Frederik Berrevoet

Diensthoofd

Algemene en Hepatobiliaire Heelkunde

Huidige aanpak en nieuwe technologie bij Pancreascarcinoom

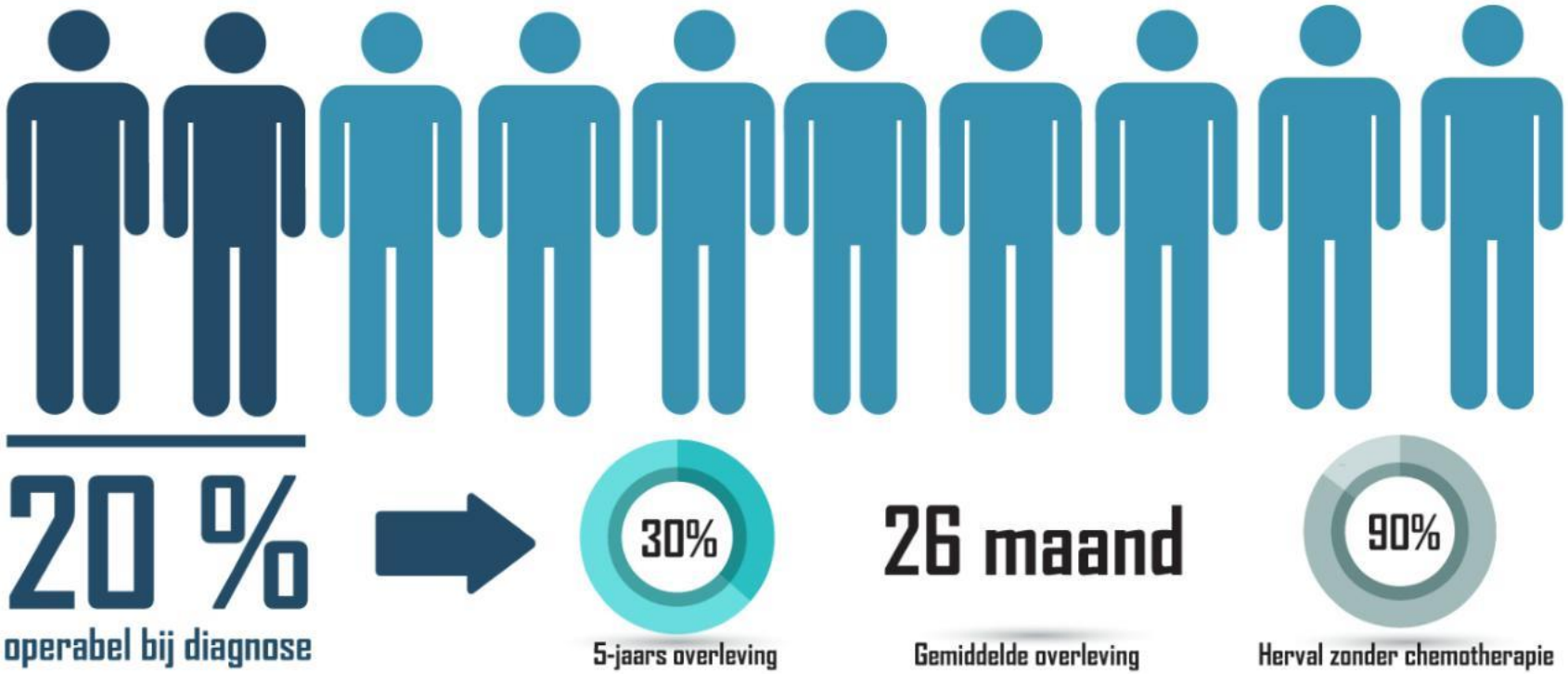
UZ Gent
26/10/2022

UZ GENT

UNIVERSITEIT GENT

- Huidige rol van neo-adjuvante therapie op basis van lokale staging
- Electroporatie als extra behandeling tot verkrijgen van R0
- Is er een plaats voor immunotherapie anno 2022
- Rol van de robot in de pancreaschirurgie

PANCREATIC DUCTAL ADENOCARCINOMA



PANCREATIC DUCTAL ADENOCARCINOMA

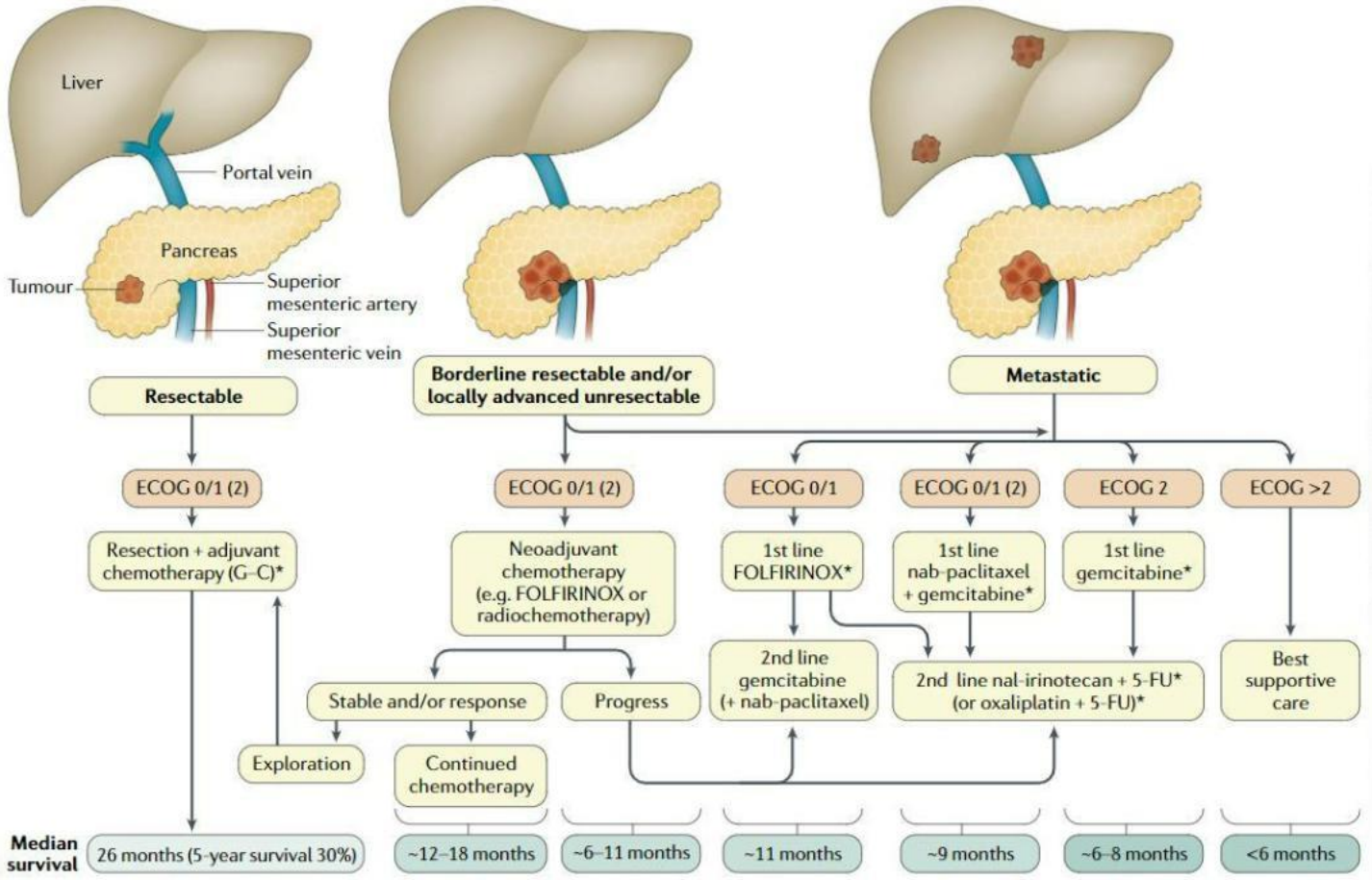
Standard of Care

PANCREATIC DUCTAL ADENOCARCINOMA

Current Survival Standard of Care

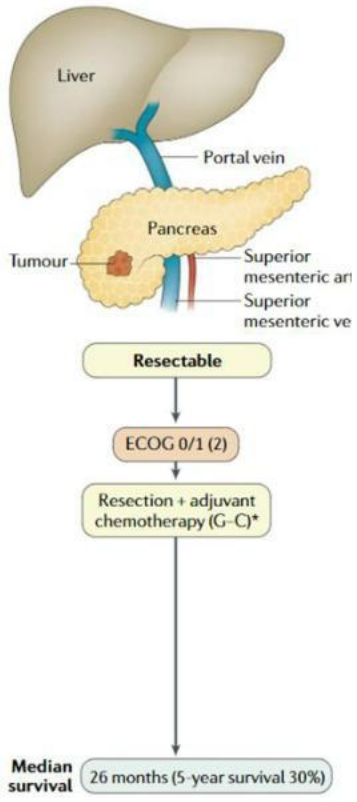
Therapeutic developments in pancreatic cancer: current and future perspectives

John P. Neoptolemos[1]*, Jörg Kleeff[2,3]*, Patrick Michl[4], Eithne Costello[5], William Greenhalf[5] and Daniel H. Palmer[5]



Current Treatment Strategies

Resection is Key



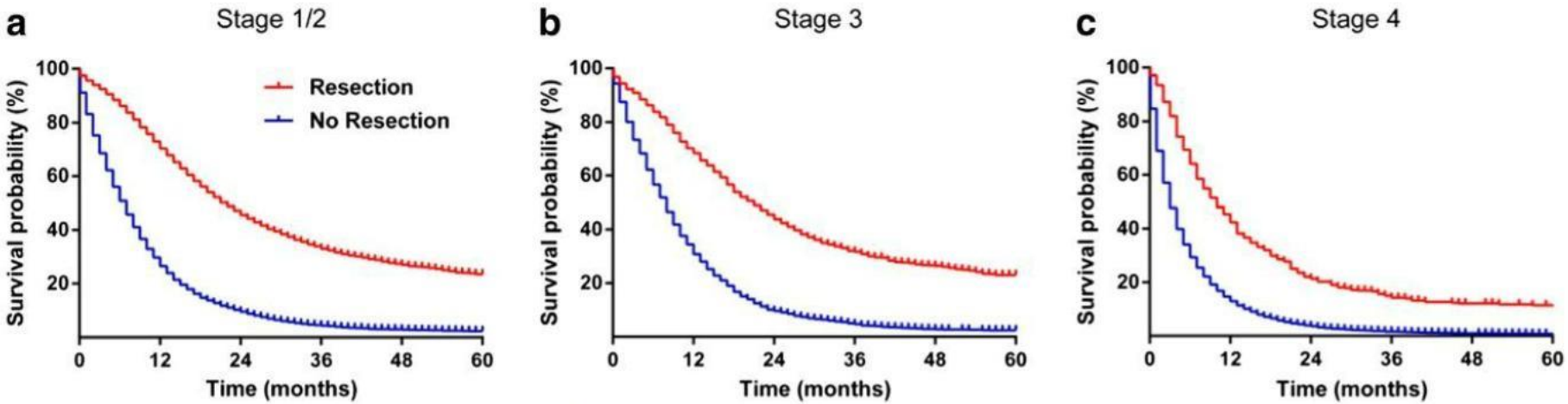


Fig. 1 Overall stage-specific survival. **a** Stage 1/2. **b** Stage 3. **c** Stage 4

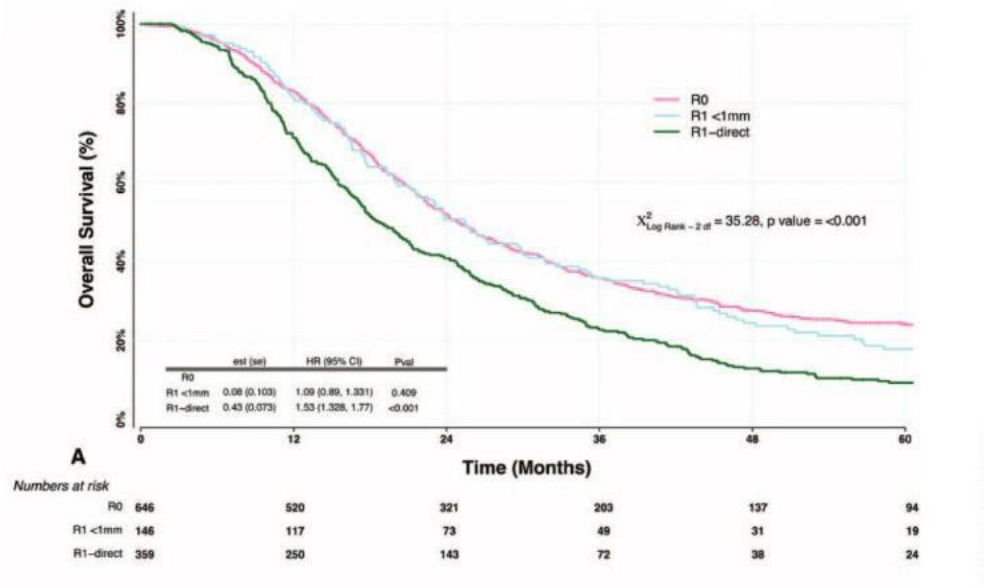
Underutilization of Surgery in Periampullary Cancer Treatment

