CÂNCER DO PÂNCREAS

QUANDO INDICAR ABORDAGEM CIRÚRGICA "UP FRONT" OU NEOADJUVÂNCIA

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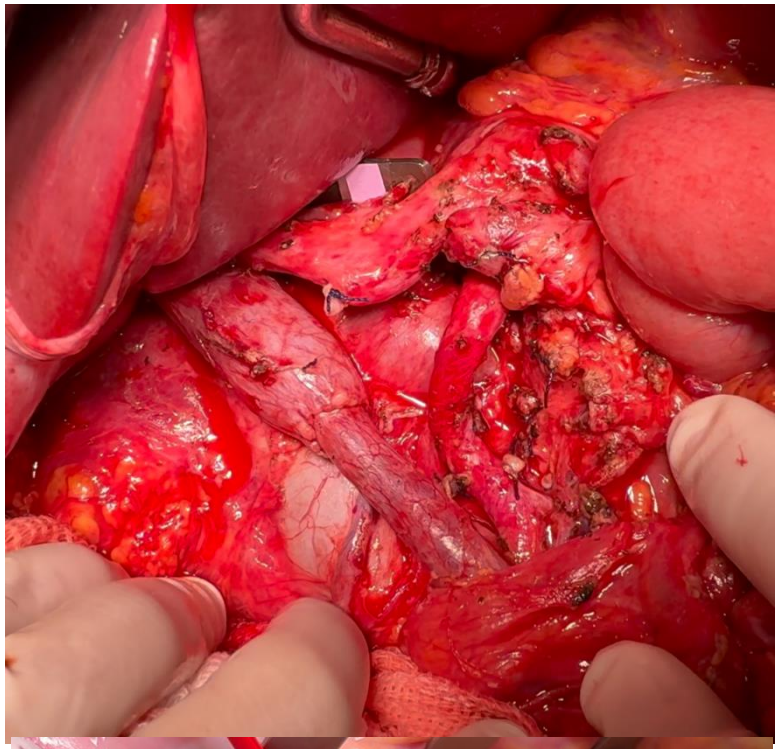
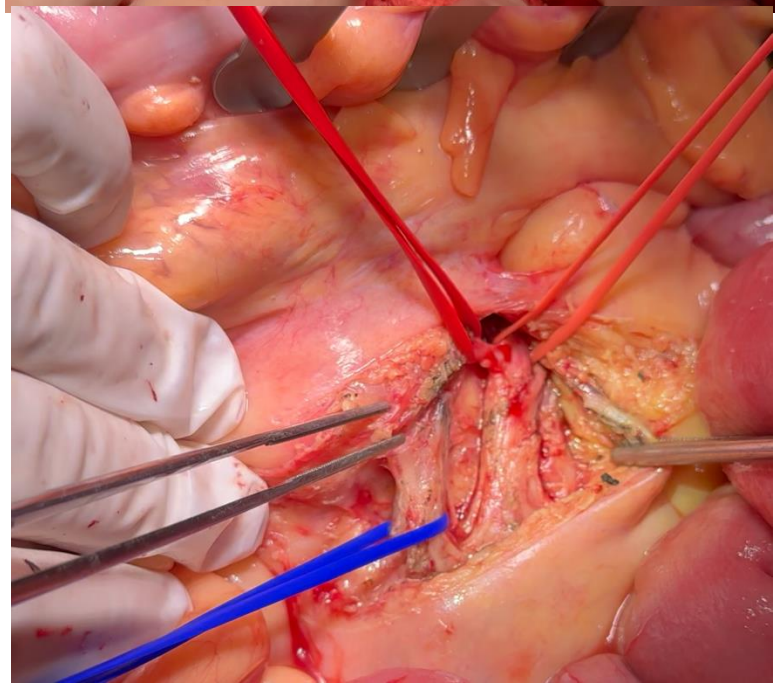
CÂNCER DO PÂNCREAS





STATE OF THE ART

Pancreatoduodenectomy

Total mesopancreas excision

"Artery first"

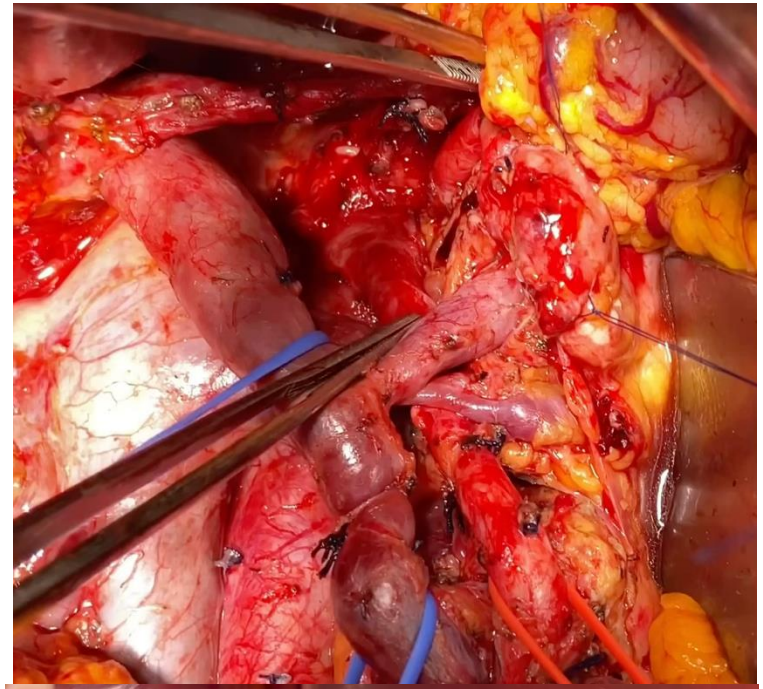
Level 3 dissection

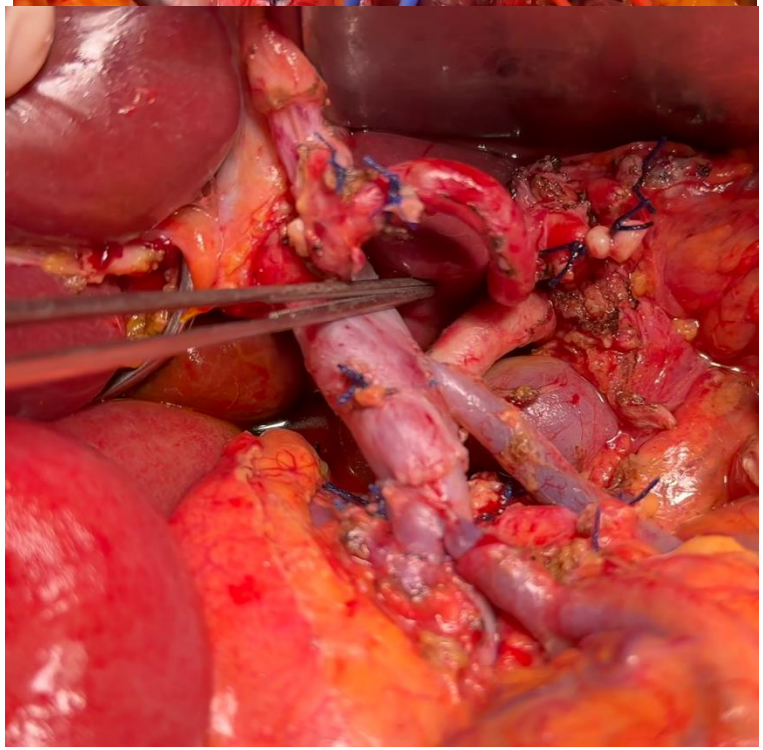
"Triangle operation"

Extended resection

+/- portal/SM vein

Torres anastomosis[6]





