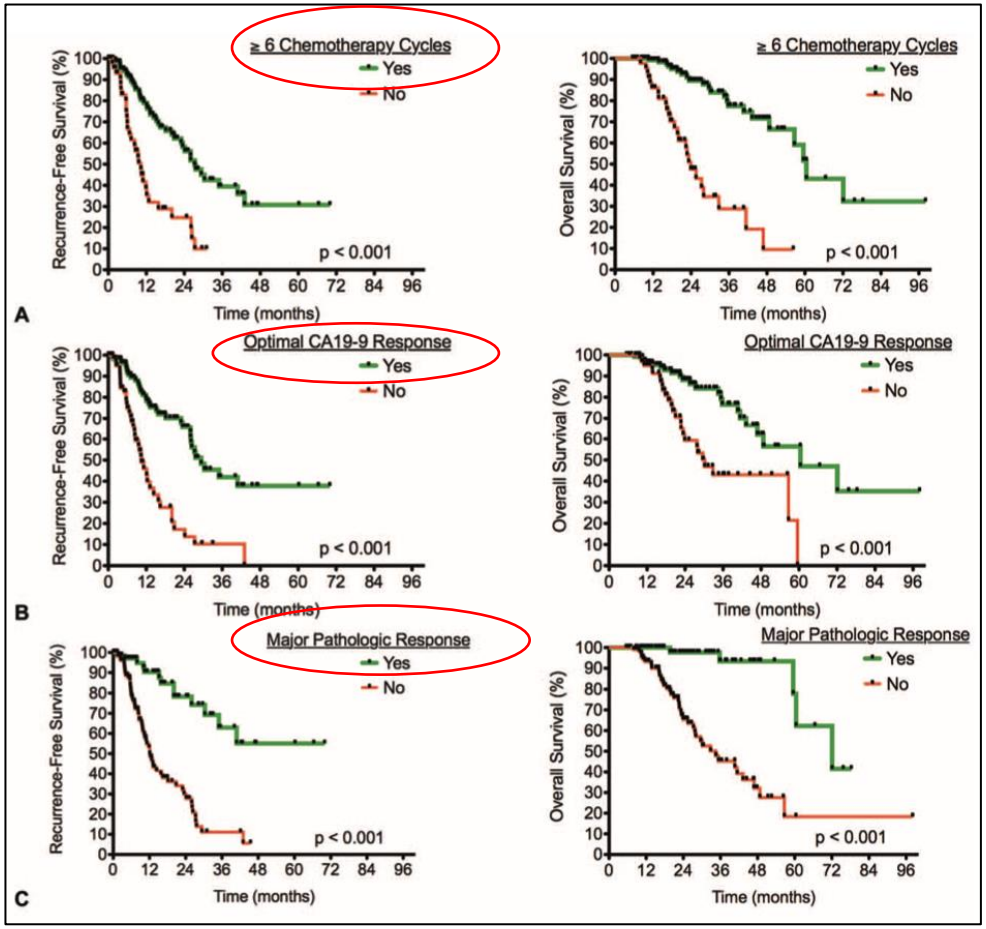
Resected: 66% **R0: 95%**

Factors Predicting Response, Perioperative Outcomes, and Survival Following Total Neoadjuvant Therapy for Borderline/Locally Advanced Pancreatic Cancer

Mark J. Truty, MD, MSc, FACS, Michael L. Kendrick, MD,* David. M. Nagorney, MD,* Rory L. Smoot, MD,* Sean P. Cleary, MD,* Rondell P. Graham, MD,† Ajit H. Goenka, MD,¶ Christopher L. Hallemeier, MD,§ Michel G. Haddock, MD,§ William S. Harmsen, MS,|| Amit Mahipal, MBBS,‡ Robert R. McWilliams, MD,‡ Thorvardur R. Halfdanarson, MD,‡ and Axel F. Grothey, MD‡*