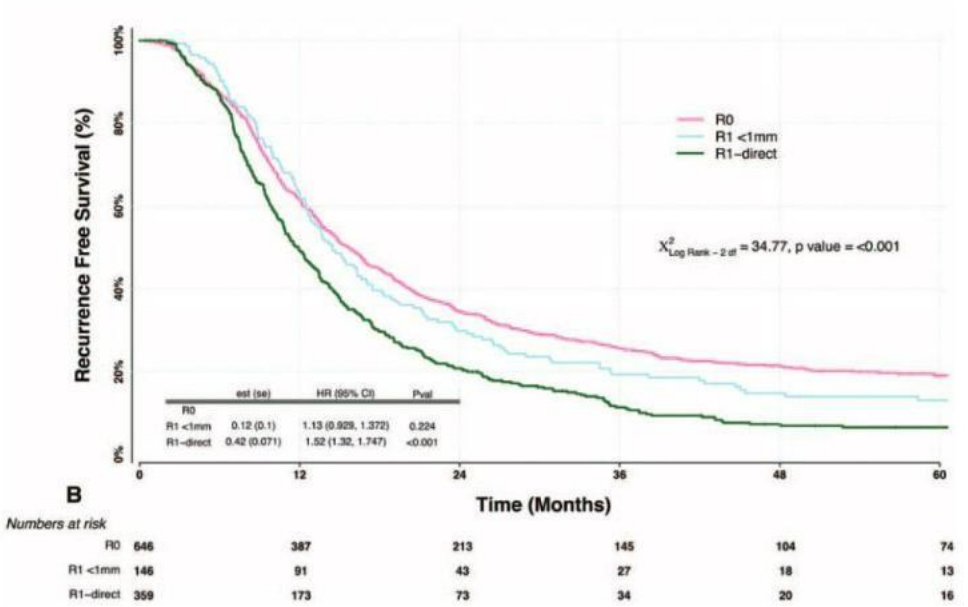
Christoph W. Michalski[1,2] · Bing Liu[1] · Max Heckler[1] · Susanne Roth[1] · Huihui Sun[1] · Ulrike Heger[1] · Markus W. Büchler[1] · Thilo Hackert[1]

Received: 26 February 2018 / Accepted: 23 July 2018

Current Treatment Strategies

R0 resection is the goal



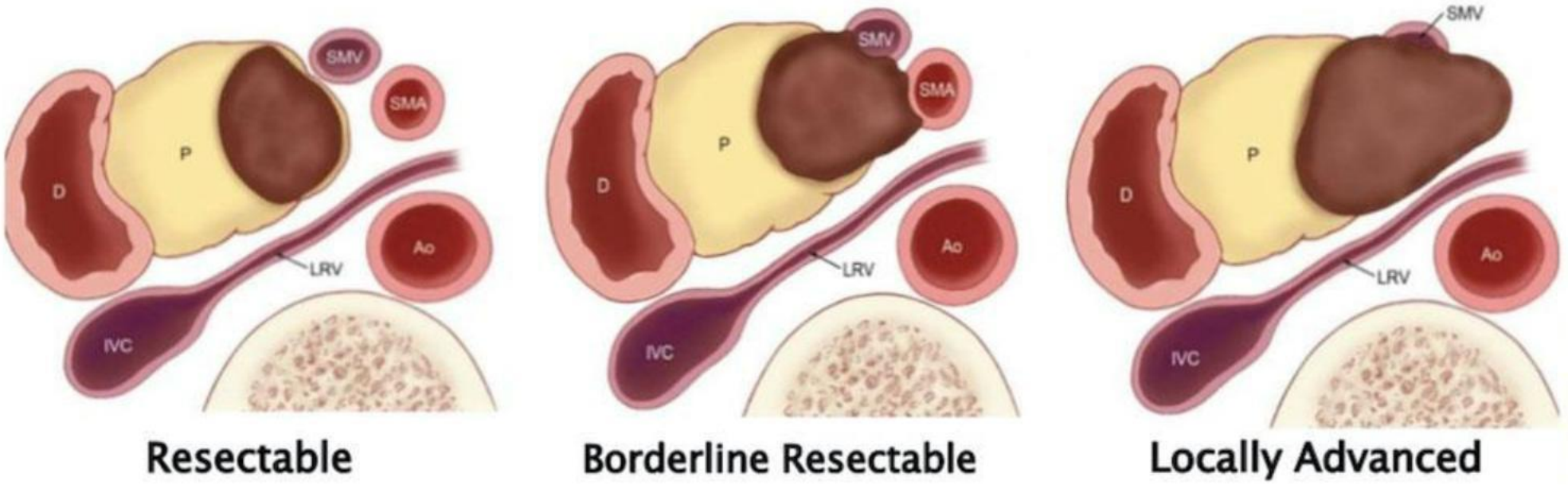


The Impact of Positive Resection Margins on Survival and Recurrence Following Resection and Adjuvant Chemotherapy for Pancreatic Ductal Adenocarcinoma

Paula Ghaneh, MD,† Jorg Kleeff, MD,† Christopher M. Halloran, MD,† Michael Raraty, MD,† Richard Jackson, PhD,* James Melling, MD,† Owain Jones, MD,† Daniel H. Palmer, MD,* Trevor F. Cox, PhD,* Chloe J. Smith, MSc,* Derek A. O'Reilly, MD,‡ Jakob R. Izbicki, MD,§ Andrew G. Scarfe, MD,¶ Juan W. Valle, MD,|| Alexander C. McDonald, MD,** Ross Carter, MD,†† Niall C. Tebbutt, PhD,‡‡ David Goldstein, MB,§§ Robert Padbury, MB,¶¶ Jennifer Shannon, PhD, FRACP,|||| Christos Dervenis, MD,*** Bengt Glimelius, MD,††† Mark Deakin, MD,‡‡‡ Alan Anthoney, MD,§§§ Markus M. Lerch, MD,¶¶¶ Julia Mayerle, MD,¶¶¶ Attila Oláh, MD,|||||| Charlotte L. Rawcliffe, MSc,* Fiona Campbell, MD,**** Oliver Strobel, MD,†††† Markus W. Büchler, MD,†††† and John P. Neoptolemos, MD*†, for the European Study Group for Pancreatic Cancer*