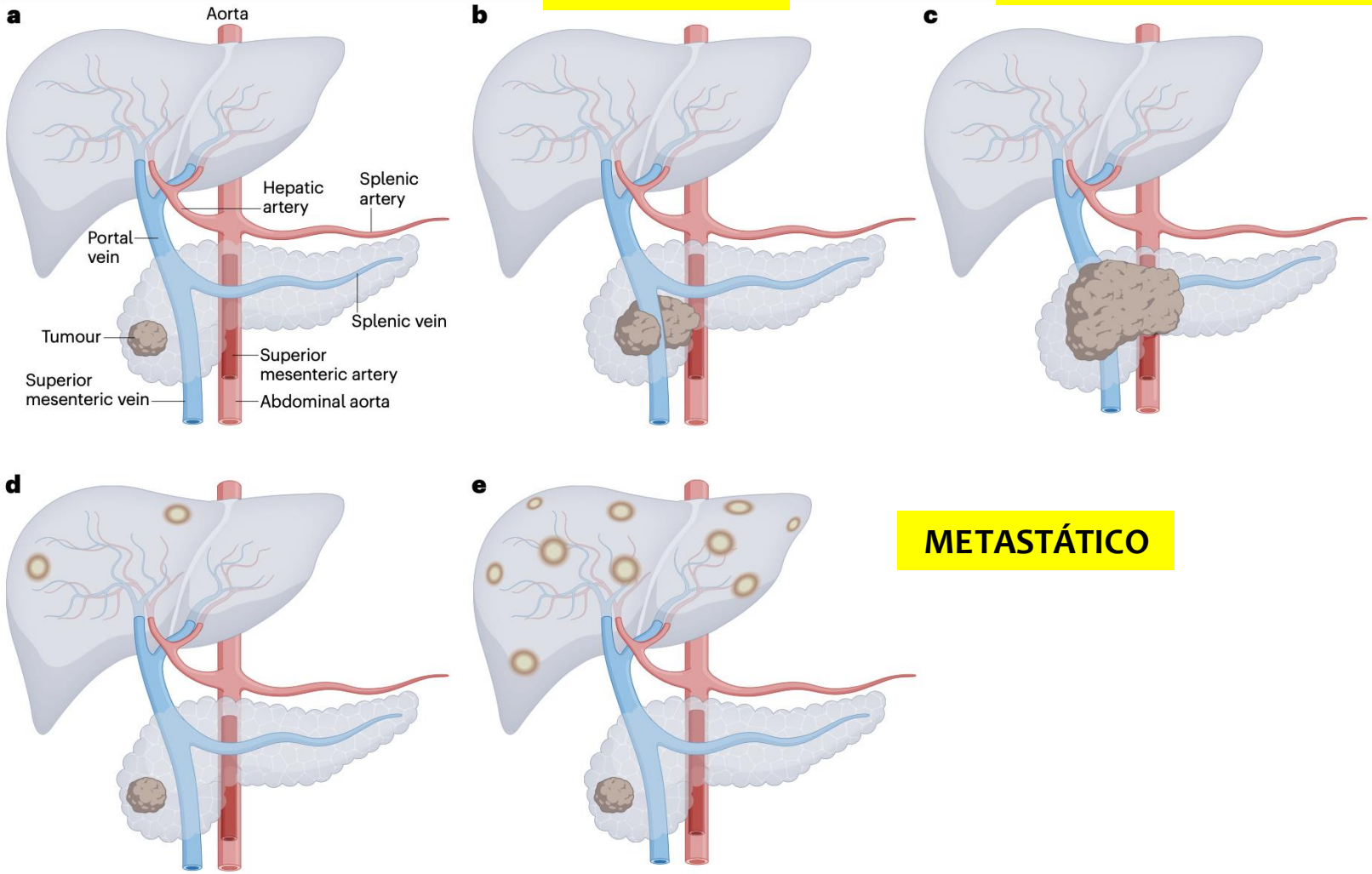
NÃO TRATA SEM CIRURGIA

ANATOMICAL FACTORS

RESSECÁVEL

BORDERLINE

LOCALMENTE AVANÇADO

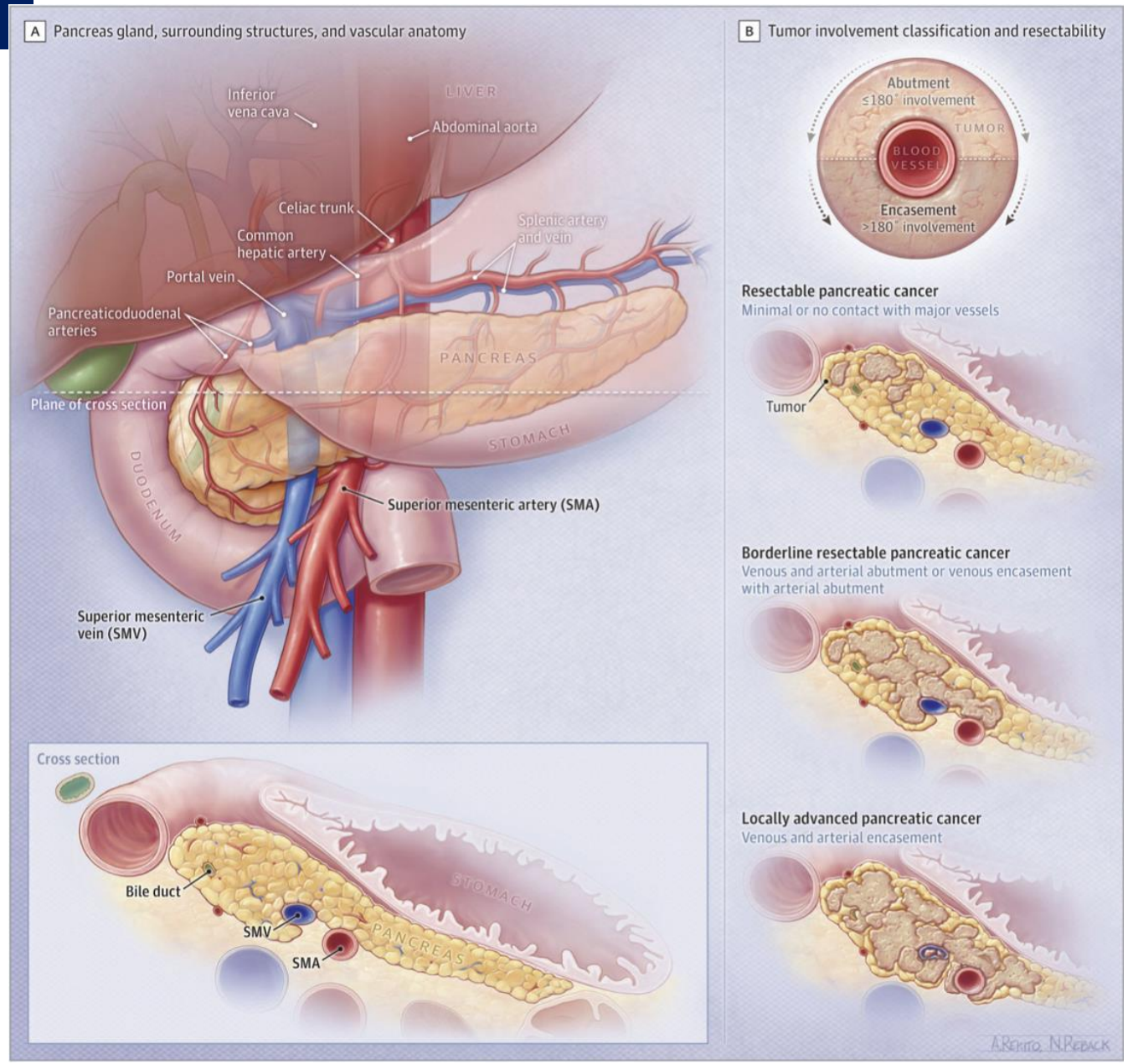


OLIGOMETASTÁTICO

METASTÁTICO

Springfeld C, et al. Nat Rev Clin Oncol 2023; 20:318–337

ANATOMICAL FACTORS



Park W, et al. JAMA. 2021; 326(9): 851–62.

Table 1 | Radiographic criteria used to assess, classify and communicate PDAC resectability

Classification	AHPBA/SSAT/SSO[20]	MD Anderson[21]	Alliance[22]	NCCN[16]
Superior mesenteric vein–portal vein				
Resectable	No abutment, encasement or occlusion	Abutment or encasement without occlusion	Interface between tumour and vessel measuring <180°	No tumour contact or ≤180° contact without vein contour irregularity
Borderline-resectable	Abutment, encasement or occlusion	Occlusion	Interface between tumour and vessel measuring ≥180°, and/or reconstructable[a] occlusion	Solid tumour contact measuring >180°, or solid tumour contact ≤180° with contour irregularity or thrombosis
Locally advanced	Unreconstructable	Unreconstructable	Unreconstructable	Unreconstructable
Superior mesenteric artery				
Resectable	No abutment	No abutment	No interface between tumour and vessel	No solid tumour contact
Borderline-resectable	Abutment	Abutment	Interface between tumour and vessel measuring <180°	Solid tumour contact ≤180°
Locally advanced	Encasement	Encasement	Interface between tumour and vessel measuring ≥180°	Solid tumour contact >180°
Common hepatic artery or its first-order branches				
Resectable	No abutment or encasement	No abutment or encasement	No interface between tumour and vessel	No solid tumour contact
Borderline-resectable	Abutment or short-segment encasement	Abutment or short-segment encasement	Reconstructable[a], short-segment interface between tumour and vessel of any degree	Solid tumour contact without extension to the coeliac artery or hepatic artery bifurcation
Locally advanced	Unreconstructable	Unreconstructable	Unreconstructable	Unreconstructable
Coeliac trunk				
Resectable	No abutment or encasement	No abutment or encasement	No interface between tumour and vessel	No solid tumour contact
Borderline-resectable	No abutment or encasement	Abutment	Interface between tumour and vessel measuring <180°	Solid tumour contact ≤180°
Locally advanced	Abutment or encasement	Encasement	Interface between tumour and vessel measuring ≥180°	Solid tumour contact >180°

AHPBA, Americas Hepato-Pancreato-Biliary Association; Alliance, Alliance for Clinical Trials in Oncology; NCCN, National Comprehensive Cancer Network; SSAT, Society for Surgery of the Alimentary Tract; SSO, Society of Surgical Oncology. [a]Normal vein or artery proximal and distal to the site of suggested tumour, vessel involvement suitable for vascular reconstruction.