123 pts BR/LA PDAC
TNT Folfirinox/Gem ± EBRT

CT downstage:	28%
Venous/art:	65%
R0 resection:	94%
DFS:	23.5mo
OS:	58.8mo



Ann Surg 2020

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Pancreatic Adenocarcinoma

NCCN Guidelines Index
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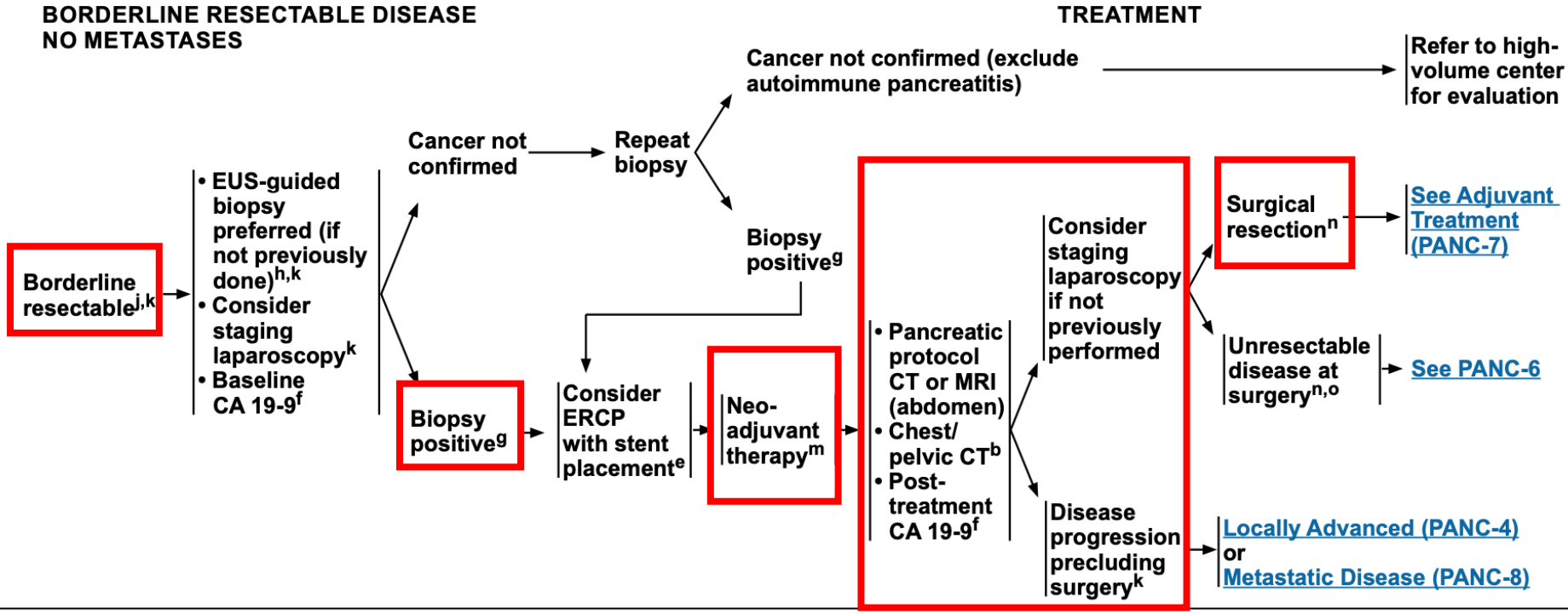
Discussion



NCCN 2022

Impact of neoadjuvant therapy on post-operative pancreatic fistula: a systematic review and meta-analysis

Sivesh K. Kamarajah,*† James R. Bundred,‡ Charles Boyle,* June Oo ,§ Sanjay Pandanaboyana* and Benjamin Loveday§¶‖