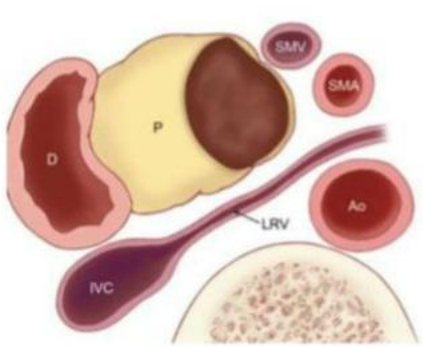
STANDARD OF CARE

Resectability Criteria

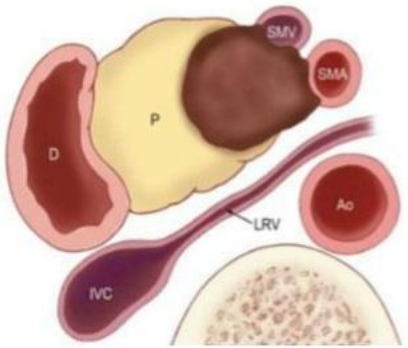


STANDARD OF CARE

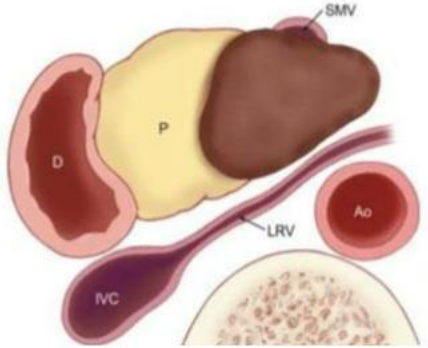
Resectability Criteria

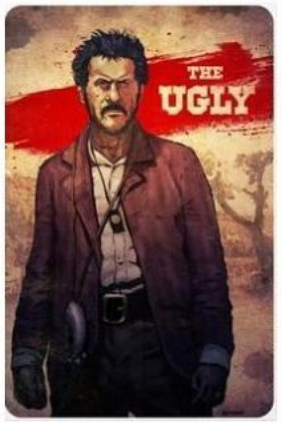


Primair operabel



Borderline



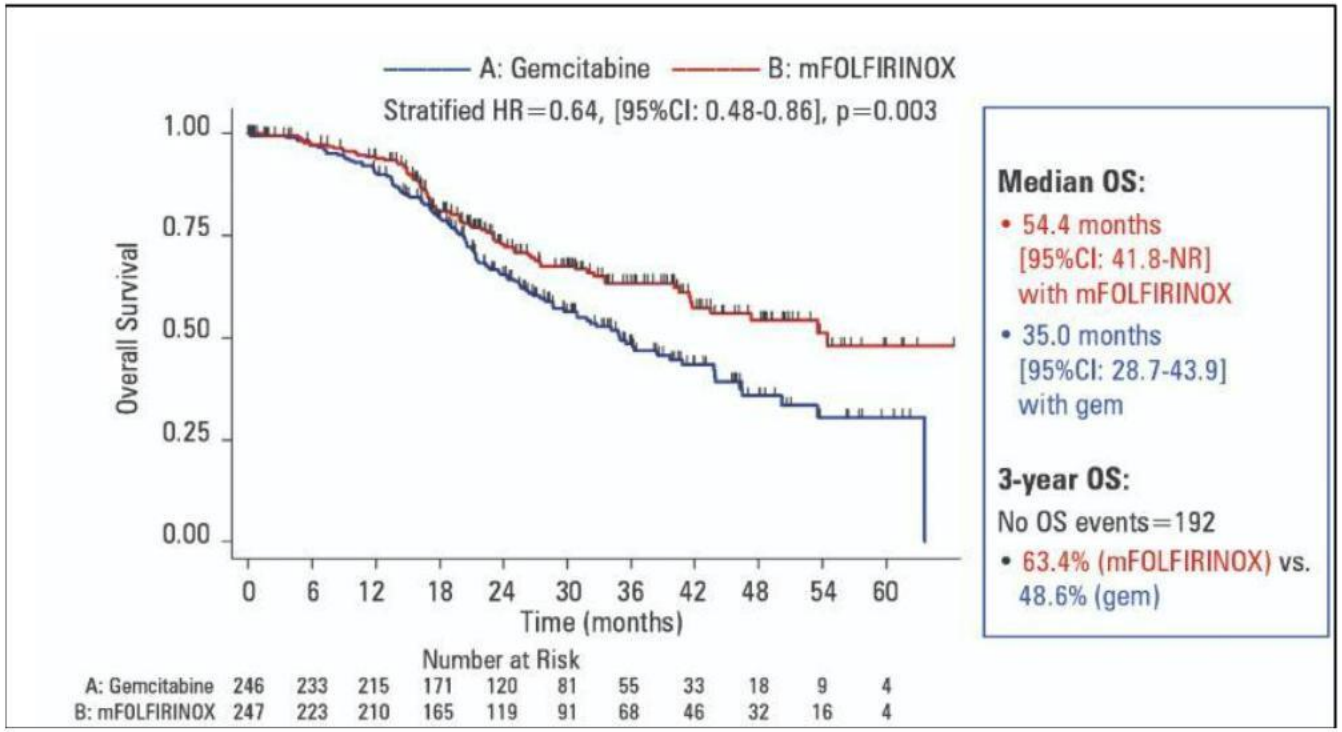


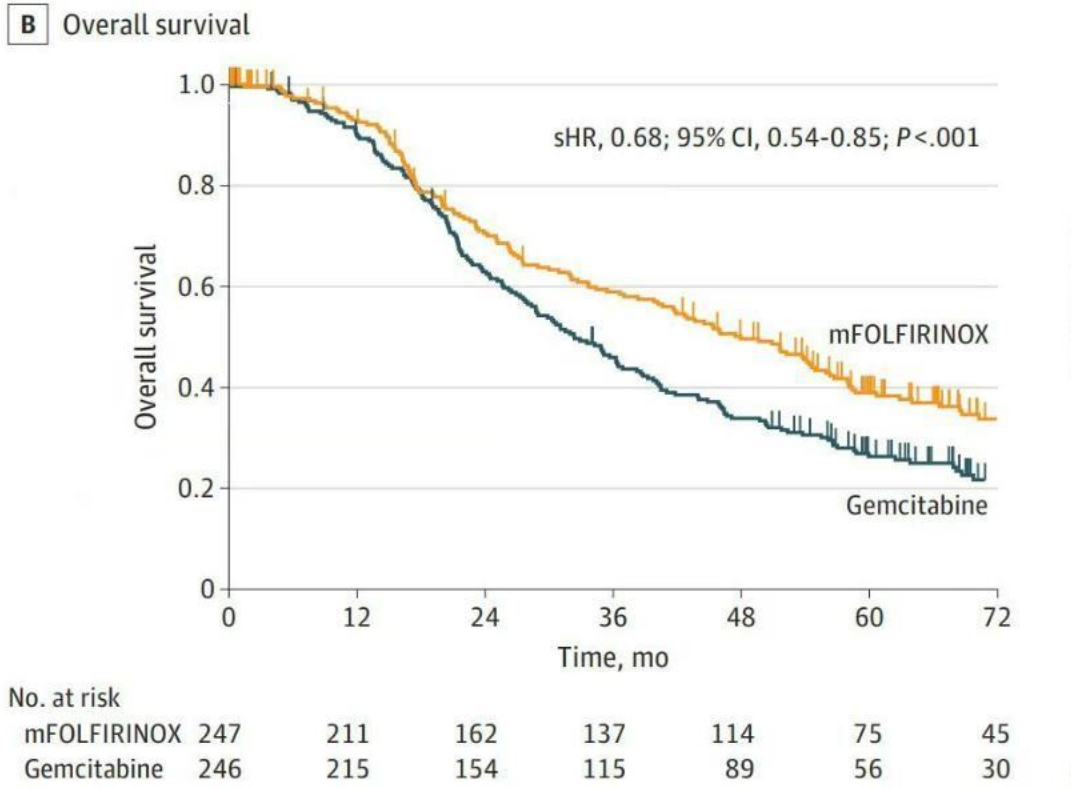
Locally advanced

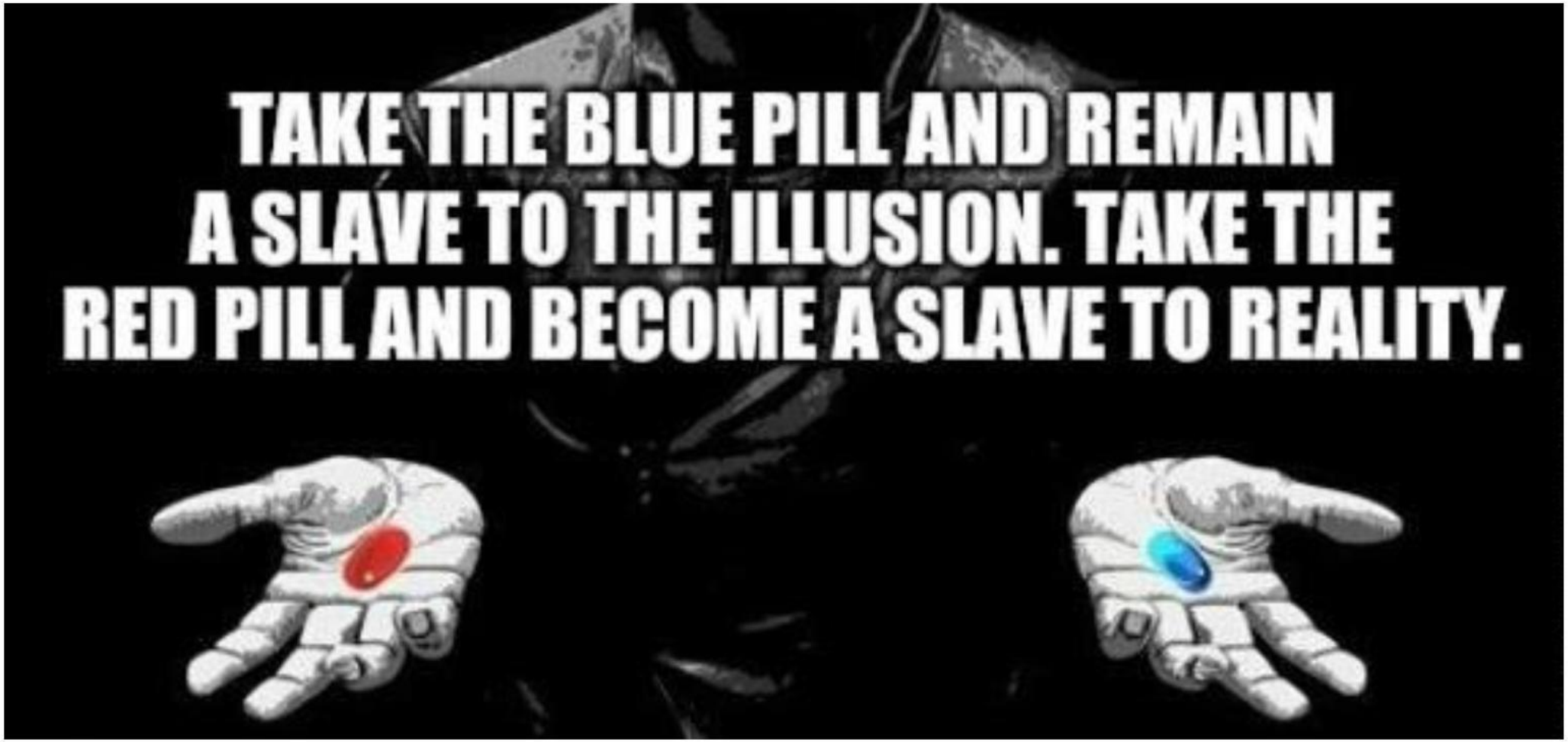
R1-resectie

STANDARD OF CARE

Systemic therapy







PANCREATIC DUCTAL ADENOCARCINOMA

Real World data

REAL WORLD DATA

Selection Bias

VS

REAL WORLD DATA

Selection Bias

VS

REAL WORLD DATA

Selection Bias

Clinical Adjuvant trials

- No metastatic disease at the time of planned pancreatectomy
- Survive surgery
- Recover in a timely fashion and are agreeable to further treatment
- No evidence of early disease progression on postsurgical re-staging evaluation
- Pass the assessment of the medical oncologist – (quid Folfirinox)

REAL WORLD DATA

Selection Bias

Real World Data

Adjuvant therapy

- Global: 40-60%
- ≥ 1 serious complication: 43%
- 28% incomplete therapy
- 7% complete therapy

Number of cycles (%)[a]	Overall (n = 778)	GEMCAP (n = 164)	GEM (n = 614)
>6	17 (2.2)	3 (1.8)	14 (2.3)
6	482 (62.0)	111 (67.7)	371 (60.4)
5	67 (8.6)	14 (8.5)	53 (8.6)
4	45 (5.8)	6 (3.7)	39 (6.4)
3	63 (8.1)	12 (7.3)	51 (8.3)
2	42 (5.4)	6 (3.7)	36 (5.9)
1	50 (6.4)	6 (3.7)	44 (7.2)
Unknown	12 (1.5)	6 (3.7)	6 (1.0)

TABLE 3 Number of completed chemotherapy cycles in patients treated with gemcitabine with capecitabine (GEMCAP) or gemcitabine (GEM)

CANCER THERAPY AND PREVENTION

Real-world evidence of adjuvant gemcitabine plus capecitabine vs gemcitabine monotherapy for pancreatic ductal adenocarcinoma

Table 3. Number of Patients Receiving Therapy in Resected or Resectable Pancreatic Adenocarcinoma Randomized Clinical Trials (RCTs)

	Experimental group							Control group						
	No.				% Adjuvant CTX[a]		CTX relative dose intensity, median, %	No.				% Adjuvant CTX[a]		CTX relative dose intensity, median, %
RCT	Randomized	CTX Began	CTX Completed	Resected	Began	Completed		Randomized	CTX Began	CTX Completed	Resected	Began	Completed	
Adjuvant RCTs in resected pancreatic cancer														
APACT,[20] 2019	432	NA	NA	432	99	66	NR	434	NA	NA	434	97	71	NR
PRODIGE 24,[18] 2018	247	NA	NA	247	93	64	≥70 in 49	243	NA	NA	243	99	79	≥70 in 91
ESPAC-4,[17] 2017	365	NA	NA	365	96	53	78/83	367	NA	NA	367	98	65	93
RTOG 0848,[16] 2020	159	NA	NA	159	99	NR	≥85 in 60	163	NA	NA	163	98	NR	≥85 in 69
CONKO-005,[15] 2017	219	NA	NA	219	96	66	NR	217	NA	NA	217	99	74	NR
JASPAC 01,[14] 2016	192	NA	NA	192	97	65	98	193	NA	NA	193	98	62	84
ESPAC-3,[13] 2010	551	NA	NA	551	88	56	79	537	NA	NA	537	89	60	89
JSAP-02,[12] 2009	58	NA	NA	58	98	76	89	60	NA	NA	60	NA	NA	NA
CONKO-001,[11] 2013	179	NA	NA	79	94	62	86	182	NA	NA	175	NA	NA	NA
Neoadjuvant and perioperative RCTs in resectable pancreatic cancer														
SWOG S1505,[21,25] 2020	55	53	46	40	83	68	NR	47	45	40	33	85	58	NR
JSAP-05[22] 2019	182	172	NR	157[b]	NR	NR	NR	180	NR	NR	157[a]	NR	NR	NR
PREOPANC,[c,19] 2020	120	91	81	72	76	47	NR	128	NA	NA	92	71	38	NR

Abbreviations: CTX, systemic chemotherapy; NA, not applicable; NR, not reported.

[a] Percentages of patients starting and completing adjuvant CTX refer to the number of patients with resection (denominator: No. resected).

[b] In each group, 157 patients underwent a pancreatectomy, but only 140 (experimental group) and 129 (control group) had a resection with curative intent.

[c] The PREOPANC trial[19] included patients with upfront resectable (54%) and borderline resectable (46%) pancreatic cancer.

Postoperative Complications Reduce Adjuvant Chemotherapy Use in Resectable Pancreatic Cancer

Ryan P. Merkow, MD, MS,*† Karl Y. Bilimoria, MD, MS,*† James S. Tomlinson, MD, PhD,‖ Jennifer L. Paruch, MD,*† Jason B. Fleming, MD,¶ Mark S. Talamonti, MD,‡‖ Clifford Y. Ko, MD, MS, MSHS,*‖ and David J. Bentrem, MD, MS†**

Completion of Adjuvant Chemotherapy After Upfront Surgical Resection for Pancreatic Cancer Is Uncommon Yet Associated With Improved Survival

Ariella M. Altman, MD[1], Keith Wirth, MD[1], Scholoma Marmor, MPH, PhD[2], Emil Lou, MD, PhD[2], Katherine Chang, MD[2], Jane Y. C. Hui, MD, MS[1], Todd M. Tuttle, MD, MS[1], Eric B. Jensen, MD[1], and Jason W. Denbo, MD[1,2]

REAL WORLD DATA

Selection Bias

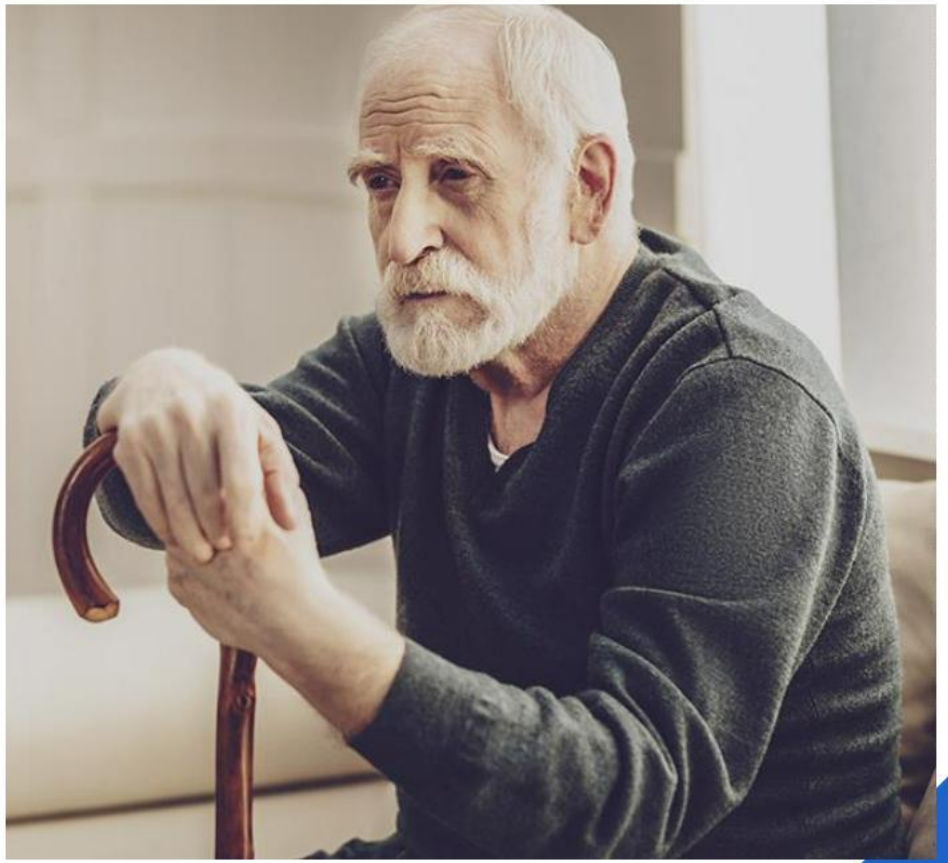
Real World Data

Adjuvant therapy

- Global: 40-60%
- ≥ 1 serious complication: 43%
- 28% incomplete therapy
- 7% complete therapy

Risk of not receiving adjuvant therapy

- Older age
- Higher ECOG
- Postoperative complications (CR-POPF, PPH)
- Poor tumor differentiation grade
- Annual center volume < 40 PD's



ORIGINAL ARTICLE

The risk of not receiving adjuvant chemotherapy after resection of pancreatic ductal adenocarcinoma: a nationwide analysis