Springfeld C, et al. Nat Rev Clin Oncol 2023; 20:318–337

ADENOCARCINOMA DUCTAL DO PÂNCREAS

RESSECÁVEL

- ❑ DUODENOPANCREATECTOMIA
- ❑ QUIMIOTERAPIA ADJUVANTE

Estado da arte

Conroy T, et al. Ann Oncol 2023

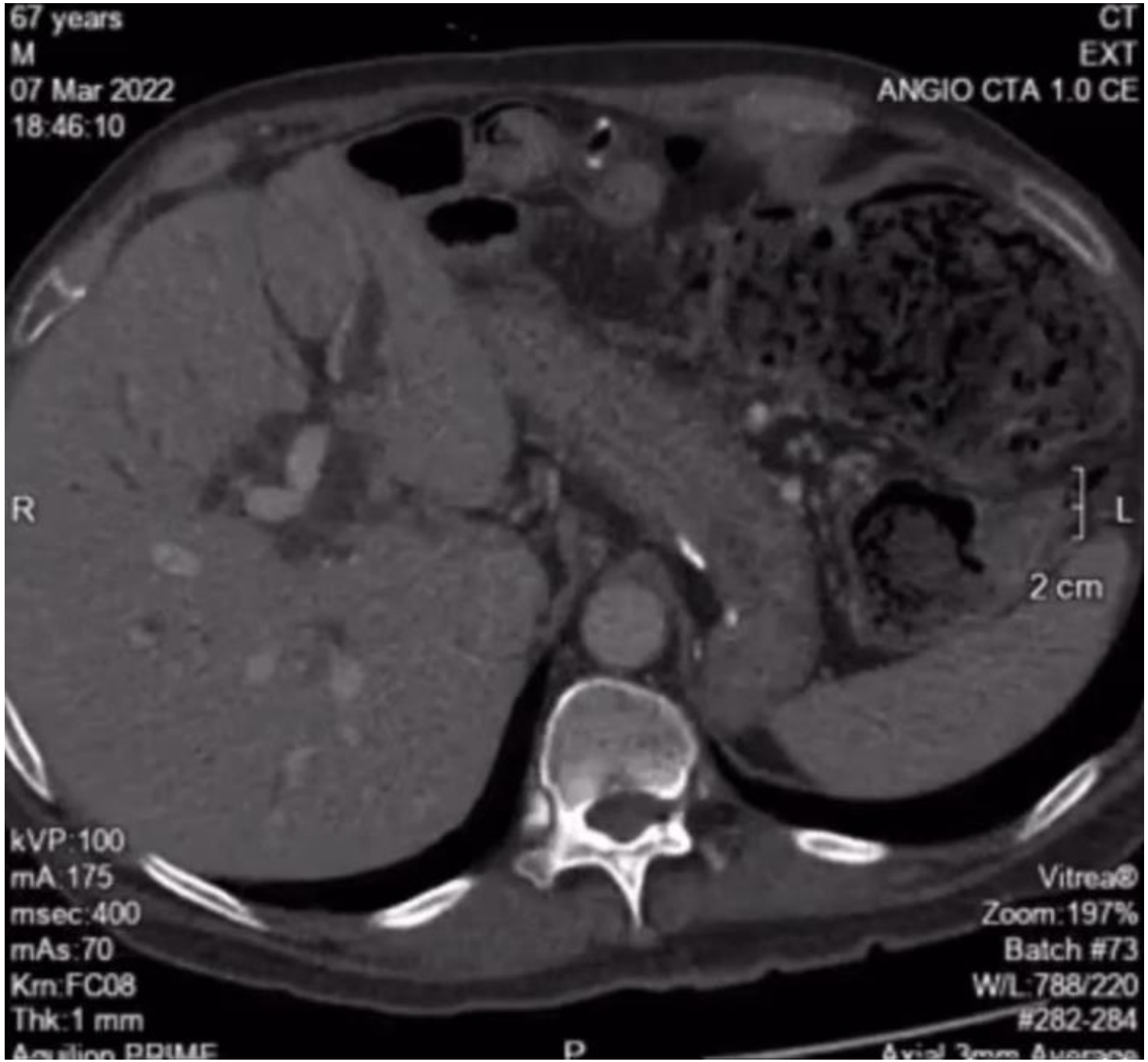
QUIMIOTERAPIA ADJUVANTE

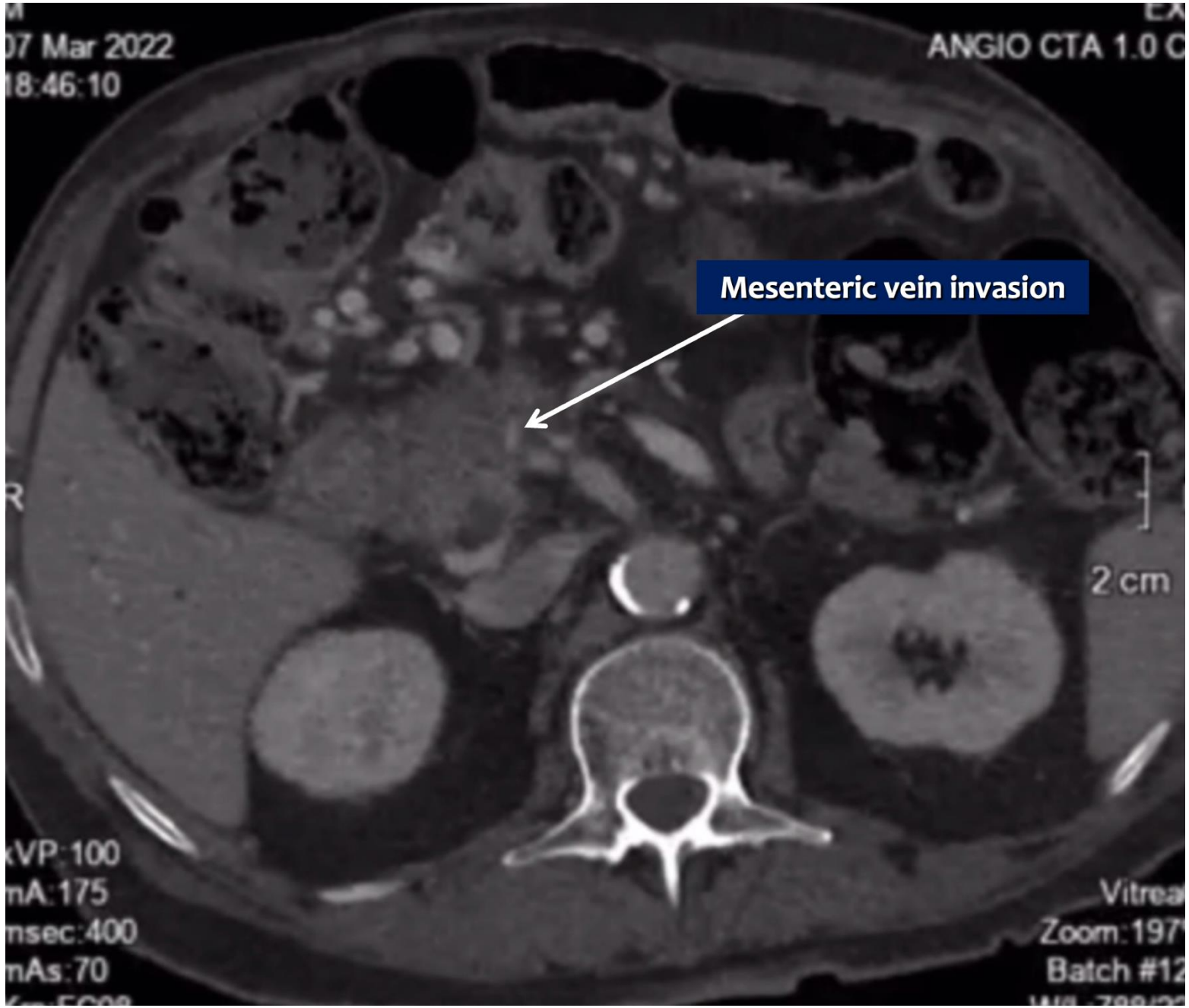
Table 3 Uni- and multivariable analysis for the association between the various individual complications with adjuvant chemotherapy after surgical resection for PDAC

	Univariable		Multivariable	
	OR (95% CI)	**p-value**	**OR (95% CI)[a]**	**p-value**
Pancreatic fistula (ISGPS 2005)				
None or grade A	Ref		Ref	
Grade B/C	**0.46 (0.31–0.68)**	**<0.001**	**0.51 (0.33–0.79)**	**0.003**
Pancreatic fistula (ISGPS 2016)				
None or biochemical leak	Ref			
Grade B/C	**0.48 (0.23–0.99)**	**0.050**		
Delayed gastric emptying				
None or grade A	Ref			
Grade B/C	0.79 (0.57–1.11)	0.173		
Bile leakage				
None or grade A	Ref			
Grade B/C	**0.45 (0.22–0.92)**	**0.038**		
Post-pancreatectomy hemorrhage				
None or grade A	Ref		Ref	
Grade B/C	**0.35 (0.22–0.55)**	**<0.001**	**0.36 (0.22–0.59)**	**<0.001**
Chyle leakage				
None or grade A	Ref			

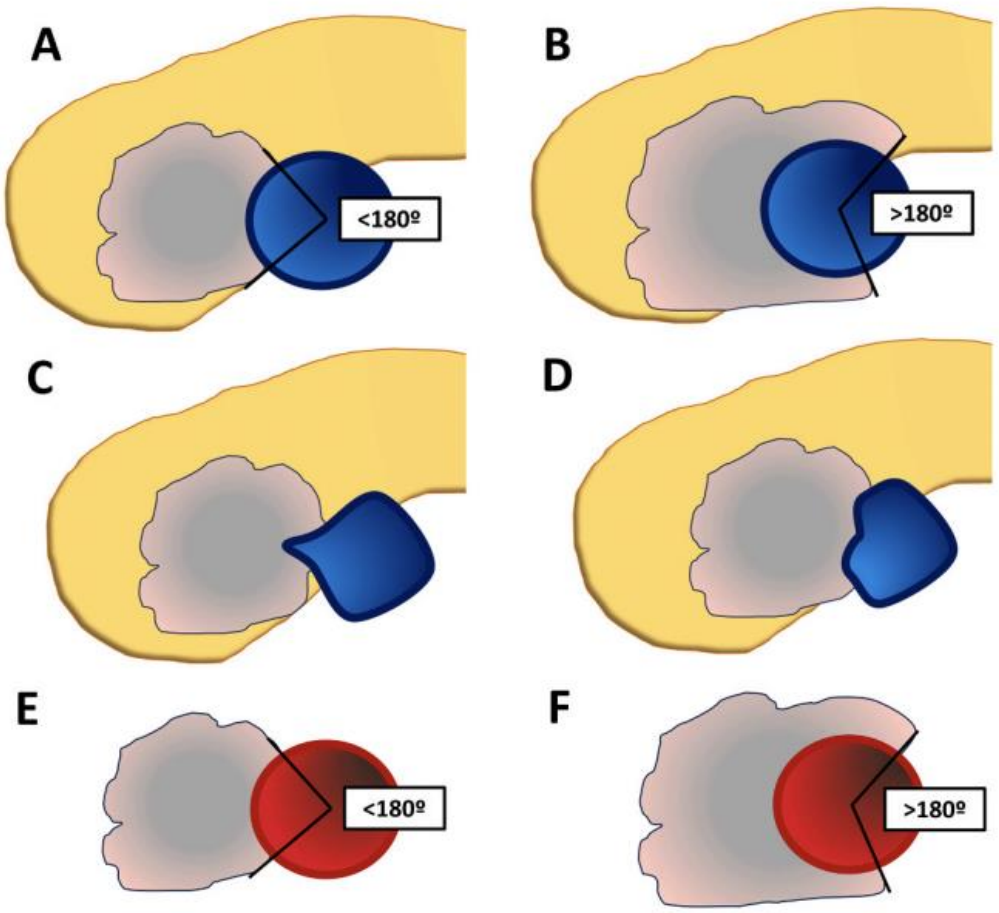
Anastomose padronizada (Heidelberg modificada)
Ligadura central vascular

Conroy T, et al. Ann Oncol 2023


67 years
M
07 Mar 2022
18:46:10
CT
EXT
ANGIO CTA 1.0 CE
R
L
2 cm
kVP:100
mA:175
msec:400
mAs:70
Krn:FC08
Thk:1 mm
Vitrea®
Zoom:197%
Batch #73
W/L:788/220
#282-284
P