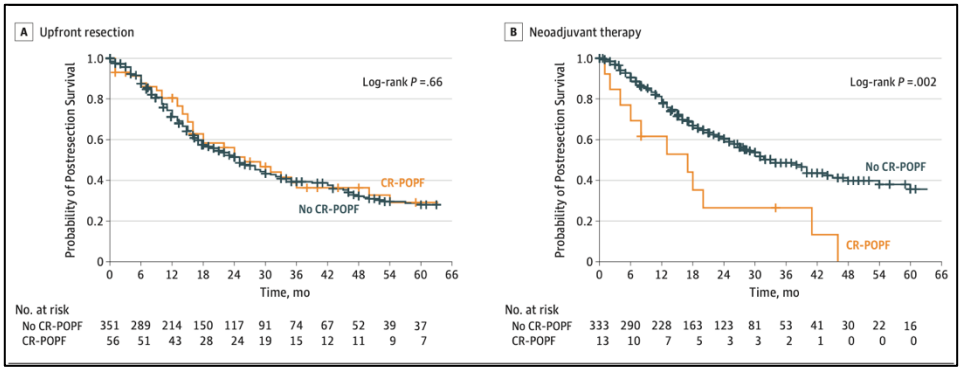
ANZ Ann Surg 2020

19 studies
19416 pts PD
5 studies
477 pts DP

Overall POPF					
Any neoadjuvant	14	0.5690 [0.4581; 0.7067]	−5.15	**<0.001**	9
Chemo/CRT	4	0.4800 [0.3599; 0.6403]	−4.99	**<0.001**	0
CRT	7	0.5897 [0.4684; 0.7425]	−4.49	**<0.001**	0
Chemotherapy	1	—	—	—	—
Grade B/C POPF					
Any neoadjuvant	8	0.5516 [0.4268; 0.7130]	−4.54	**<0.001**	25
Chemo/CRT	6	0.4476 [0.3764; 0.5322]	−9.10	**<0.001**	1
CRT	1	—	—	—	—
Chemotherapy	0	—	—	—	—
Overall DGE					
Any neoadjuvant	11	0.9604 [0.6974; 1.3226]	−0.25	0.8	42
Chemo/CRT	4	1.0726 [0.5816; 1.9781]	0.22	0.8	56
CRT	6	1.1543 [0.6154; 2.1651]	0.45	0.7	42
Chemotherapy	0	—	—	—	—
Grade B/C DGE					
Any neoadjuvant	1	—	—	—	—
Chemo/CRT	1	—	—	—	—
CRT	0	—	—	—	—
Chemotherapy	0	—	—	—	—
Overall PPH					
Any neoadjuvant	9	0.7270 [0.3867; 1.3670]	−0.99	0.3	23
Chemo/CRT	3	0.7761 [0.3216; 1.8728]	−0.56	0.6	20
CRT	4	0.4129 [0.1619; 1.0534]	−1.85	0.064	0
Chemotherapy	0	—	—	—	—
Grade B/C PPH					
Any neoadjuvant	1	—	—	—	—
Chemo/CRT	1	—	—	—	—
CRT	0	—	—	—	—
Chemotherapy	0	—	—	—	—
Overall complications					
Any neoadjuvant	16	1.1006 [0.8037; 1.5071]	0.60	0.6	80
Chemo/CRT	7	0.8686 [0.6377; 1.1831]	−0.89	0.4	63
CRT	7	1.2162 [0.5261; 2.8117]	0.46	0.6	83
Chemotherapy	0	—	—	—	—
Major complications					
Any neoadjuvant	6	0.9299 [0.7860; 1.1002]	−0.85	0.4	0
Chemo/CRT	4	0.9700 [0.6917; 1.3602]	−0.18	0.9	0
CRT	1	—	—	—	—
Chemotherapy	0	—	—	—	—

Association Between Pancreatic Fistula and Long-term Survival in the Era of Neoadjuvant Chemotherapy

Thomas Hank, MD; Marta Sandini, MD; Cristina R. Ferrone, MD; Clifton Rodrigues, MD; Maximilian Weniger, MD; Motaz Qadan, MD; Andrew L. Warshaw, MD; Keith D. Lillemoe, MD; Carlos Fernández-del Castillo, MD



JAMA Surg 2021

2020

JAMA Oncology | Original Investigation

Evaluation of Adjuvant Chemotherapy in Patients With Resected Pancreatic Cancer After Neoadjuvant FOLFIRINOX Treatment