SYSTEMIC TREATMENT

Efficacy

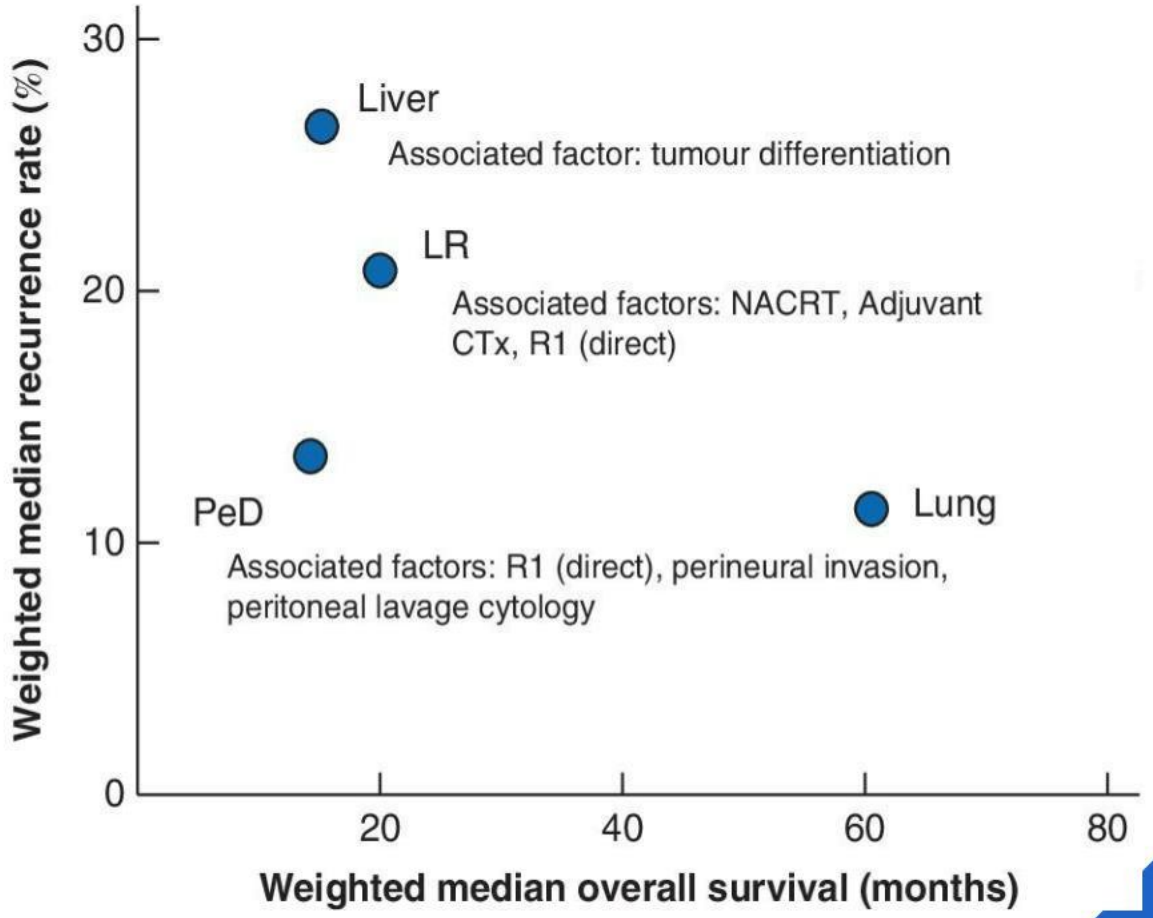
Recurrence after resection: 76.7%

Median RFS: 11.7 months

PANCREATIC CANCER

=

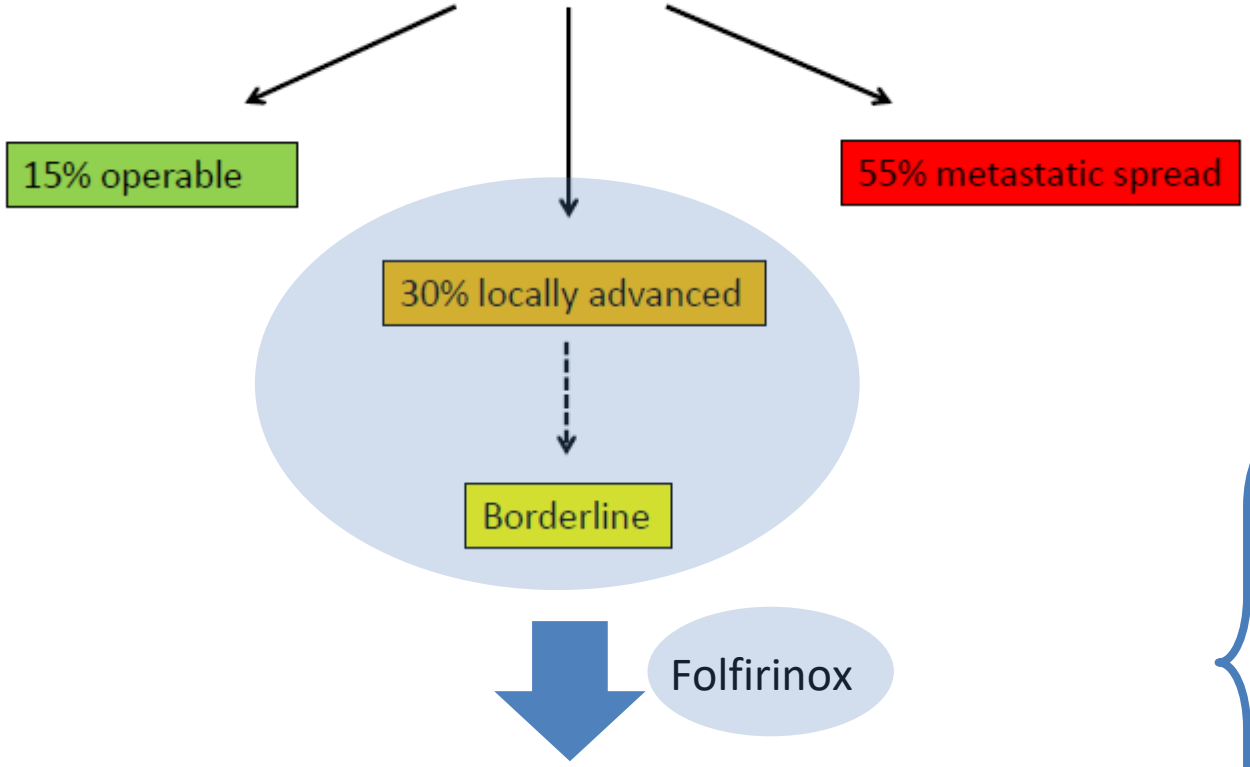
SYSTEMIC DISEASE



NEOADJUVANT TREATMENT

Setting the scene

Pancreatic cancer



+- 40% resectability

When R0 resection → prognosis = initially resectable disease

Response?

CT, MRI: no progression

CA 19.9: no increase

TREATMENT SEQUENCE RESECTABLE PANCREATIC CANCER

Upfront Surgery Versus Neoadjuvant treatment

UPFRONT SURGERY

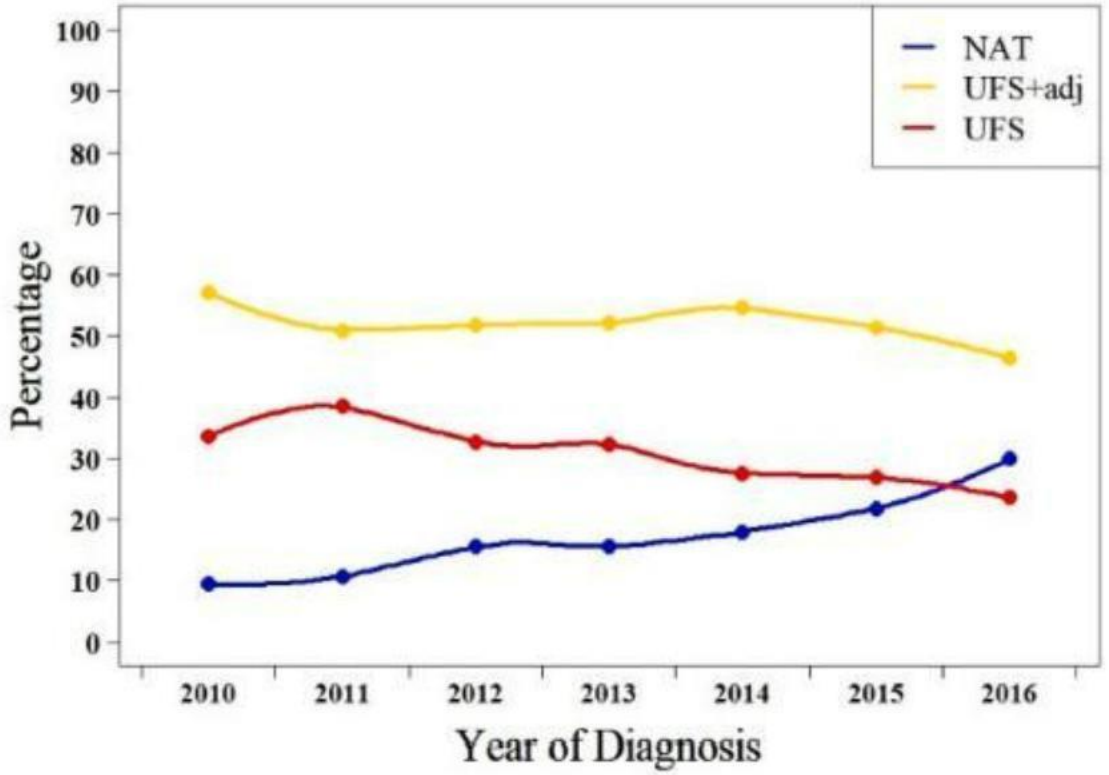
- Biliary stenting ommited
- No risk preoperative clinical detoriation
- Risk of progression to unresectable tumor

- Delay/ommission chemotherapy
- R0 – resection
- Sugery in “metastatic” setting

NEO ADJUVANT TREATMENT

- Rapid delivery systemic therapy
- More chance of R0
- Prevent futile surgery (rapidly progressive)

- Lower resection rates (+- 66%)
- EUS/ERCP needed
- SAE systemic treament



PANCREATIC DUCTAL ADENOCARCINOMA

Neoadjuvant Treatment

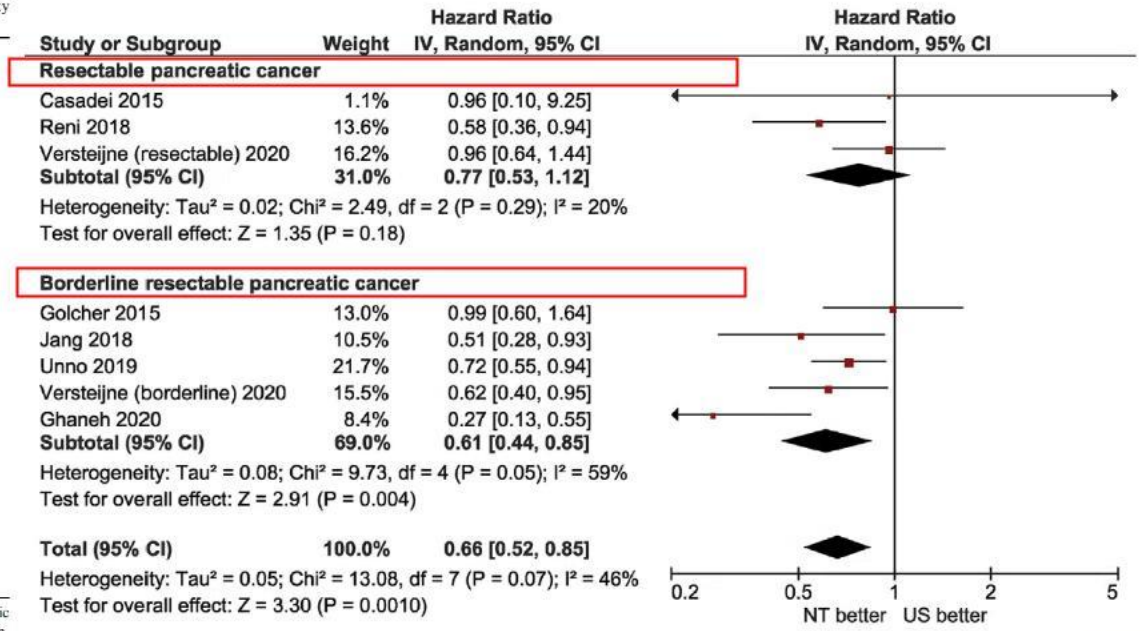
NEOADJUVANT TREATMENT

Level 1 Evidence

Table 1
Study characteristics.

Reference	Year of publication	Country	Accrual years	Number of patient	Intervention (cycles)	Comparator (cycles)	Criteria arterial	Criteria venous	Resectability status[a]
Golcher [21]	2015	Germany, Switzerland	2003–09	66	Neoadj. gemcitabine/cisplatin based CRT (55.8 Gy) + adj. gemcitabine (6)	Adj. gemcitabine (6)	HA/SMA/ CA ≤ 180°	SMV/PV ≤ 180°	R/BR
Casadei [22]	2015	Italy	2007–13	38	Neoadj. gemcitabine-based CRT (54 Gy) + adj. gemcitabine (6)	Adj. gemcitabine (6)	No contact with HA/ CA/SMA	SMV/PV ≤ 180°	R
Reni [23]	2018	Italy	2010–15	88	C: Periop. gemcitabine/cisplatin/ epirubicin/capecitabine (3 + 3)	A: Adj. gemcitabine (6) B: Adj. gemcitabine/ cisplatin/epirubicin/ capecitabine (6)	Absence of invasion in HA/CA/SMA	Absence of invasion in SMV/PV	R
Jang [24]	2018	South Korea	2012–14	50	Neoadj. gemcitabine-based CRT (54 Gy) + adj. gemcitabine (4)	Adj. gemcitabine-based CRT (54 Gy) + adj. gemcitabine (4)	2012 NCCN: HA encasement allowed, tumour abutment with SMA ≤180°	2012 NCCN: Venous reconstructible (SMV/PV encasement allowed)	BR
Unno [14]	2019	Japan	2013–16	362	Neoadj. gemcitabine/S-1 (2) + adj. S-1 (6 mo)	Adj. S-1 (6 mo)	No arterial abutment of HA/CA/SMA	Venous reconstructible (SMV/PV encasement allowed)	R/BR
Versteijne [15]	2020	The Netherlands	2013–17	246	Neoadj. gemcitabine-based CRT (36 Gy) (3) + adj. gemcitabine (4)	Adj. gemcitabine (6)	R: No arterial contact BR: Arterial contact ≤90°	R: Venous ≤90° BR: Venous >90° −270° without occlusion	R/BR
Ghaneh [16]	2020	United Kingdom, Germany	2014–18	88	B: Neoadj. gemcitabine/ capecitabine (2) C: Neoadj. mFOLFIRINOX (4) D: Neoadj. capecitabine-based CRT (50.4 Gy) All arms received adj. gemcitabine or adj. 5-FU/FA (6)	A: Adj. 5-FU/FA or adj. gemcitabine (6)	2013 NCCN: HA encasement allowed, tumour abutment with SMA ≤180°	2013 NCCN: Venous reconstructible (SMV/PV encasement allowed)	BR

5-FU/FA, fluorouracil with folinic acid; Adj, adjuvant; BR, borderline ectable; CA, coeliac axis; CRT, chemoradiotherapy; HA, he ic artery; mFOLFIRINOX, modified fluorouracil with folinic acid, irinotecan, oxaliplatin; NCCN, National Comprehensive Cancer N work; Neoadj, neoadjuvant; PV, portal vein; R, resectable; S A, superior mesenteric artery; SMV, superior mesenteric vein.
[a] Resectability status according to NCCN definitions.



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

Jacob L. van Dam [a,*], Quisette P. Janssen [a], Marc G. Besselink [b], Marjolein Y.V. Homs [c], Hjalmar C. van Santvoort [d], Geertjan van Tienhoven [e], Roeland F. de Wilde [f], Johanna W. Wilmink [g], Casper H.J. van Eijck [a], Bas Groot Koerkamp [a] for the Dutch Pancreatic Cancer Group

NEOADJUVANT TREATMENT

Future Evidence

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.

NEOADJUVANT TREATMENT

State of the Art?