07 Mar 2022
18:46:10
ANGIO CTA 1.0 C
Mesenteric vein invasion
2 cm
kVP:100
mA:175
msec:400
mAs:70
Zoom:197
Batch #12

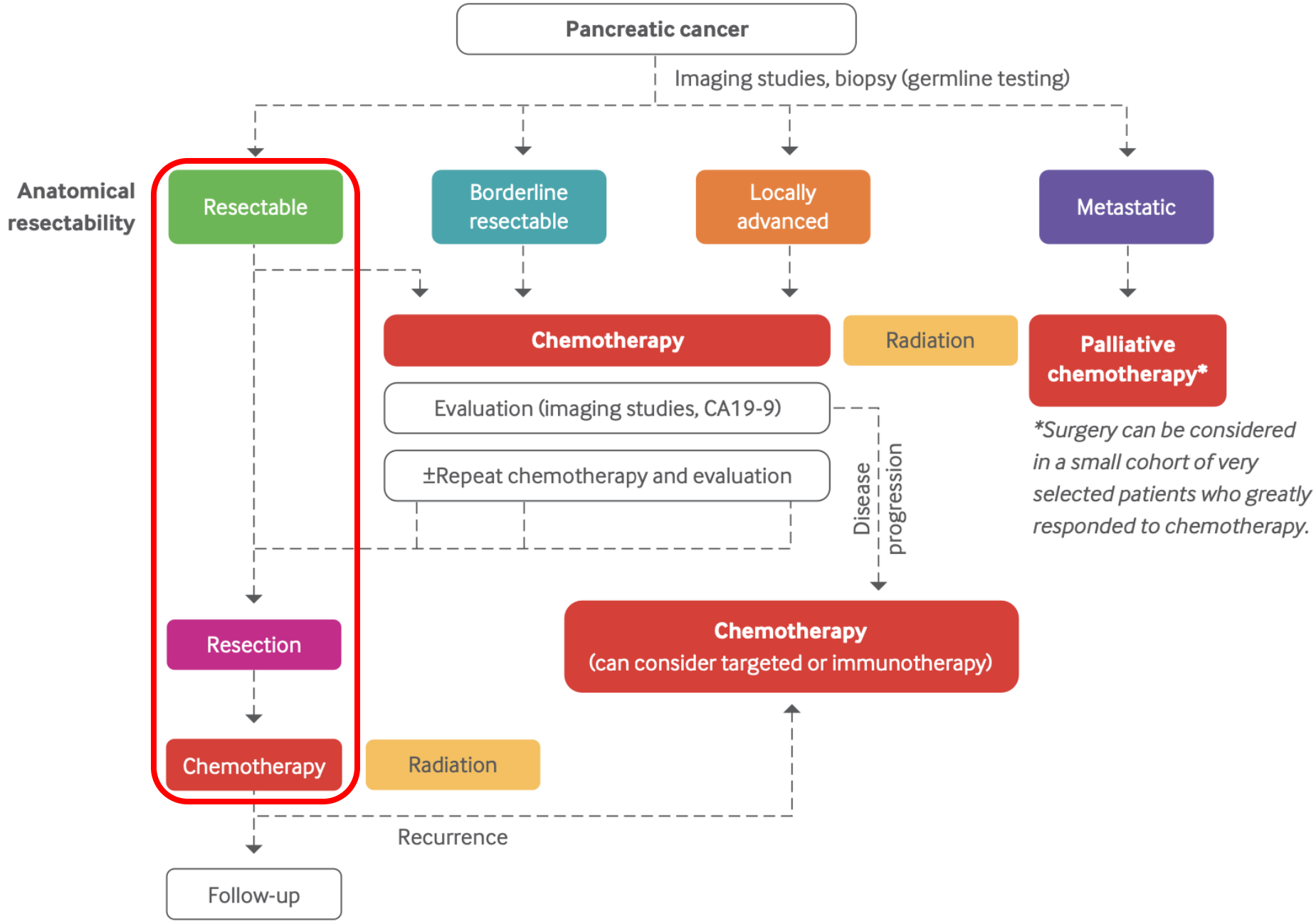
NCCN



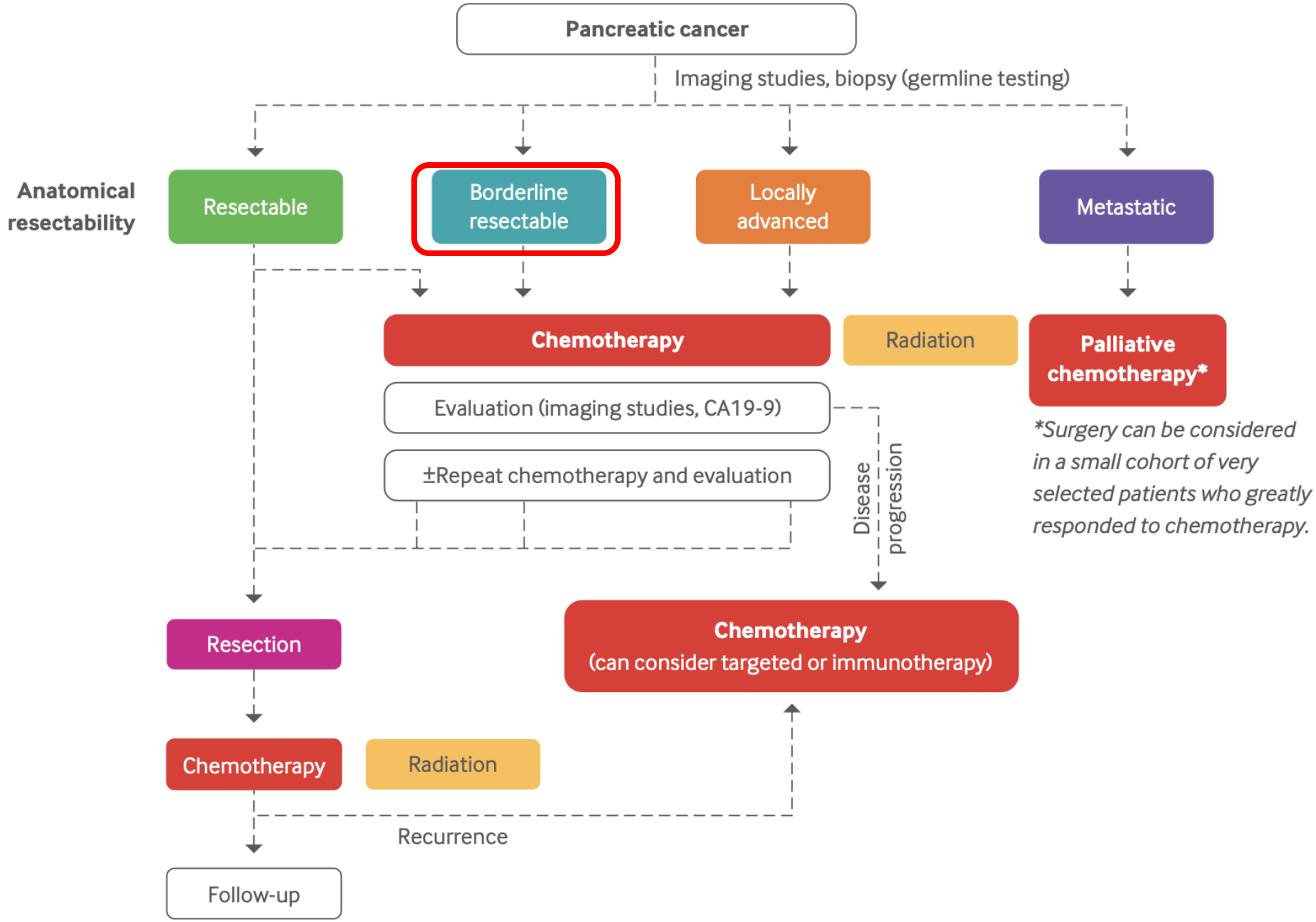
Resectable	Arteries	No tumoral contact
	Veins	No tumoral contact / ≤ 180° PV or SMV contact without deformity
Borderline	Arteries	≤ 180° SMA or CT contact Limited CHA contact (not extending to its bifurcation nor the CT) Anatomical variant with arterial involvement allowing for surgical management
	Veins	≤ 180° PV or SMV contact with deformity > 180° PV or SMV contact but surgically repairable Tumoral contact with IVC
Unresectable	Arteries	> 180° SMA or CT contact; extensive HA involvement
	Veins	> 180° PV or SMV contact non-surgically repairable

CHA: common hepatic artery; CT: celiac trunk; IVC: inferior vena cava; HA: hepatic artery; NCCN: National Comprehensive Cancer Network; PV: portal vein; SMA: superior mesenteric artery; SMV: superior mesenteric vein. Abutment and encasement are considered synonyms with < 180° and > 180° tumoral contact, respectively.

Bilreiro C, et al. Eur J Radiol Open 2024



Del Chiaro M, et al. BMJ 2023;383



Del Chiaro M, et al. BMJ 2023;383

❑ Terapia neoadjuvante

Table 4 | Survival outcomes from randomized studies of neoadjuvant therapies in patients with borderline-resectable pancreatic cancer

Trial	Recruitment period	Treatment arms	Survival outcomes	Comments
Jang et al.[52]	2012–2014	CRT+GEM>surgery>GEM+CRT (*n*=27) vs surgery>GEM+CRT (*n*=23	Median OS 21 vs 12 months (*P*=0.028 by intention-to-treat, preplanned analysis)	Data analyses are premature owing to an unacceptable number of deaths in the surgery-first arm (target enrolment was 110 patients); per-protocol analyses revealed no significant difference; PP1,17 patients who had both CRT>surgery vs 12 with upfront surgery (*P*=0.34); PP2, only eight patients who had CRT>surgery>chemotherapy versus six who had upfront surgery (*P*=0.32)
PREOPANC1 (refs. [49,50])	2013–2017	CRT+GEM>surgery>GEM (*n*=54) vs upfront resection>GEM (*n*=59)	Median OS 15.7 vs 14.3 months (*P*=0.025)[a] (ref. [50]), significant only in patients with borderline-resectable disease (HR 0.67, 95% CI 0.45–0.99)[50]	Combined OS in patients with borderline-resectable and resectable disease was the primary end point; median OS by intention-to-treat was 16.0 months with preoperative CRT vs 14.3 months with immediate surgery (HR 0.78, 95% CI 0.58–1.05; *P*=0.096)[49]
ESPAC-5 (ref. [17])	2014–2018	Surgery>adjuvant CTX (*n*=32) vs neoadjuvant therapy (GEMCAP (*n*=20), FOLFIRINOX (*n*=20) or CAP-CRT (*n*=16))>surgery>adjuvant CTX	1-year OS 39% vs 76% for the combined neoadjuvant therapy groups (*P*=0.0052); 1-year OS 78%, 80% and 60% in neoadjuvant GEMCAP, FOLFIRINOX and CAP–CRT subgroups, respectively	1-year OS and resection rate were the primary end points; R0 resection was achieved in 14% vs 23% of patients in the adjuvant-only group vs the combined neoadjuvant group
NUPAT-01 (ref. [161])	2015–2020	FOLFIRINOX>surgery>adjuvant CTX (*n*=26) vs GEM-NabP>surgery>adjuvant CTX (*n*=25)	3-year OS 55.3% vs 54.4% (NS)	R0 resection (the primary end point) was achieved in 73.1% vs 56.0%
Alliance A021501 (ref. [29])	2016–2019	mFOLFIRINOX>surgery (*n*=54) vs mFOLFIRINOX>SBRT>surgery (*n*=56)	18-month OS 66.7% vs 47.3%; median OS 29.8 vs 17.1 months	SBRT after mFOLFIRINOX did not improve OS

CAP–CRT, capecitabine plus chemoradiotherapy; CRT, chemoradiotherapy; CTX, chemotherapy; FOLFIRINOX, folinic acid, 5-fluorouracil, irinotecan and oxaliplatin; GEM, gemcitabine; GEMCAP, GEM plus capecitabine; GEM-NabP, GEM–nab-paclitaxel; mFOLFIRINOX, modified FOLFIRINOX; NS, not significant; OS, overall survival; SBRT, stereotactic body radiotherapy.
[a]Includes patients with resectable or borderline-resectable PDAC.

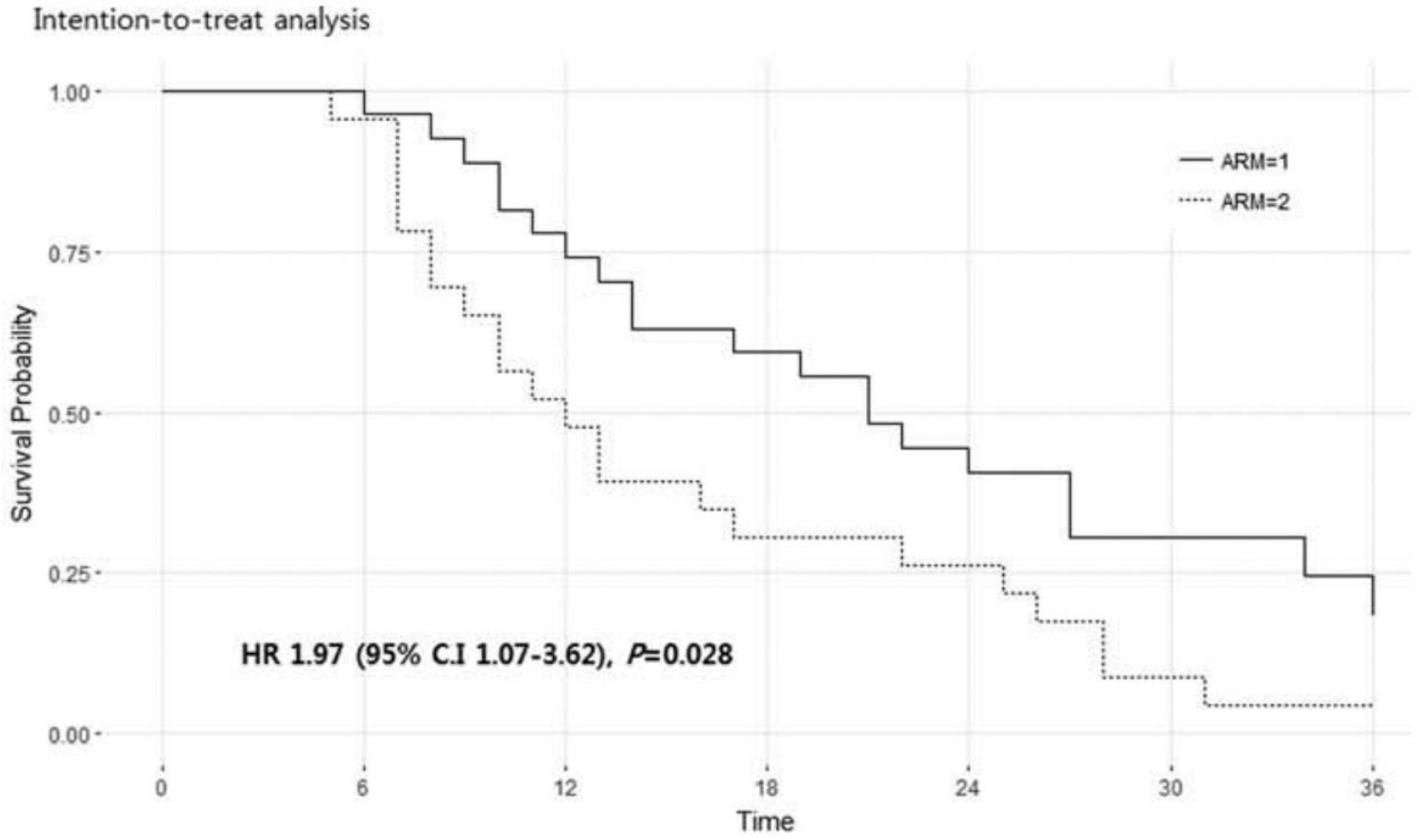
Borderline-resectable

Springfeld C, et al. Nat Rev Clin Oncol 2023; 20:318–337

❑ Terapia neoadjuvante

Oncological Benefits of Neoadjuvant Chemoradiation With Gemcitabine Versus Upfront Surgery in Patients With Borderline Resectable Pancreatic Cancer