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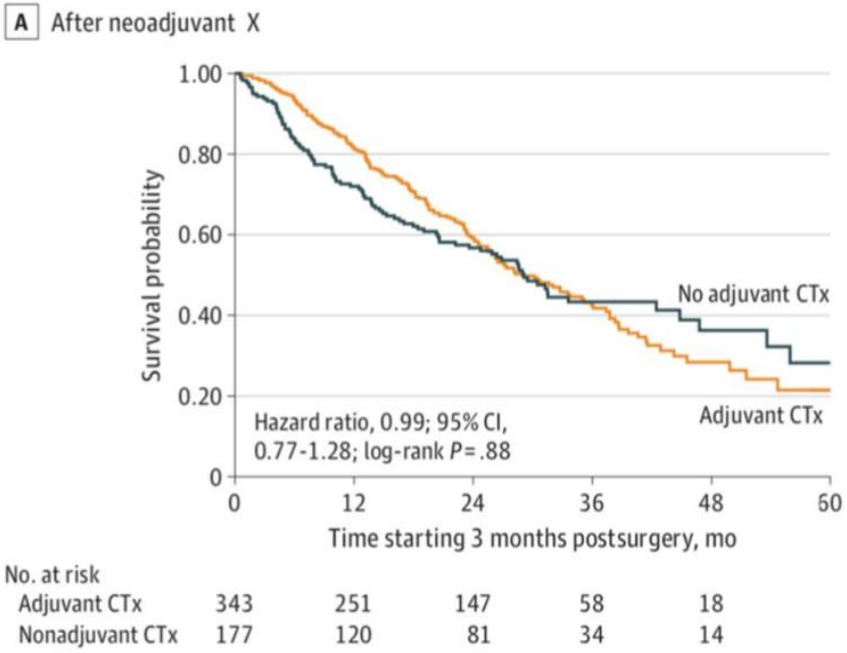
536 patients surgery
NAT (FOLFIRINOX)
31 centers/19 countries



2020

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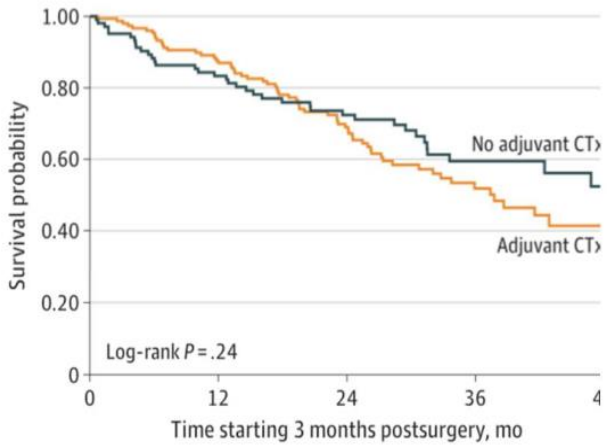
B With node-negative disease

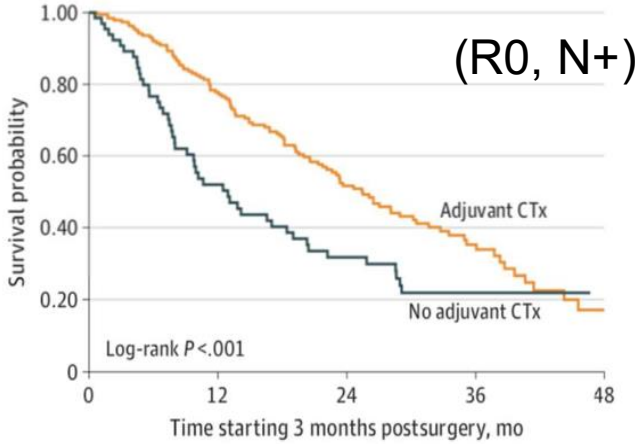


No. at risk

uvant CTx	151	121	79	32
adjuvant CTx	105	83	60	29

C With node-positive disease

(R0, N+)



No. at risk

Adjuvant CTx	189	130	68	68
Nonadjuvant CTx	65	31	17	17

Συμπεράσματα

- BR-PDAC είναι ξεχωριστή οντότητα
- Κοινός ορισμός με συγκεκριμένα χαρακτηριστικά
- Περιορισμένο *level of evidence*
- Σύσταση για νέο-επικουρική θεραπεία
- Χημειοθεραπεία με Gem/Folfirinox
- Ακτινοθεραπεία???
- Ανεπαρκής αξιολόγηση NT
- Χειρουργική διερεύνηση σε μη πρόοδο νόσου
- Έκβαση παγκρεατεκτομής μετά NT
- Επικουρική θεραπεία σε N+
- Νεότεροι βιοδείκτες
- Εξατομικευμένη προσέγγιση