Available Literature:

- Not upfront comparable with adjuvant trials (Standard of Care)
  - “Darwinian selection”
  - Low accrural rates (Prodige, conko, espac: enrolled 0,6-1,5 patients per center per year)

- Neoadjuvant trials plagued with
  - Subjective classifications (resectable/borderline)
  - Problems of adequate pretreatment staging (mainly AMS)
  - < 50% completed all intended chemotherapy
  - Use of “lesser” chemotherapy regimens
  - No optimalisation of neoadjuvant treatment/delivery/support

PANCREAS CANCER TREATMENT

Food for thoughts

- *The obvious concern is that as systemic therapies become even more effective, they will never reach the patient if a surgery-first approach is taken*
- *Risking the ability to deliver systemic therapy to patients with resectable pancreatic cancer, by embarking on a surgery first approach, may negatively impact the survival of those patients most likely to benefit from multimodality therapy*.
- *Surgery first is an easier paradigm to complete for the medical team as no one is responsible for those patients who drop out along the way.*

PANCREAS CANCER TREATMENT

Food for thoughts

- *Downstaging on coaxial imaging is not related to resectability and local control does not equate to greater survival. This approach has thus so far never been shown to significantly improve OS in a randomized, prospective trial.*

NEOADJUVANT TREATMENT

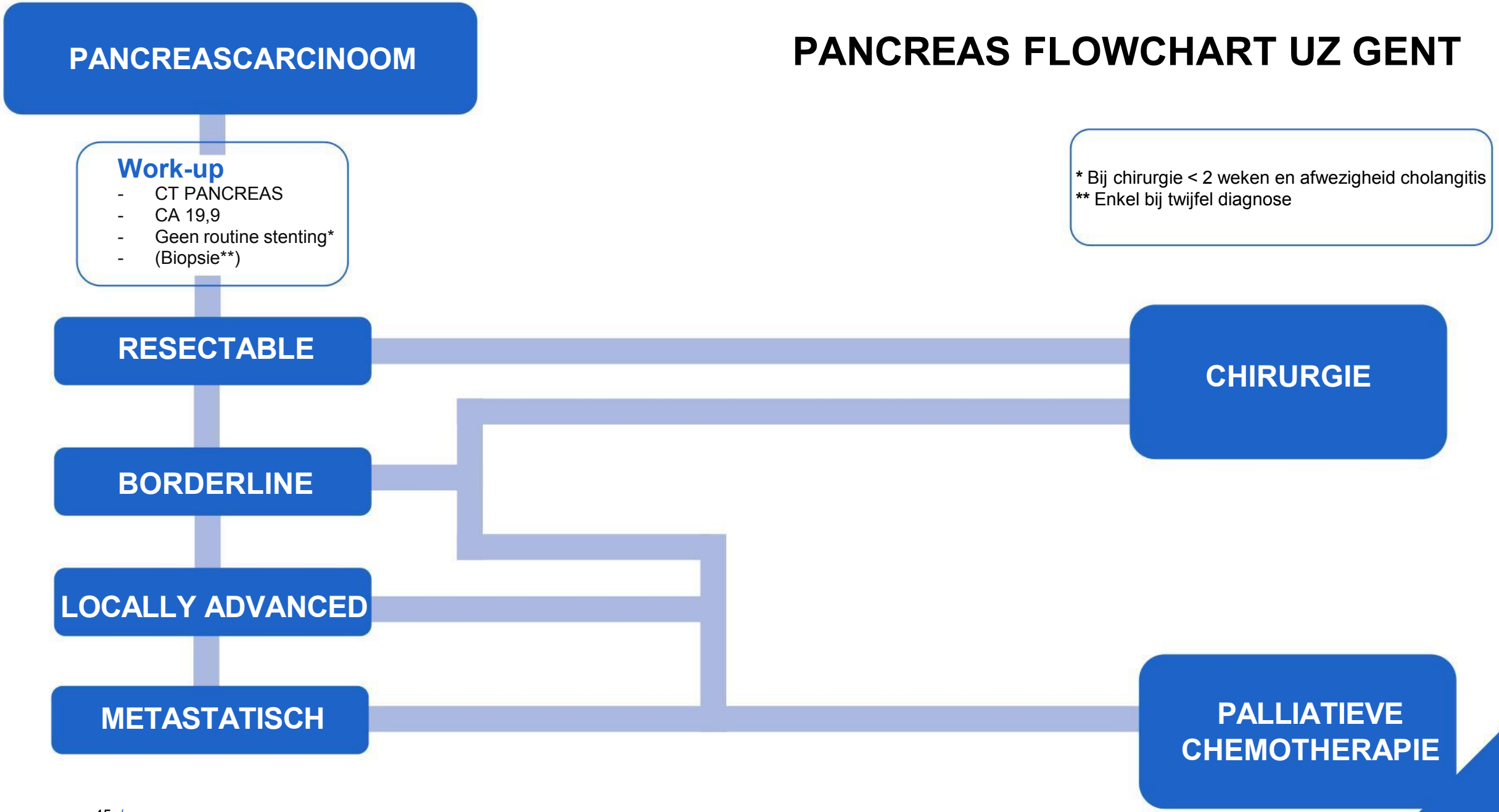
State of the Art?

Resectable PDAC

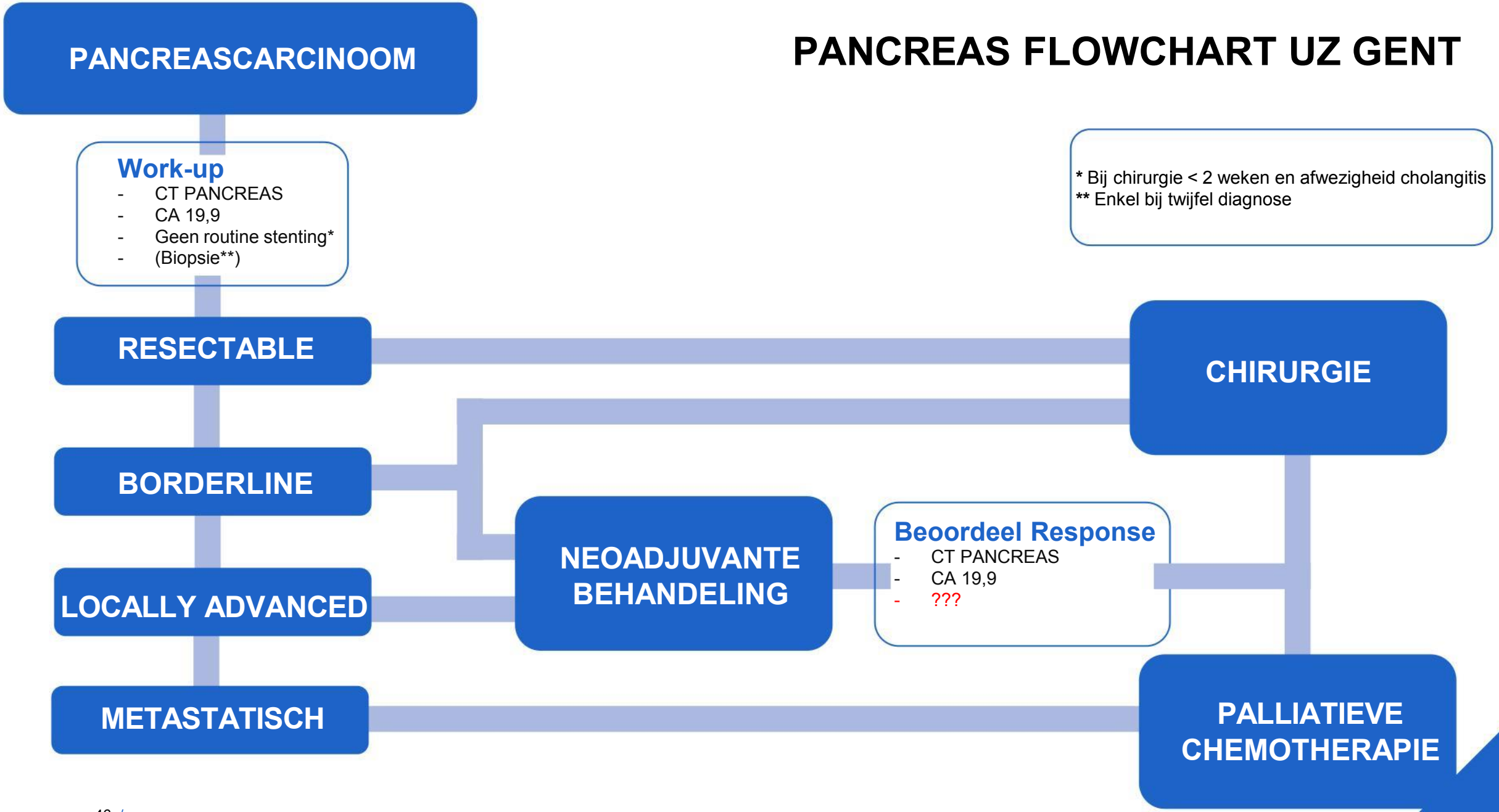
=

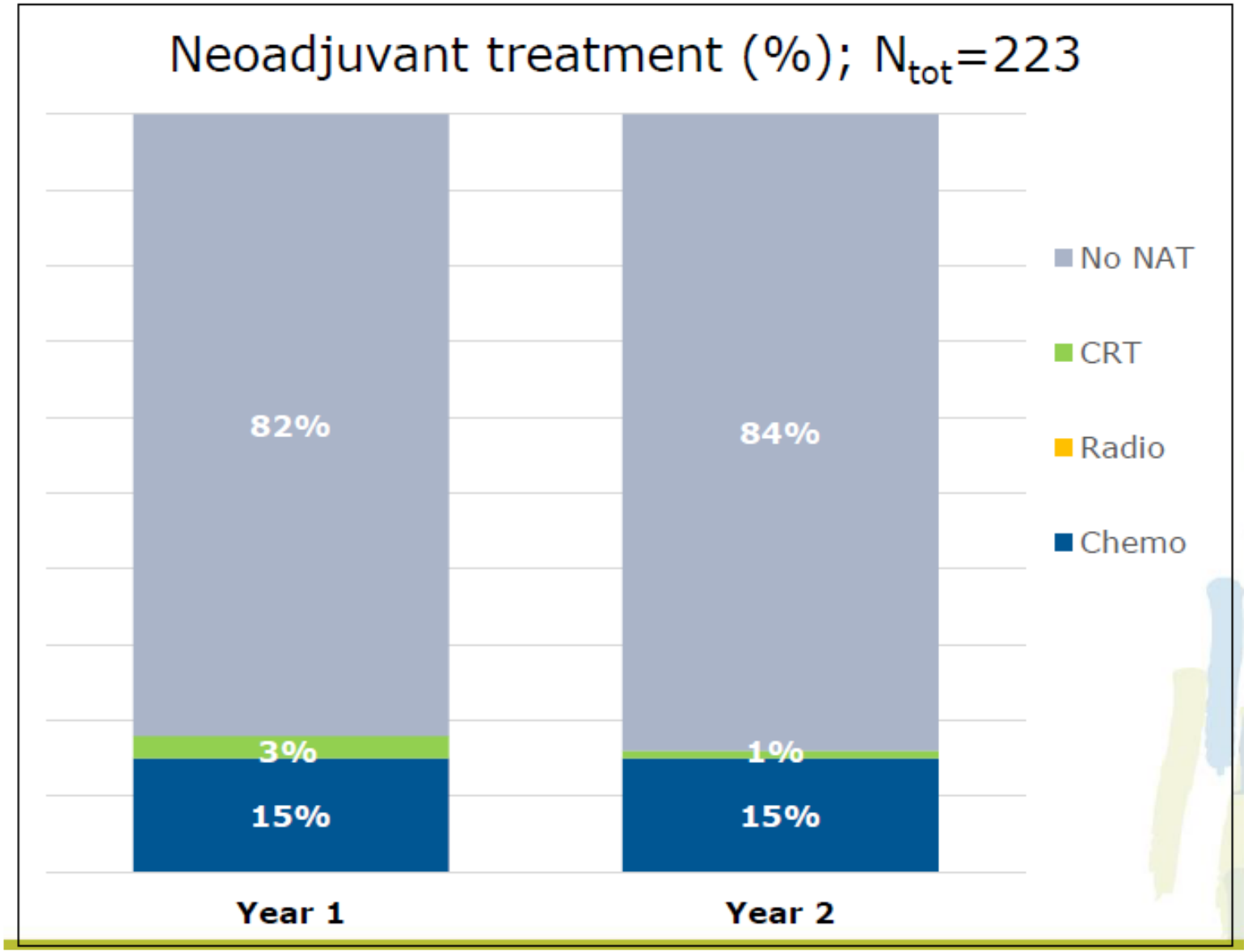
Spectrum of Disease with Heterogeneous Biological Behaviour

PANCREAS FLOWCHART UZ GENT



PANCREAS FLOWCHART UZ GENT




Neoadjuvant treatment (%); N$_{tot}$=223
82%
3%
15%
84%
1%
15%
No NAT
CRT
Radio
Chemo
Year 1
Year 2

Neo-adjuvante therapie

Neoadjuvant treatment

	Your hospital				Belgium			
	Year 1		Year 2		Year 1		Year 2	
Characteristic	N	%	N	%	N	%	N	%
Chemotherapy	9	15.3	15	17.6	88	14.9	107	14.7
Radiotherapy	0	0.0	0	0.0	0	0.0	1	0.1
Chemoradiotherapy	0	0.0	0	0.0	16	2.7	11	1.5
No chemo or radiation treatment	50	84.7	70	82.4	485	82.3	611	83.7