A Prospective, Randomized, Open-label, Multicenter Phase 2/3 Trial



p=0.028

Borderline-resectable

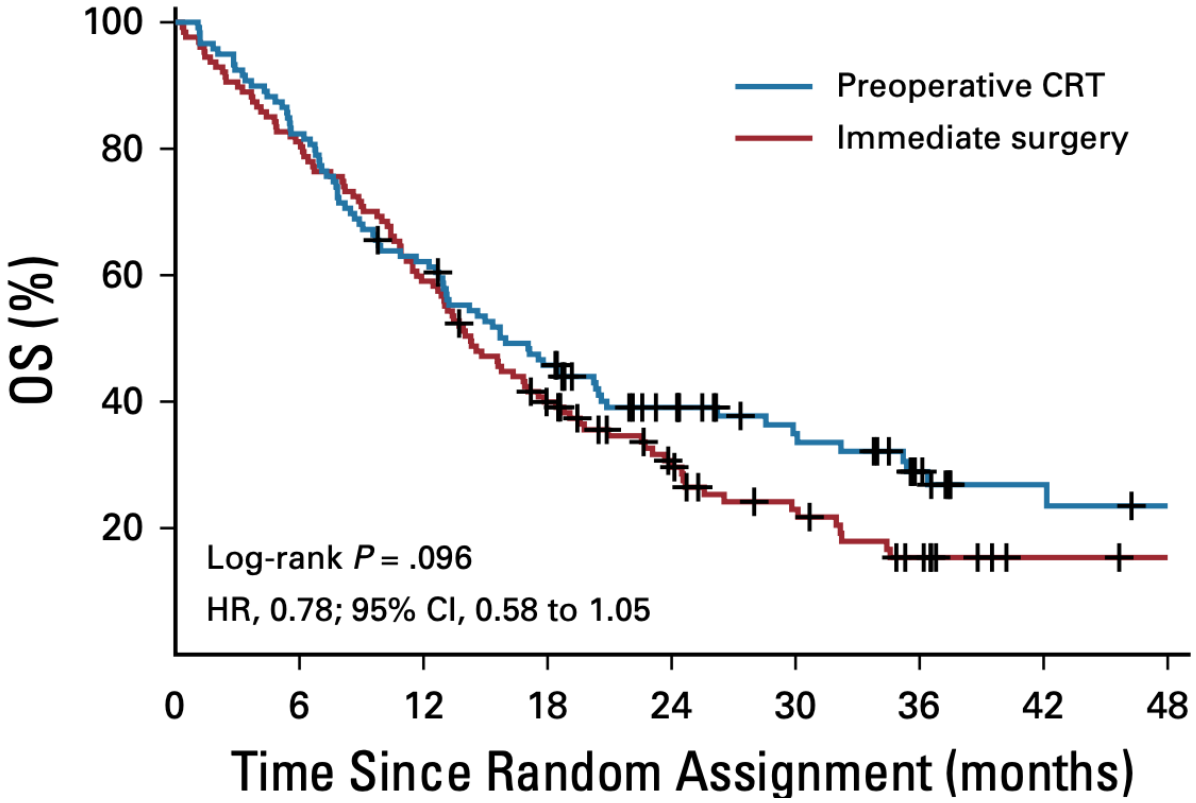
Jang JY, et al. Ann Surg 2018

❑ Terapia neoadjuvante

original reports

Preoperative Chemoradiotherapy Versus Immediate Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Results of the Dutch Randomized Phase III PREOPANC Trial

Eva Versteijne, MD[1]; Mustafa Suker, MD, PhD[2]; Karin Groothuis, MSc[3]; Janine M. Akkermans-Vogelaar, BSc[3];



p=0.096

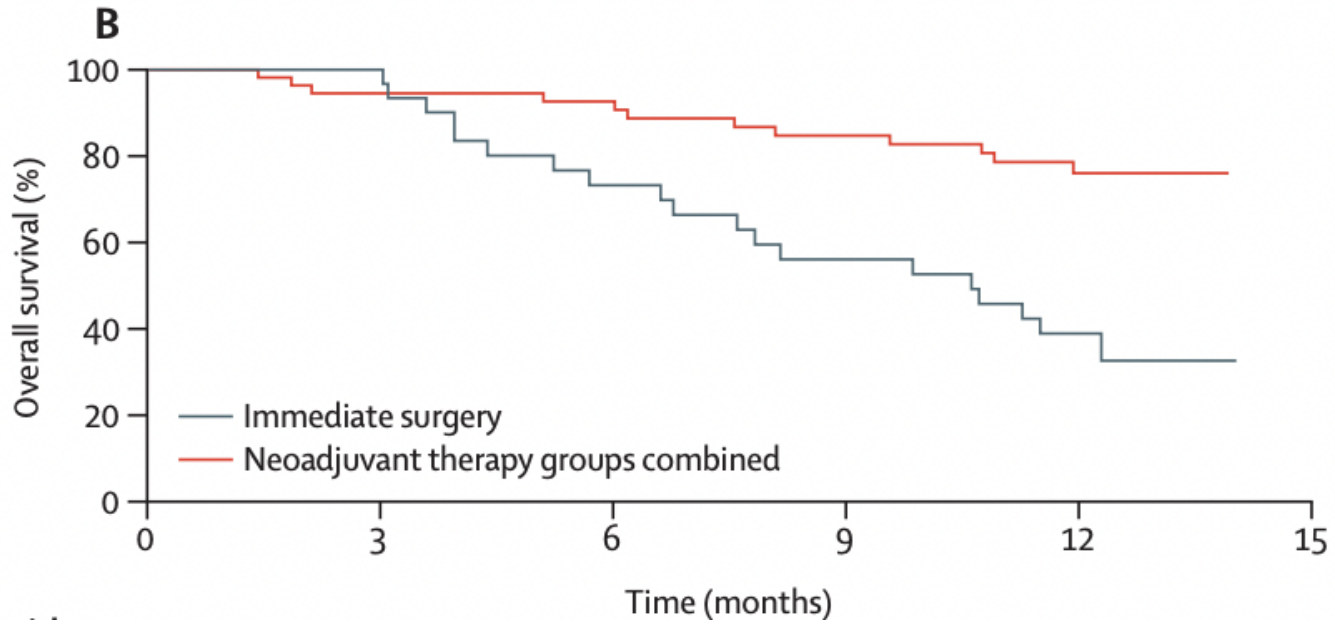
Borderline-resectable

Springfeld C, et al. Nat Rev Clin Oncol 2023; 20:318–337

❑ Terapia neoadjuvante

Immediate surgery compared with short-course neoadjuvant gemcitabine plus capecitabine, FOLFIRINOX, or chemoradiotherapy in patients with borderline resectable pancreatic cancer (ESPAC5): a four-arm, multicentre, randomised, phase 2 trial

ESPAC 5



p=0.0001

Borderline-resectable

Ghaneh P, et al. Lancet Gastroenterol Hepatol 2023; 8: 157–68

NEOADJUVÂNCIA

RACIONAL

- ❑ Eliminate presumed occult metastatic disease
- ❑ Give some patients time to allow for preoperative conditioning.
- ❑ Increase complete resection (R0) rates.
- ❑ Evaluate the histological response to therapy.
- ❑ Shrink tumor size and reduce involvement of vascular structures
- ❑ Downstage the tumor and reduce regional nodal disease

Lambert A, et al. Cancers 2021, 13, 4724

NEOADJUVÂNCIA

RACIONAL

- ❑ Reduce surgical complexity and postoperative complications
- ❑ Maximize the number of patients completing chemo (radio)
- ❑ Improve tolerance
- ❑ Identify patients with rapidly progressive disease
- ❑ Test in vivo chemosensitivity
- ❑ Increase overall survival (OS) and quality of life

Lambert A, et al. Cancers 2021, 13, 4724

NEOADJUVÂNCIA

- ❑ Histological or cytological diagnosis
- ❑ Biliary stenting for obstructive jaundice

Lambert A, et al. Cancers 2021, 13, 4724

COLANGIOPANCREATOGRAFIA ENDOSCÓPICA RETRÓGRADA

- ❑ Pancreatite
- ❑ Colangite
- ❑ Sangramento
- ❑ Perfuração

Lambert A, et al. Cancers 2021, 13, 4724

CÂNCER DO PÂNCREAS

- ❑ Ressecável e “borderline”
- ❑ Quimioterapia

QUIMIOTERAPIA NEOADJUVANTE

EVENTOS ADVERSOS

TABLE 2 Adverse events (related or not), maximum grade by patient and category

	Arm A: adjuvant gemcitabine ($N = 21$)			Arm B: perioperative FOLFIRINOX ($N = 19$)		
	Grades 1–2	Grades 3–4	Grade 5	Grades 1–2	Grades 3–4	Grade 5
Abdominal pain	2 (10%)	1 (5%)		1 (5%)	2 (11%)	
Anorexia	3 (14%)			4 (21%)		
Biliary tract infection					2 (11%)	
Diarrhea	5 (24%)	1 (5%)		3 (16%)	2 (11%)	
Dizziness	3 (14%)			4 (21%)		
Fatigue	5 (24%)	1 (5%)		5 (26%)		
Fever	5 (24%)	1 (5%)		3 (16%)		
GGT increased		1 (5%)		1 (5%)	2 (11%)	
Hepatic failure			1 (5%)			
Nausea	1 (5%)	2 (10%)		5 (37%)		
Neutropenia	1 (5)	3 (14%)		1 (5%)		
Sepsis					2 (11%)	2 (11%)

Except for grade 5, adverse events are displayed when they were observed in > 20% patients at grades 1 or 2 or > 5% patients at grades 3 or 4 in at least one of both arms

Perda do status

Goetze TO, et al. Ann Surg Oncol 2024; 31:4073–83

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN CANCER HORIZONS

REVIEW

Neoadjuvant chemotherapy with or without radiotherapy versus upfront surgery for resectable pancreatic adenocarcinoma: a meta-analysis of randomized clinical trials

Table 1. Characteristics of clinical trials included in the meta-analysis

Study	Country	Phase	NC arm Neoadjuvant regimen (weeks)	NC arm Adjuvant chemotherapy (weeks)	US arm Adjuvant chemotherapy (weeks)	Sample size, *n*
Seufferlein et al.[26]	Germany	II	NabP-Gem (8)	NabP-Gem (16)	NabP-Gem (24)	118
Versteijne et al.[24]	The Netherlands	III	Gem (10) + RT	Gem (16)	Gem (24)	133[a]
Reni et al.[20]	Italy	II/III	PEXG (12)	PEXG (12)	1. Gem (24) 2. PEXG (24)	88
Birrer et al.[12]	Switzerland	III	Gem-Ox (8)	Gem (24)	Gem (24)	34
Casadei et al.[b,10]	Italy	II	Gem (12) + RT	Gem (24)	Gem (24)	38
Golcher et al.[b,11]	Germany	II	Cis-Gem (6) + RT	Gem (24)	Gem (24)	58[a]

Cis, cisplatin; Gem, gemcitabine; NabP, nab-paclitaxel; NC, neoadjuvant chemotherapy; Ox, oxaliplatin; PEXG, cisplatin, epirubicin, capecitabine, gemcitabine; RT, radiation therapy; US, upfront surgery.

[a]Patients with borderline resectable pancreatic cancer not included in the analysis.

[b]Actualized data from these studies were collected from Birrer et al.[12]

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN CANCER HORIZONS

REVIEW

Neoadjuvant chemotherapy with or without radiotherapy versus upfront surgery for resectable pancreatic adenocarcinoma: a meta-analysis of randomized clinical trials

Table 2. Resection rate and R0 resection rate for neoadjuvant chemotherapy (NC) and upfront surgery (US) approaches in each clinical trial

Study	Resection rate NC, %	Resection rate US, %	R0 resection rate NC, %	R0 resection rate US, %
Seufferlein et al.[26]	69	78	88	67
Versteijne et al.[24]	68	79	66	59
Reni et al.[20]	84	87	63	33
Birrer et al.[a,12] Casadei et al.[a,10] Golcher et al.[a,11]	84	89	70	53

[a]Data from these studies were updated and collected as a whole from Birrer et al.[12]

RESECTION RATE

Table 2. Randomized controlled trials comparing neoadjuvant chemotherapy with upfront surgery for resectable and borderline resectable pancreatic cancer

Author	Country	Treatment arm	*N*	Primary endpoint	OS	Resection rate	R0 rate
Resectable PDAC							
Golcher et al. [66]	Germany	GEM/CIS + RT	33	OS	17.4	19/33 (58)	17/19 (89)
	Switzerland	Upfront surgery	33		14.4	23/33 (70)	16/23 (70)
Casadei et al. [67]	Italy	GEM + RT	18	R0 resection rate	22.4	11/18 (61)	7/11 (64)
		Upfront surgery	20		19.5	15/20 (75)	5/15 (33)
Reni et al. [68]	Italy	PEXG	32	Event-free at 1 year[b]	38.2	27/32 (84)	17/27 (63)
		Upfront surgery (+PEXG)	30		26.4	27/30 (90)	10/27 (37)
		Upfront surgery (+GEM)	26		20.4	22/26 (85)	6/22 (27)
Resectable/borderline resectable PDAC							
Unno et al. [63]	Japan	GEM + S-1	182	OS	36.7[a]	140/182 (77)	–
		Upfront surgery	180		26.6[a]	130/180 (72)	–
Versteijne et al. [62]	Netherlands	GEM + RT	119	OS	16.0	72/119 (61)	51/72 (71)[a]
		Upfront surgery	127		14.3	92/127 (72)	37/92 (40)[a]
Borderline resectable PDAC							
Jang et al. [61]	Korea	GEM + RT	27	2-year survival rate	21[a]	17/27 (63)	14/17 (82)[a]
		Upfront surgery	23		12[a]	18/23 (78)	6/18 (33)[a]

Data are given as *n* (%). CIS, cisplatin; GEM, gemcitabine; OS, median overall survival in months by intention-to-treat analysis; PDAC, pancreatic ductal adenocarcinoma; RT, radiotherapy; S-1, oral fluoropyrimidine derivative; PEXG, cisplatin, epirubicin, capecitabine, and gemcitabine. [a] $p < 0.05$. [b] Events defined as progression, relapse, new tumor, distant metastases, or death.

Muller PC, et al. Pharmacology 2020

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

ORIGINAL RESEARCH

Does neoadjuvant treatment in resectable pancreatic cancer improve overall survival? A systematic review and meta-analysis of randomized controlled trials

Gemcitabine-based neoadjuvant treatment

Table 1. Studies included in meta-analysis

Study	Trial phase	Age (range), years	Laparoscopy	TNM	Intervention	*n*	mOS (95% CI), months	OS HR (95% CI)	mDFS (95% CI), months	mDFS HR (95% CI)	R0	R0 HR (95% CI)
Casadei et al.[11] Di Marco et al.[12]	II	71.5 (51-78)	72.2%	I: 22% II: 78%	GEM + RDT > surgery > GEM	18	24.35 (8.04-40.66)	$P = 0.174$	18.03 (2.58-33.48)	$P = 0.242$	38.9%	OR = 1.91 (0.48-7.64)
		67.5 (48-79)	100%	I: 0% II: 100%	Surgery > GEM	20	21.17 (8.37-33.96)		8.53 (4.47-12.59)		25%	$P = 0.489$
Golcher et al.[13]	II	62.5 (33-76)	39%	I: 39% II: 55% IV: 6%	GEM + CDDP + RDT > surgery > GEM	33	17.4	$P = 0.96$	—	—	52%	$P = 0.81$
		65.1 (46-73)	46%	I: 48% II: 52%	Surgery > GEM	33	14.4		—		48%	
PACT-15 Reni et al.[14]	II	64 (39-75)	Not evaluated	I or II: 100%	PEXG > surgery > PEXG	32	38.2 (27.3-49.1)	—	16.9 (3.7-28.7)	—	63%	—
		68 (49-75)			Surgery > PEXG	30	26.4 (15.8-26.7)		12.4 (5.4-19.4)		37%	
		65 (37-74)			Surgery > GEM	26	20.4 (14.6-25.8)		4.7 (0.9-8.9)		27%	
Prep-02/JSAP-05 Satoi et al.[15]	III	Not presented	Not evaluated	I or II: 100%	GEM + S1 > surgery > S1	182	36.7 (28.6-43.3)	0.72 (0.55-0.94)	—	—	—	—
					Surgery > S1	180	26.6 (21-31.3)	$P = 0.015$	—		—	
PREOPANC Versteijne et al.[10]	III	66 (59-71)	100%	I or II: 100%	GEM + RDT > surgery > GEM	65	14.6	0.96 (0.64-1.44)	9.2	0.88 (0.60-1.28)	66%	OR = 1.33 (0.58-3.04)
		67 (60-73)	Not necessary		Surgery > GEM	68	15.6	$P = 0.830$	9.3	$P = 0.52$	59%	$P = 0.540$
NEONAX Seufferlein et al.[16]	II	Not presented	Not evaluated	I or II: 100%	GEM + NAB-PACL > surgery	59	25.2	1.26 (0.80-1.97)	11.5	1.31 (0.86-1.99)	87.8%	
					Surgery > GEM + NAB-PACL	59	16.7		5.9		67.4%	

CDDP, cisplatin; CI, confidence interval; GEM, gemcitabine; HR, hazard ratio; mDFS, median disease-free survival; mOS, median overall survival; NAB-PACL, nab-paclitaxel; RDT, radiotherapy; TNM, tumor—node—metastasis staging.

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ORIGINAL RESEARCH

Does neoadjuvant treatment in resectable pancreatic cancer improve overall survival? A systematic review and meta-analysis of randomized controlled trials

Gemcitabine-based neoadjuvant treatment

Conclusion

In this meta-analysis of six randomized controlled trials, no survival benefit was identified with neoadjuvant chemotherapy or chemoradiation in RPC. Upfront surgery should still be considered a standard approach in this subgroup of patients. The best treatment strategy should be discussed case by case considering multiple clinical factors and molecular biomarkers.

Uson Junior PLS, et al. Cancers 2024, 16, 2522

PANCREATIC CANCER

The role of neoadjuvant therapy for resectable pancreatic cancer remains uncertain

Christoph Springfeld and John P. Neoptolemos

PREOPANC is an important study and adds a lot of knowledge to the field of perioperative PDAC therapy. However, whether the results of PREOPANC should change current clinical practice is uncertain, and several questions remain. Adjuvant single-agent chemotherapy, which was the standard-of-care approach in the Netherlands when PREOPANC was initiated, has since been superseded by combination chemotherapy regimens, which have been shown to be superior. Furthermore, the use of chemora-

Table 1 | **Selected randomized controlled trials of perioperative therapy for patients with PDAC**

Trial name	Identifier	Disease status	*N*	Phase	Interventions
NorPACT-1	NCT02919787	Resectable	140	II	Neoadjuvant FOLFIRINOX (4) plus adjuvant chemotherapy for 4 months versus adjuvant chemotherapy for 6 months
PANACHE01	NCT02959879	Resectable	160	II	Neoadjuvant mFOLFIRINOX (4) plus adjuvant chemotherapy for 4 months versus neoadjuvant FOLFOX (4) plus adjuvant chemotherapy for 4 months versus adjuvant chemotherapy for 6 months
PREOPANC-2	EudraCT 2017-002036-17	Resectable and borderline resectable	368	III	Neoadjuvant FOLFIRINOX (8) versus neoadjuvant gemcitabine-based chemoradiotherapy plus adjuvant gemcitabine (4)
PREOPANC-3	NCT04927780	Resectable	378	III	Neoadjuvant (8) plus adjuvant (4) mFOLFIRINOX versus adjuvant FOLFIRINOX (12)
ALLIANCE A021806	NCT04340141	Resectable	352	III	Neoadjuvant (8) plus adjuvant mFOLFIRINOX (4) versus adjuvant mFOLFIRINOX (12)
ESPAC-6	EudraCT 2020-004906-79	Resected	NR	III	Adjuvant mFOLFIRINOX (12) or gemcitabine/capecitabine (6) based on transcriptomic signature versus adjuvant mFOLFIRINOX (12)

For the interventions, the number of chemotherapy cycles is shown in parentheses. FOLFIRINOX, folinic acid (400 mg/m^2), 5-fluorouracil (bolus 400 mg/m^2, then 2,400 mg/m^2), irinotecan (180 mg/m^2) oxaliplatin (85 mg/m^2); mFOLFIRINOX, FOLFRINOX with one or more dose modifications; FOLFOX, folinic acid, 5-fluorouracil and oxaliplatin; PDAC, pancreatic ductal adenocarcinoma.

Springfeld C, Neoptolemos JP, 2022.

Ann Surg Oncol (2024) 31:4956–4965
https://doi.org/10.1245/s10434-024-15070-w

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ORIGINAL ARTICLE – PANCREATIC TUMORS

BIOLOGICAL AND CONDITIONAL FACTORS

The Value of Biological and Conditional Factors for Staging of Patients with Resectable Pancreatic Cancer Undergoing Upfront Resection: A Nationwide Analysis

R_{B+} - Ressecável biologicamente desfavorável (CA 19-9 ≥ 500 U/mL)
R_{B-} - Ressecável biologicamente favorável (CA 19-9 < 500 U/mL)
R_{C+} - Ressecável condicionalmente desfavorável (ECOG performance status ≥ 2)
R_{C-} - Ressecável condicionalmente favorável (ECOG performance status 0-1)

Schouten TJ, et al. Ann Surg Oncol 2024; 31:4956–65

Ann Surg Oncol (2024) 31:4956–4965
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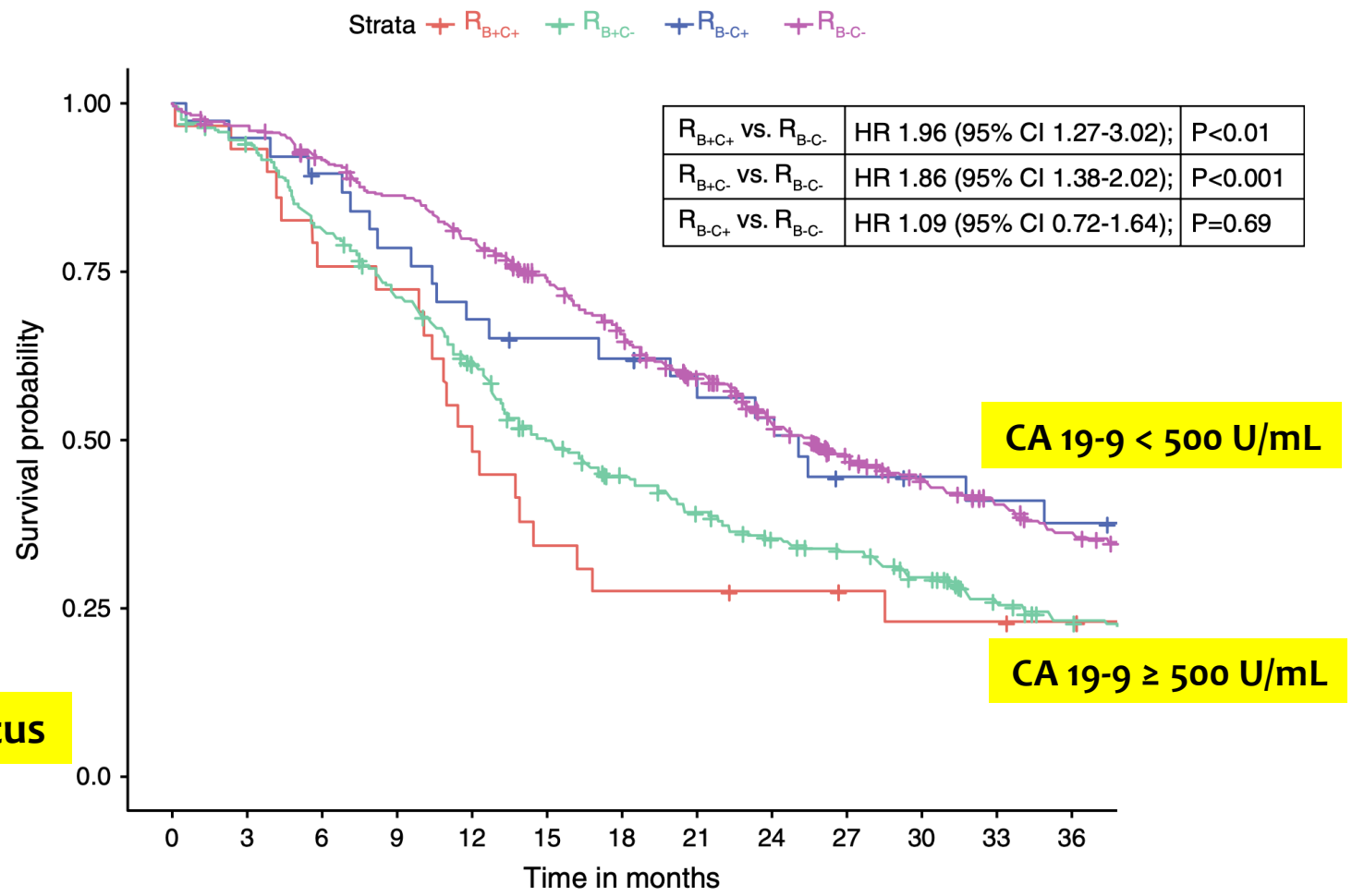