Current Treatment Strategies

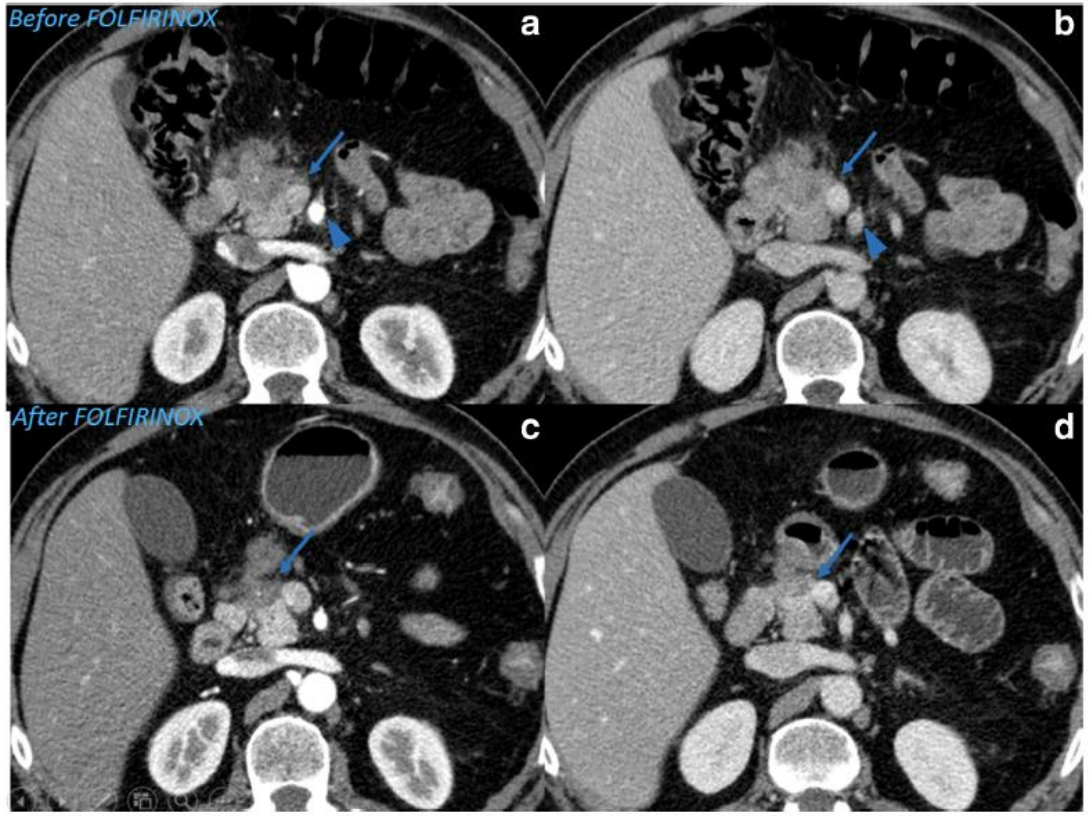
PeRFormanCe

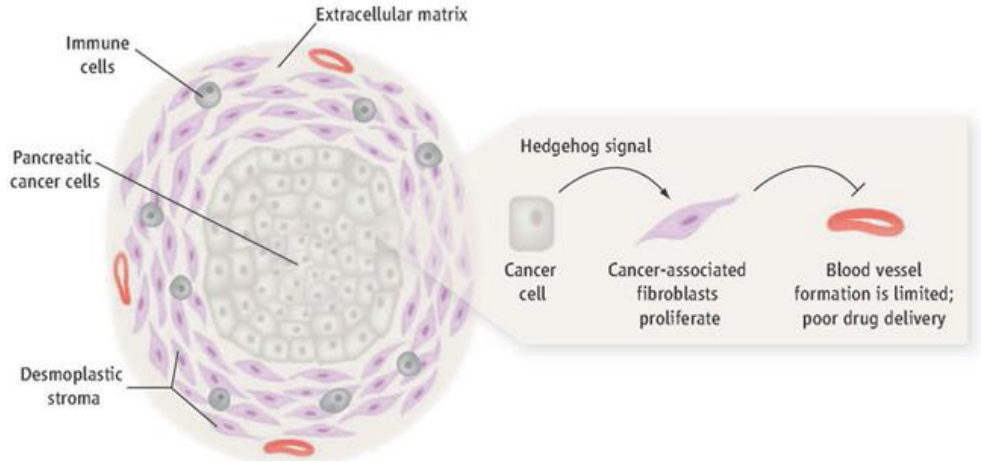
Prediction of surgical Resectability after Folfirinox treatment for borderline resectable and locally advanced pancreatic Cancer:

the role of diffusion weighted magnetic resonance imaging, radiomics and liquid biopsy

Surgery after FOLFIRINOX treatment for locally advanced and borderline resectable pancreatic cancer: increase in tumour attenuation on CT correlates with R0 resection

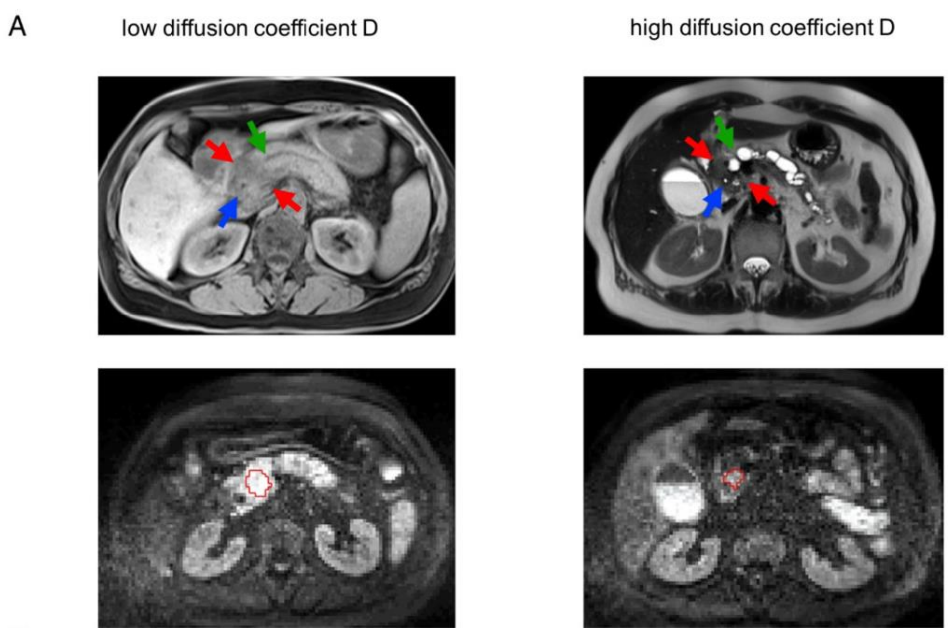
Giovanni Marchegiani[1] · Valentina Todaro[1] · Enrico Boninsegna[2] · Riccardo Negrelli[2] · Binit Sureka[3] · Debora Bonamini[1] · Roberto Salvia[1] · Riccardo Manfredi[4] · Roberto Pozzi Mucelli[2] · Claudio Bassi[1]

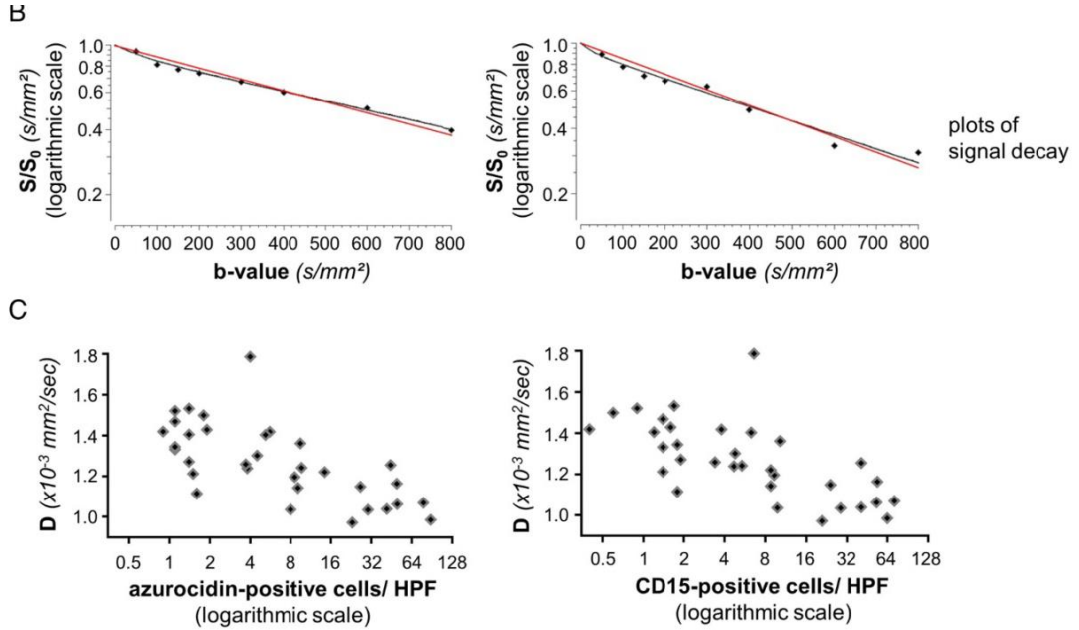




Changes in the microarchitecture of the pancreatic cancer stroma are linked to neutrophil-dependent reprogramming of stellate cells and reflected by diffusion-weighted magnetic resonance imaging

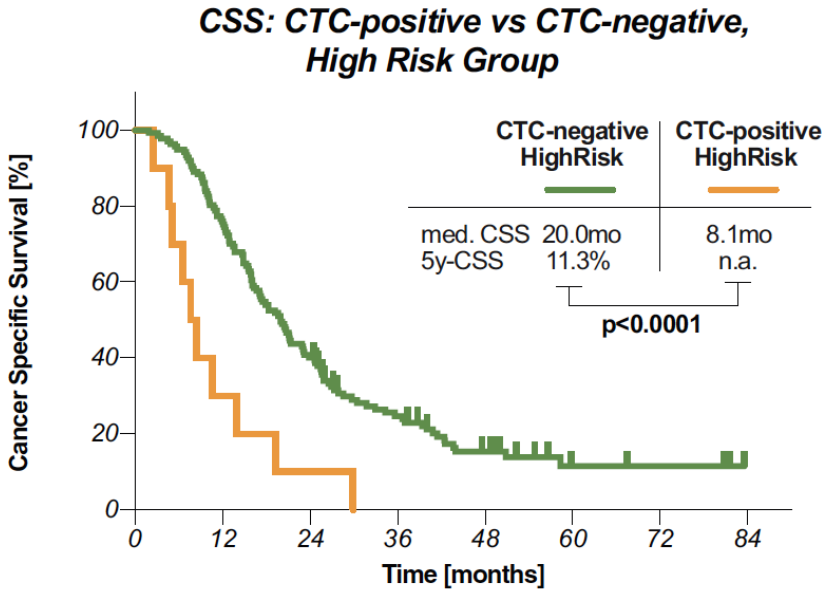
Philipp Mayer[1], Christine Dinkic[2], Ralf Jesenofsky[3], Miriam Klauss[1], Peter Schirmacher[4], Ulrike Dapunt[5], Thilo Hackert[6], Florian Uhle[7], G. Maria Hänsch[8], Matthias M. Gaida[4]✉





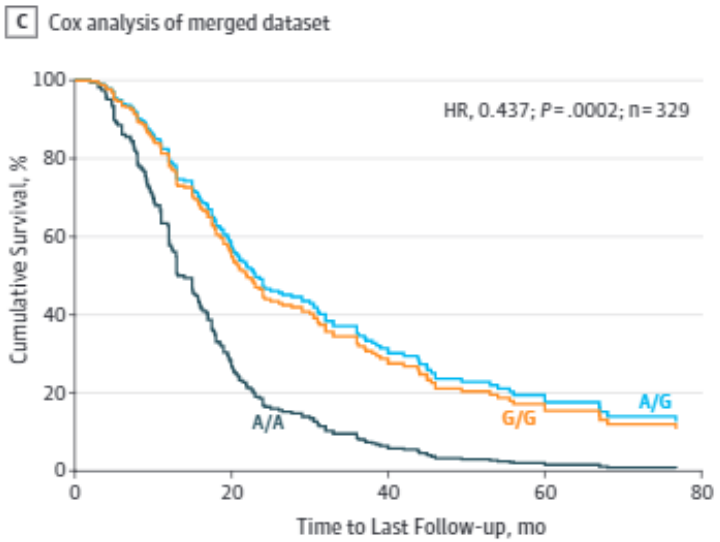
Circulating Tumor Cells are an Independent Predictor of Shorter Survival in Patients Undergoing Resection for Pancreatic and Periampullary Adenocarcinoma

Harald Hugenschmidt, MD,†‡ Knut Jørgen Labori, MD, PhD,‡ Cathrine Brunborg, MSc,§ Caroline Sophie Verbeke, MD, PhD,*¶ Lars Thomas Seeberg, MD, PhD,‡** Cecilie Bendigtsen Schirmer, MSc,¶ Anne Renolen, MSc,¶ Elin Faye Borgen, MD, PhD,¶ Bjørn Naume, MD, PhD,*|| and Gro Wiedswang, MD, PhD‡*



JAMA Surgery | Original Investigation

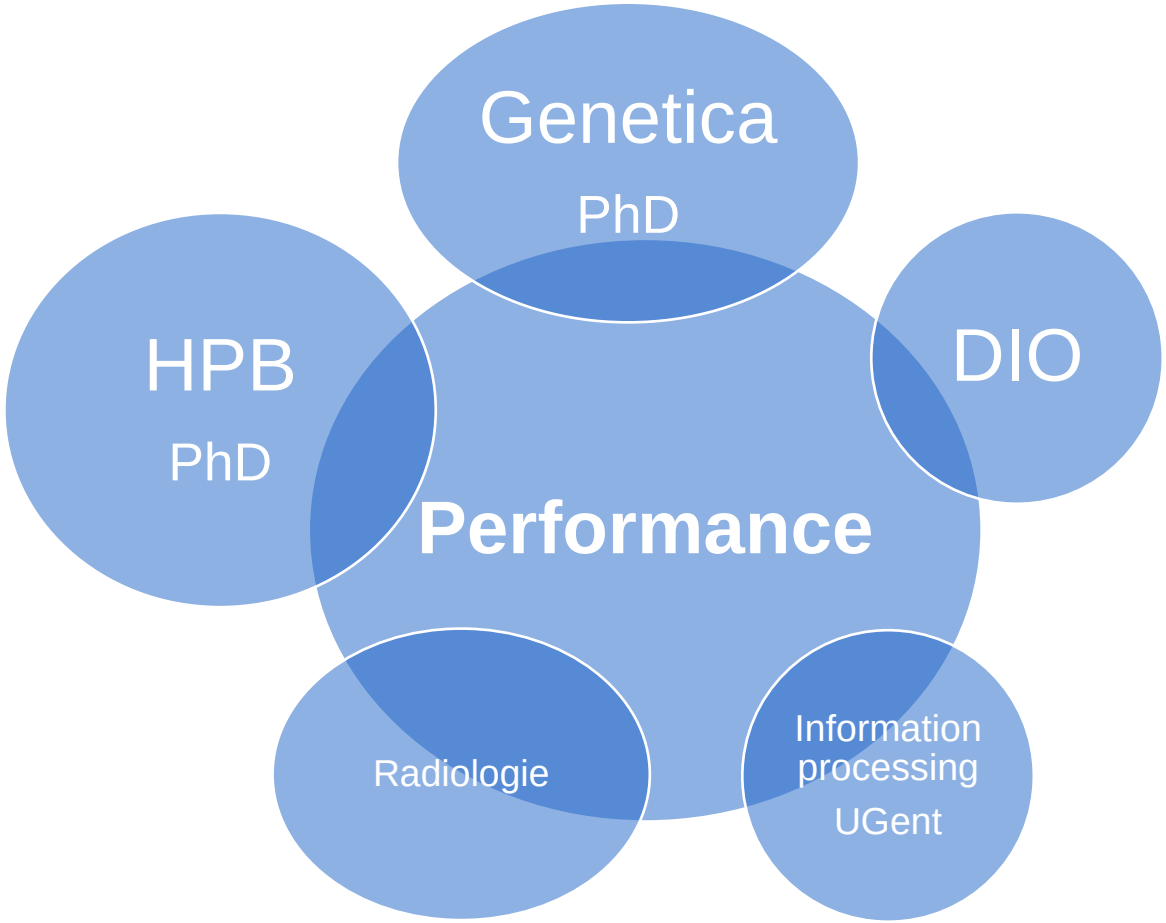
Identification and Validation of a Biomarker Signature in Patients With Resectable Pancreatic Cancer via Genome-Wide Screening for Functional Genetic Variants