R_{B+C+} vs. R_{B-C-}	HR 1.96 (95% CI 1.27-3.02);	P<0.01
R_{B+C-} vs. R_{B-C-}	HR 1.86 (95% CI 1.38-2.02);	P<0.001
R_{B-C+} vs. R_{B-C-}	HR 1.09 (95% CI 0.72-1.64);	P=0.69

CA 19-9 < 500 U/mL

CA 19-9 ≥ 500 U/mL

CA 19-9 mais importante que o performance status

Schouten TJ, et al. Ann Surg Oncol 2024; 31:4956–65

JAMA Surgery | Original Investigation

Futility of Up-Front Resection for Anatomically Resectable Pancreatic Cancer

Table 2. Modeling Futility (Recurrence or Death Within 6 Months) After Up-Front Surgery of Anatomically Resectable Pancreatic Ductal Adenocarcinoma Based on Preoperative Clinical Features in the Derivation Cohort

	k-Fold cross validation					
	1	2	3	4	5	Pooled (95% CI)
In-sample cohorts, No.	708	708	708	708	708	885
Coefficients (95% CI)						
ASA class III	0.906 (0.805-1.006)	0.681 (0.603-0.759)	0.687 (0.575-0.798)	0.781 (0.647-0.915)	0.841 (0.803-0.880)	0.779 (0.687-0.871)
Tumor size, cm	0.399 (0.301-0.496)	0.384 (0.309-0.459)	0.334 (0.250-0.417)	0.424 (0.391-0.458)	0.332 (0.148 to 0.517)	0.375 (0.280-0.469)
Ca 19-9 level (per log10)	0.450 (0.009-0.892)	0.251 (0.169-0.671)	0.409 (0.003-0.814)	0.389 (0.016-0.763)	0.392 (0.148 to 0.636)	0.378 (0.005-0.751)
Constant value	−3.775 (−0.485 to −2.901)	−3.335 (−4.233 to −2.437)	−3.493 (−4.422 to −2.564)	−3.788 (−4.944 to −2.632)	−3.524 (−3.781 to −3.266)	−3.603 (−4.442 to −2.764)
C-statistic (95% CI)	0.706 (0.657-0.754)	0.667 (0.617-0.716)	0.671 (0.621-0.720)	0.690 (0.640-0.740)	0.673 (0.624-0.723)	NA
Hosmer-Lemeshow, *P* value	.32	.33	.26	.28	.26	NA
Out-of-sample cohorts, No.	177	177	177	177	177	885
C-statistic (95% CI)	0.568 (0.465-0.672)	0.739 (0.645-0.834)	0.720 (0.620-0.820)	0.644 (0.546-0.742)	0.706 (0.608-0.803)	0.681 (0.636-0.725)
Hosmer-Lemeshow, *P* value[a]	.04	.70	.83	.17	.60	.39

Abbreviations: ASA, American Society of Anesthesiology; NA, not applicable.

[a] The Hosmer-Lemeshow $P > .05$ indicated that the model fits reasonably well. The model's linear predictor can be calculated as follows: 0.799 if ASA 3 + 0.375 × tumor size in cm + 0.378 × log10 of CA 19-9 level of -3.603. The linear predictors' tertiles were quarter 1, less than −1.961; quarter 2, between −1.961 and - 1.331; and quarter 3, less than −1.331. The probability of futility can be calculated as 1 / (1 + EXP [− linear predictor]).

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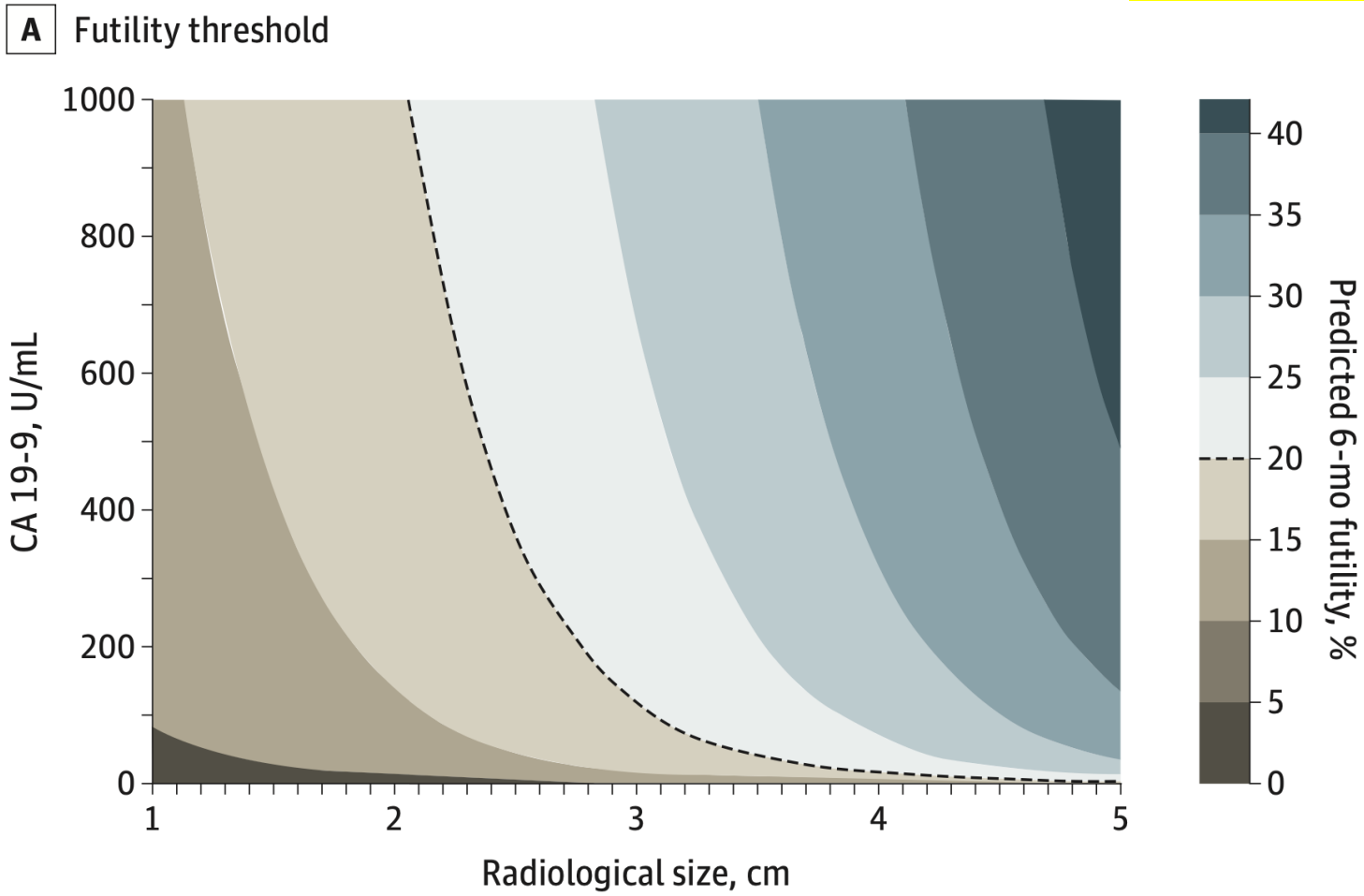
Futility of Up-Front Resection for Anatomically Resectable Pancreatic Cancer

CA 19-9 (U/mL)
Tamanho do tumor (cm)



Crippa S, et al. JAMA Surg 2024

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Futility of Up-Front Resection for Anatomically Resectable Pancreatic Cancer

CA 19-9 (U/mL)
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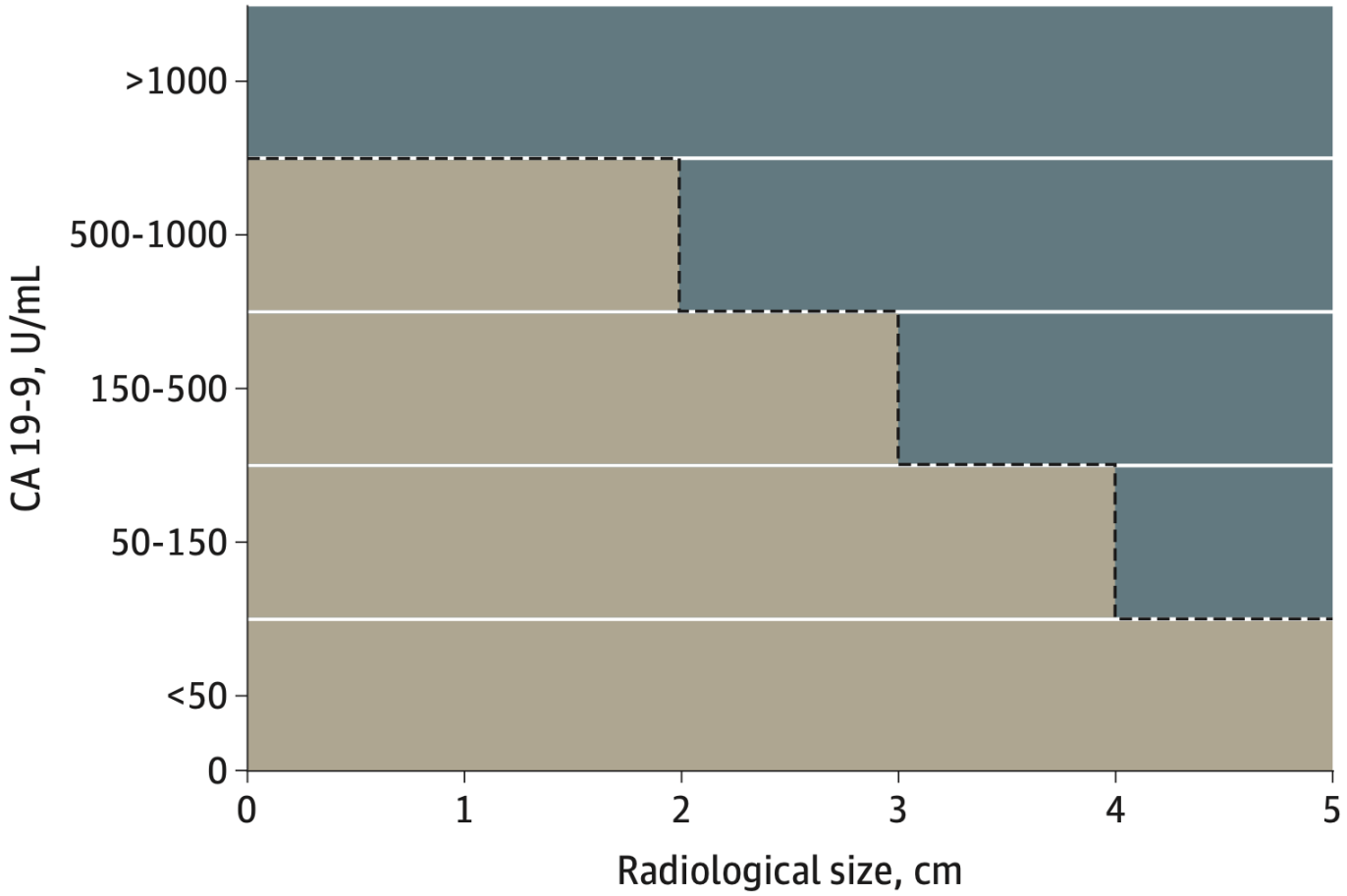

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Safety and Feasibility of Neoadjuvant-Modified FOLFIRINOX in Elderly Patients with Pancreatic Cancer

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Table 3. Adverse events.