JAMA Surg. doi:10.1001/jamasurg.2019.0484

- **Fonds voor innovatie en klinisch onderzoek (Type I mandaat)**

- **Beurs voor voltijds PhD kandidaat Genetica**



az alma zorg met een hart

AZ JAN PALFIJN GENT

AZ OUDENAARDE VZW

azsint-lucas

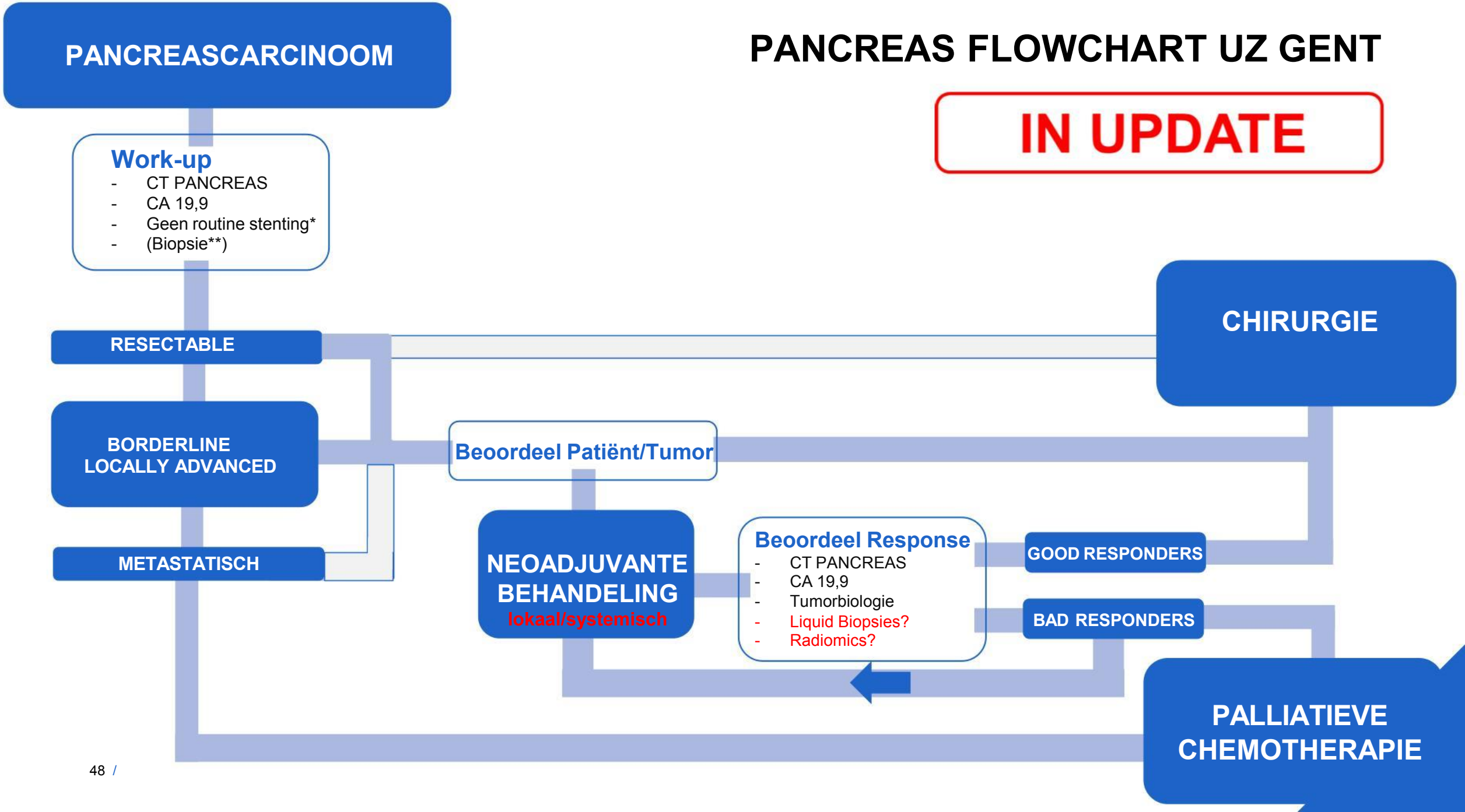
ZorgSaam

VITAZ STERK IN ZORG

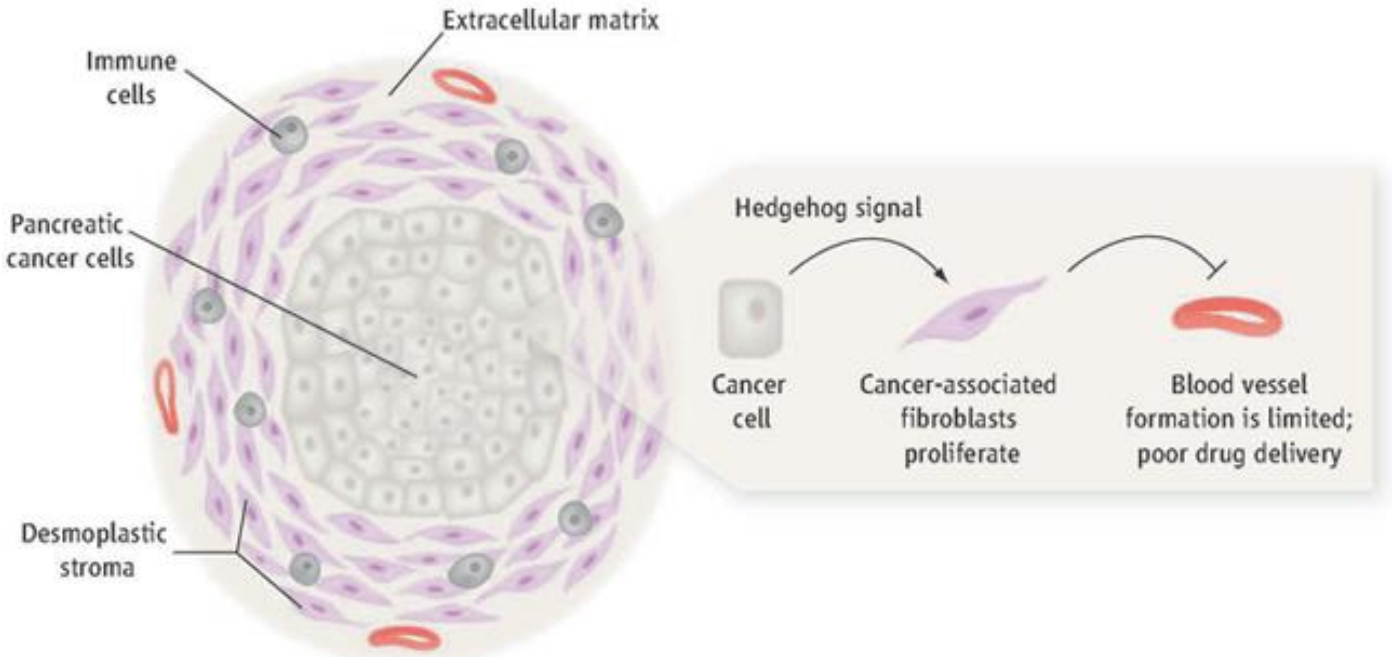
az Sint Blasius

PANCREAS FLOWCHART UZ GENT

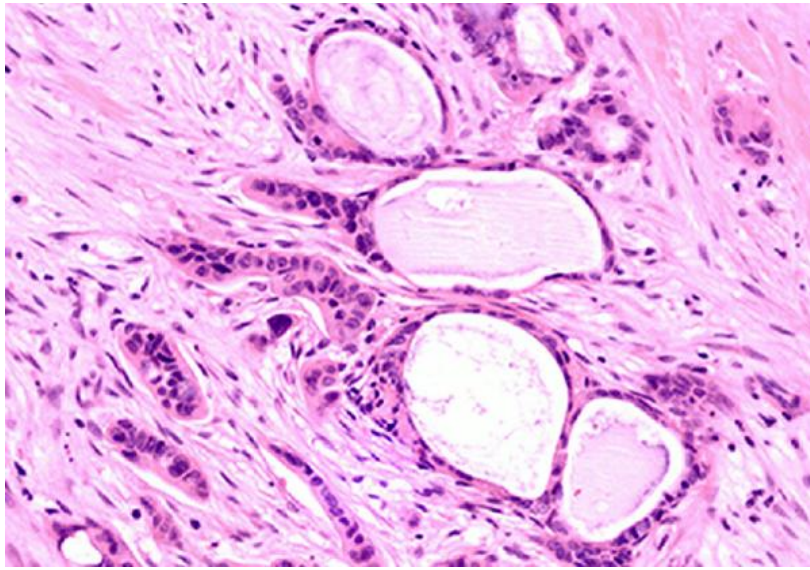
IN UPDATE



Rol voor immunotherapie?



- De moeilijkheden voor behandeling van pancreascarcinoma liggen op cellulair en genetisch vlak…..
- Voor veel tumoren biedt immunotherapie een veelbelovende behandeling (long-, blaas-, niertumoren……)
- Helaas lijkt het pancreascarcinoma eerder weerstandig tegen deze behandeling (<1% MSI). Hierbij lijkt de tumor microenvironment een essentiële rol te spelen…
- Stroma-rijke tumor met uitgesproken desmoplastische reactie en sterke bindweefsel component die het invasief carcinoma lijkt te omkapselen….
- Therapeutische medicatie lijkt dit kapsel onvoldoende te kunnen penetreren…..



Electrovaporatie

- Tot nu toe een behandeling voor lokaal inoperabele tumoren

- Gezien frekwente R1 status na resectie (50-60%) mogelijks ook een indicatie voor gebruik bij resecabele letsels…….

Multimodal therapy with or without irreversible electroporation for unresectable locally advanced pancreatic adenocarcinoma: a systematic review and meta-analysis

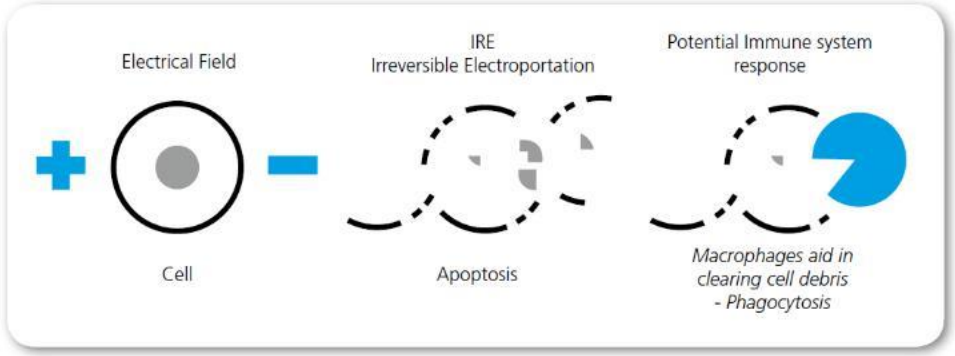
Kavin Sugumar[1], Alex Hurtado[2], Ilora Naik[2], Jonathan J. Hue[1], Luke D. Rothermel[1], John B. Ammori[1], Jeffrey M. Hardacre[1], Jordan M. Winter[1] & Lee M. Ocuin[1]

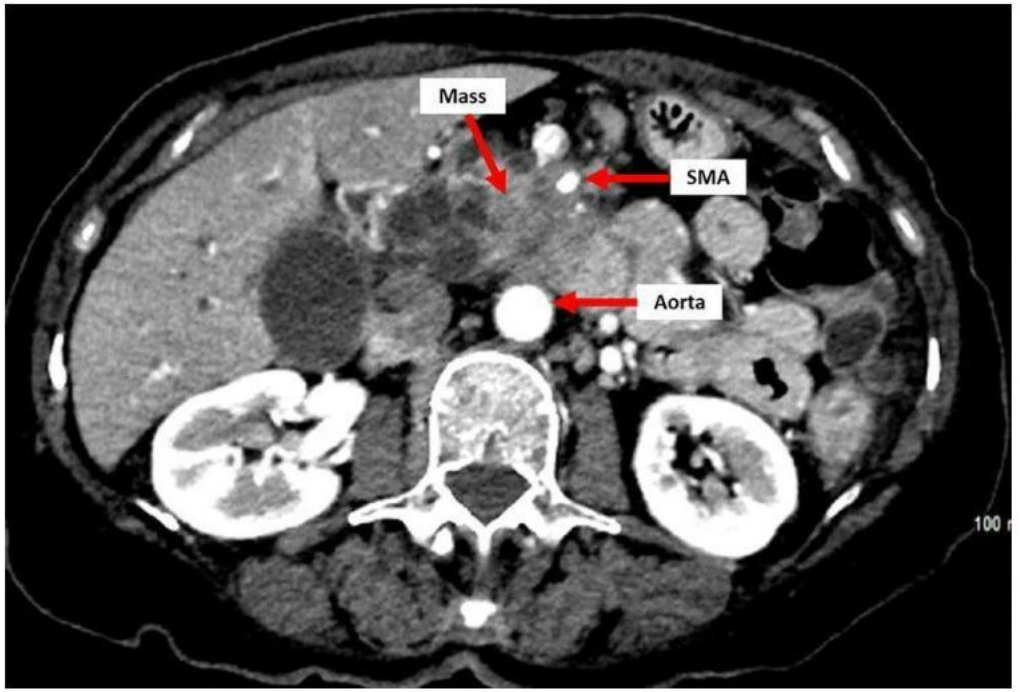
Conclusion: Multimodal therapy alone is associated with similar OS to multimodal therapy + IRE in patients with LAPC. Most patients progress and nearly half die within 1 year of the IRE procedure. Given the lack of quality prospective data, IRE should remain experimental and be used with caution in LAPC.