	Age ≥ 75 Years (n = 23)		Age < 75 Years (n = 39)		*p*-Value	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Neutropenia	18 (78)	11 (48)	26 (67)	18 (46)	0.3957	>0.9999
Anemia	21 (91)	0 (0)	32 (82)	2 (5)	0.4639	0.5256
Thrombocytopenia	16 (70)	0 (0)	28 (72)	2 (5)	>0.9999	0.5256
Febrile neutropenia	1 (4)	1 (4)	1 (3)	1 (3)	>0.9999	>0.9999
AST increased	5 (22)	0 (0)	21 (54)	2 (5)	0.0173	0.5256
ALT increased	7 (30)	0 (0)	23 (59)	2 (5)	0.0378	0.5256
Creatinine increased	2 (9)	0 (0)	2 (5)	2 (5)	0.6232	0.5256
Fatigue	10 (43)	2 (9)	23 (59)	1 (3)	0.2962	0.5494
Nausea	6 (26)	0 (0)	23 (59)	2 (5)	0.0177	0.5256
Biliary tract infection	0 (0)	0 (0)	4 (10)	4 (10)	0.2871	0.2871
Diarrhea	8 (35)	2 (9)	13 (33)	2 (5)	>0.9999	0.6232
Stomatitis	3 (13)	0 (0)	7 (18)	0 (0)	0.7313	>0.9999
Sensory neuropathy	8 (35)	0 (0)	21 (54)	0 (0)	0.1910	>0.9999
Pneumonitis	0 (0)	0 (0)	1 (3)	1 (3)	>0.9999	>0.9999

AST, Aspartate aminotransferase; ALT, alanine aminotransferase.

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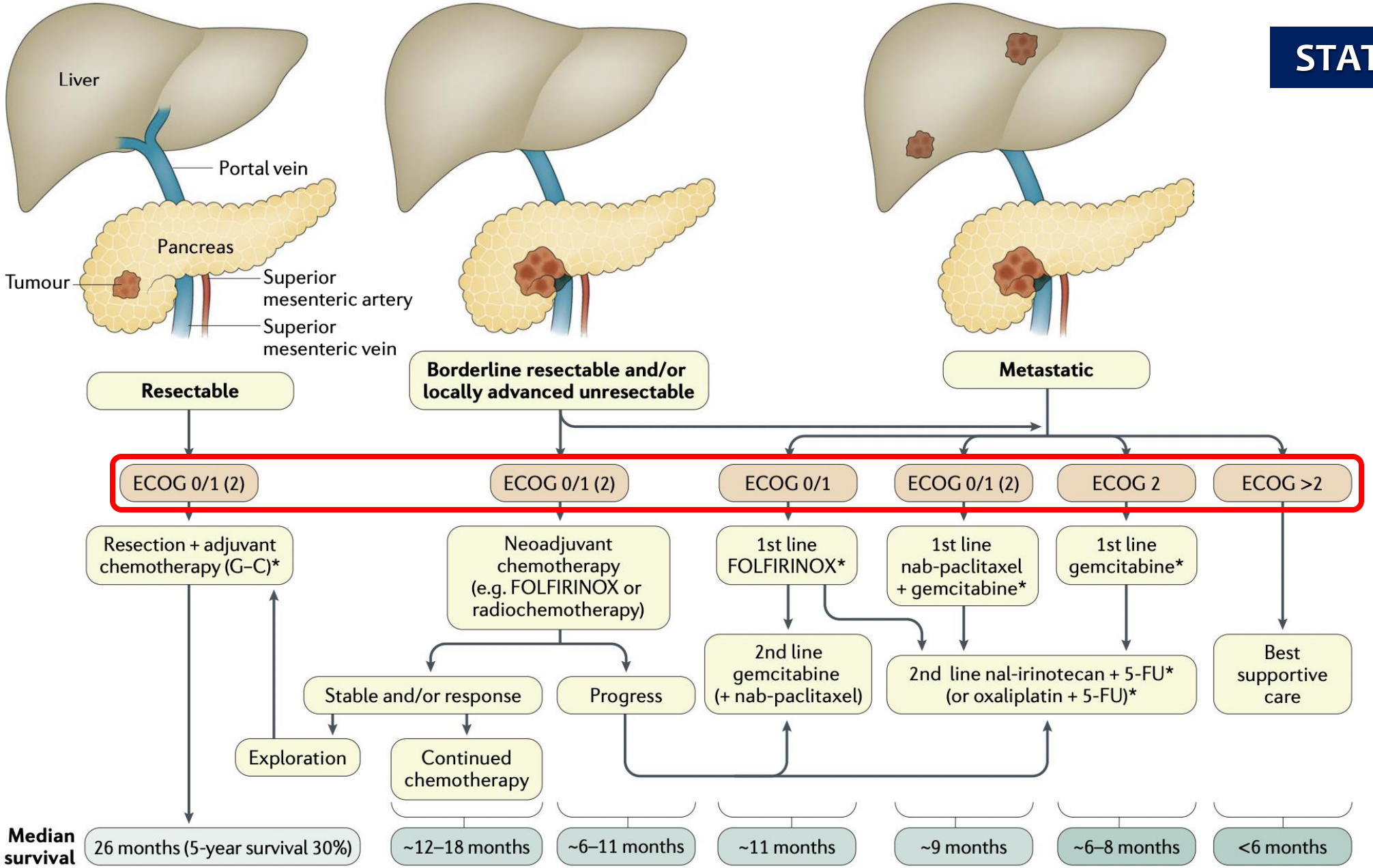
Table 2. Outcomes of neoadjuvant chemotherapy.

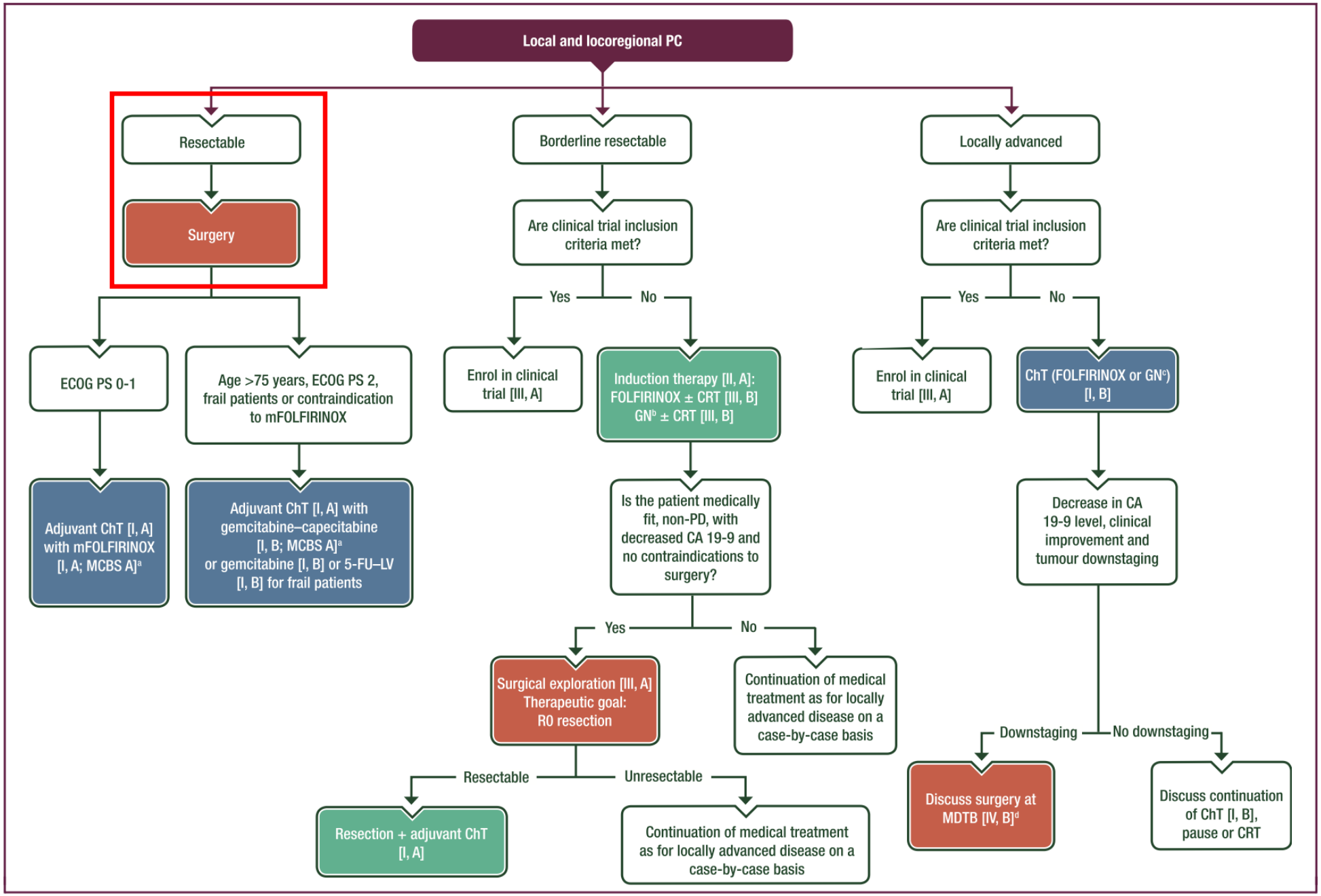
	Age ≥ 75 Years (n = 23)	Age < 75 Years (n = 39)	*p*-Value
Completion of NAC	17 (74)	30 (77)	>0.9999
Dose reduction	21 (91)	28 (72)	0.1063
ARDI	65.3 (44.3–100.0)	77.0 (45.2–100.0)	0.0665
Surgical resection feasible	20 (87)	29 (74)	0.3381
Reason for not undergoing surgical resection			0.7008
Disease progression	2 (9)	7 (18)	
Poor general condition	0 (0)	1 (3)	
Adverse event	0 (0)	1 (3)	
Others	1 (4)	1 (3)	

NAC, Neoadjuvant chemotherapy; ARDI, average relative dose intensity.

STATUS



Neoptolemos JP, et al. Nat Rev Gastroenterol Hepatol 2018



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- ❑ Pacientes ressecáveis (anatomia)
- ❑ CA 19-9 baixo (≤ 500 U/mL)
- ❑ Status ECOG 0-1
- ❑ Idosos ≥ 75a
- ❑ Pacientes borderline venoso

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