Expanding the Resection Pool

Irreversibele Electroporatie in Locally Advanced Tumoren

- **NanoKnife**
  - Hernieuwde interesse
  - Andere insteek

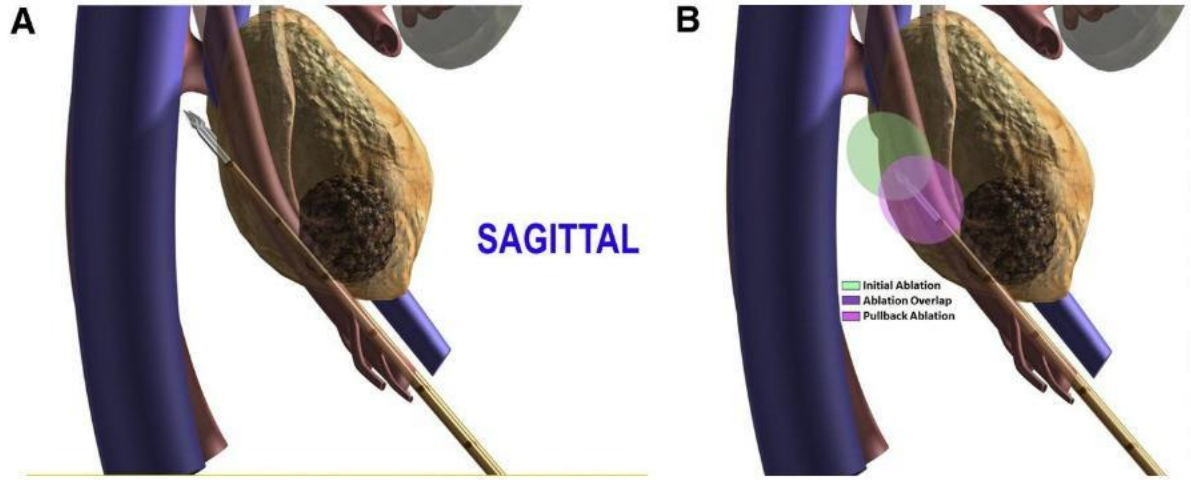


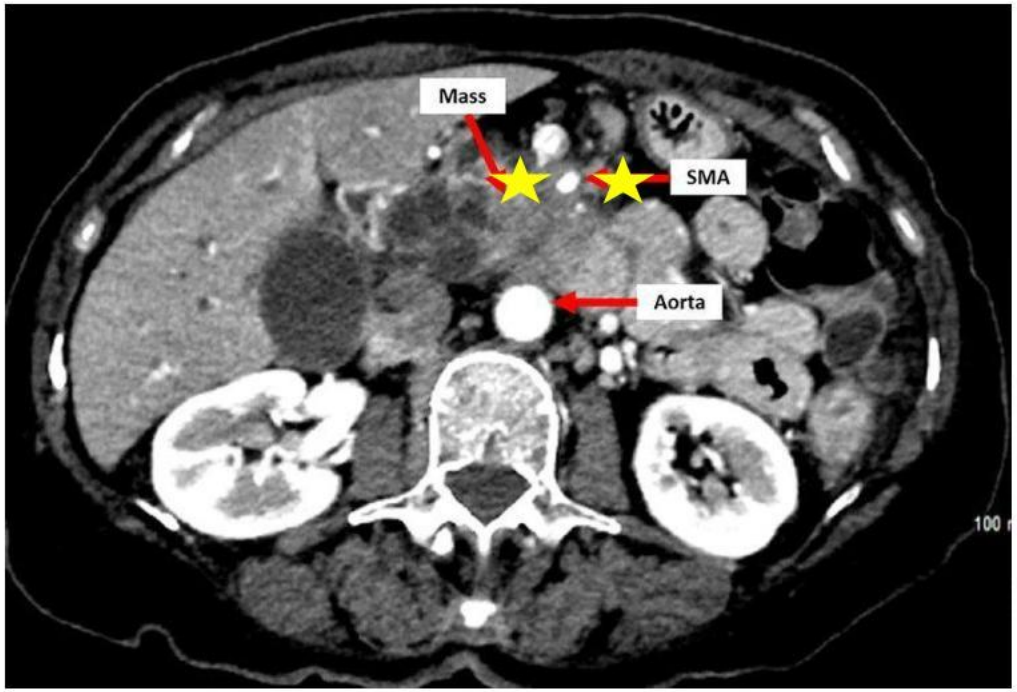


Expanding the Resection Pool

Irreversibele Electroporatie in Locally Advanced Tumoren

- NanoKnife
  - Hernieuwde interesse
  - Andere insteek
- Margin Accentuation
  - Resection + IRE





Expanding the Resection Pool

Irreversibele Electroporatie in Locally Advanced Tumoren

- NanoKnife
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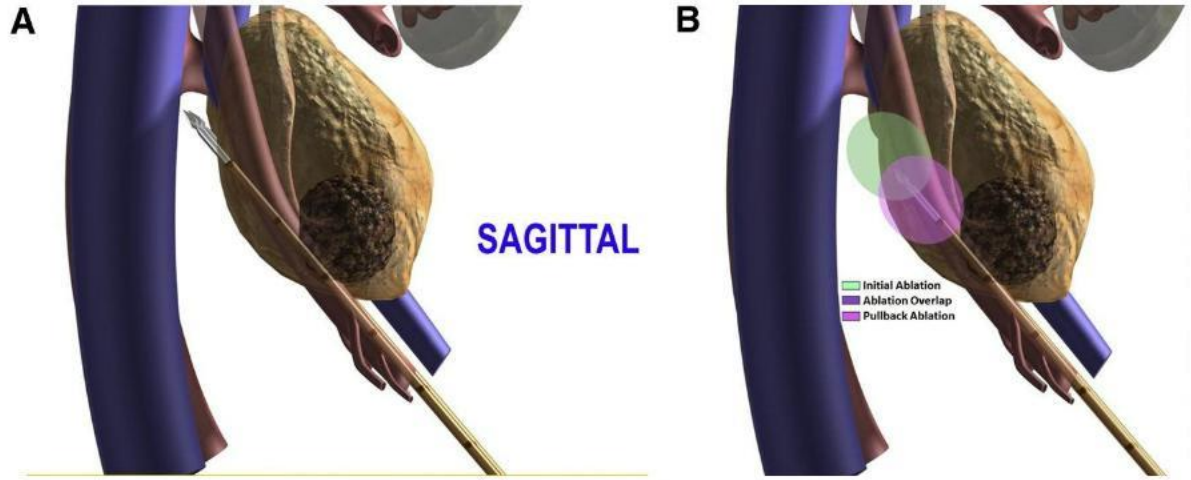
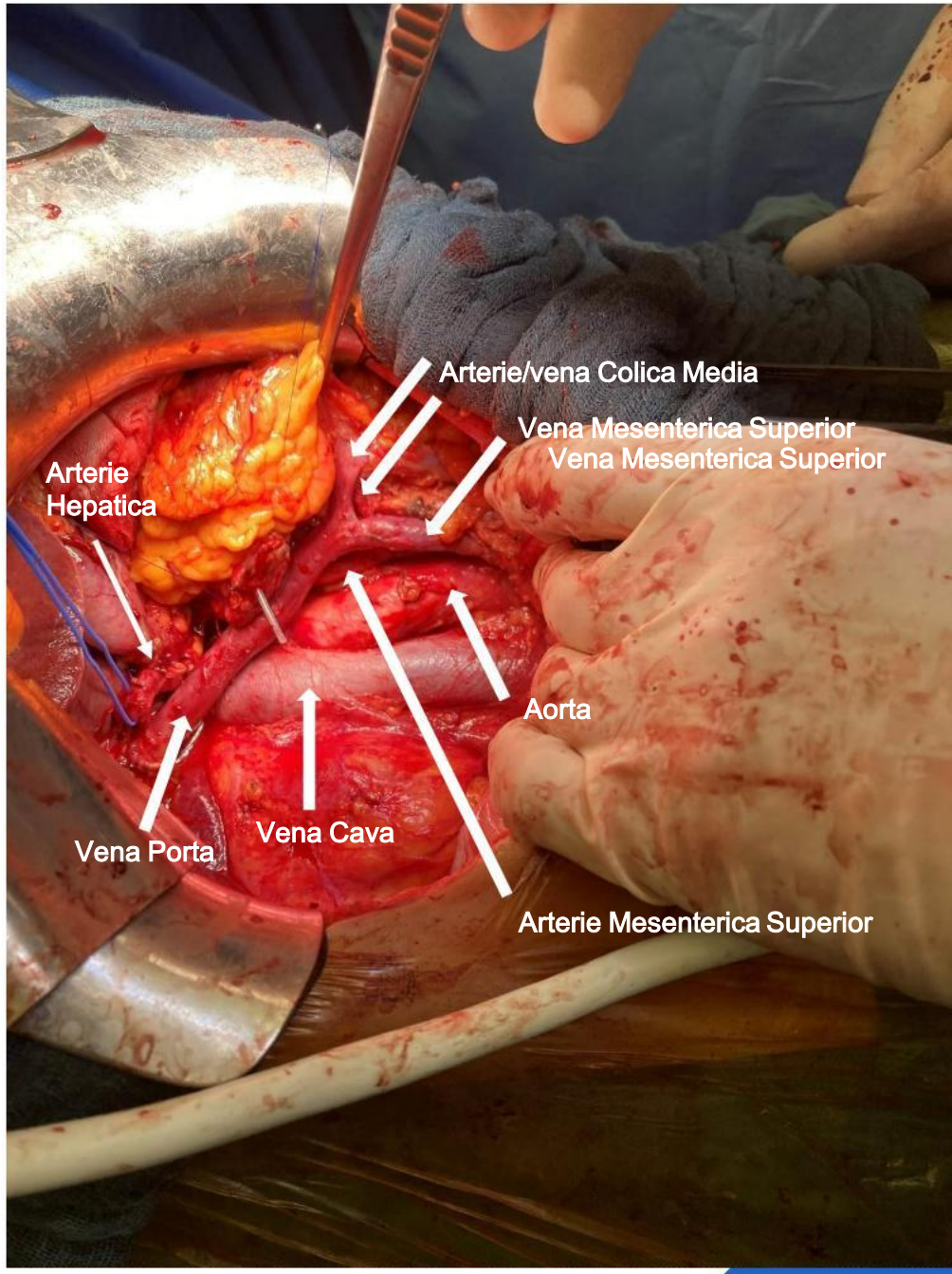
- Margin Accentuation
  - Resection + IRE





Margin ACcentuation for resectable Pancreatic cancer using Irreversible Electroporation – Results from the MACPIE-I study

Kaushal Kundalia [a], Abdul Hakeem [b], Michail Papoulas [c], Mark Mcphail [d], Shruthi Reddy [a], Praveen Peddu [a], Nabil Kibriya [a], Simon Atkinson [a], Andreas Prachalias [a], Parthi Srinivasan [a], Nigel Heaton [a], Debashis Sarker [a], Paul Ross [e], Yoh Zen [a], Krishna Menon [a, *]

Primary outcome

The percentage reduction in margin positivity in the IRE group compared to the non-IRE control group.

Secondary outcomes

1. Incidence of post-operative complications (graded as per Clavien-Dindo Classification [35]) include mortality and major morbidity (pancreatic anastomotic leak, delayed gastric emptying, bleeding and chyle leak)
2. Evaluate any local morbidity following the use of IRE
3. Length of hospital stay (LOS)
4. Disease-Free Survival (DFS)
5. Overall Survival (OS)

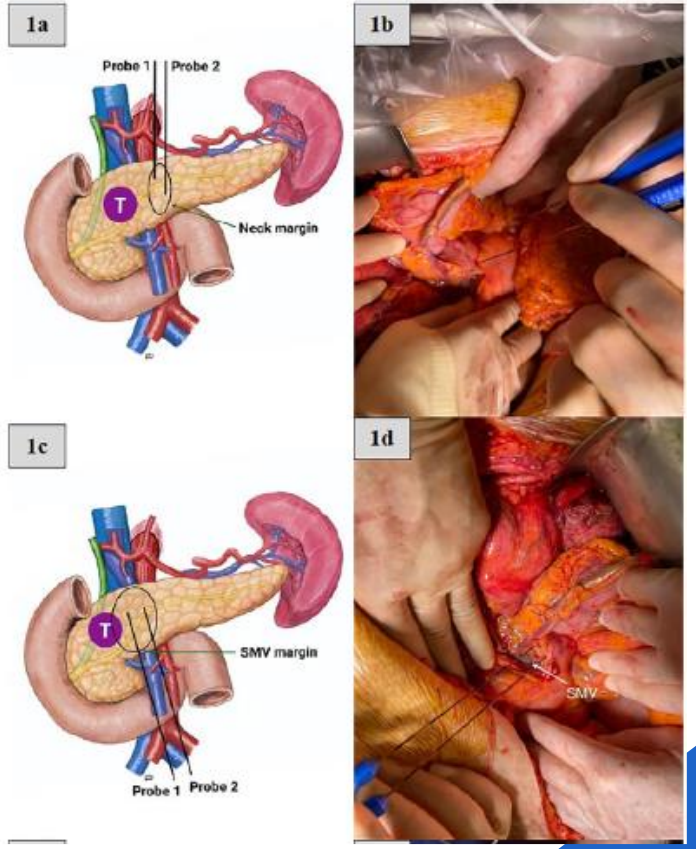


Table 2
Operative details and immediate post-operative outcomes comparing those who had IRE versus non-IRE.

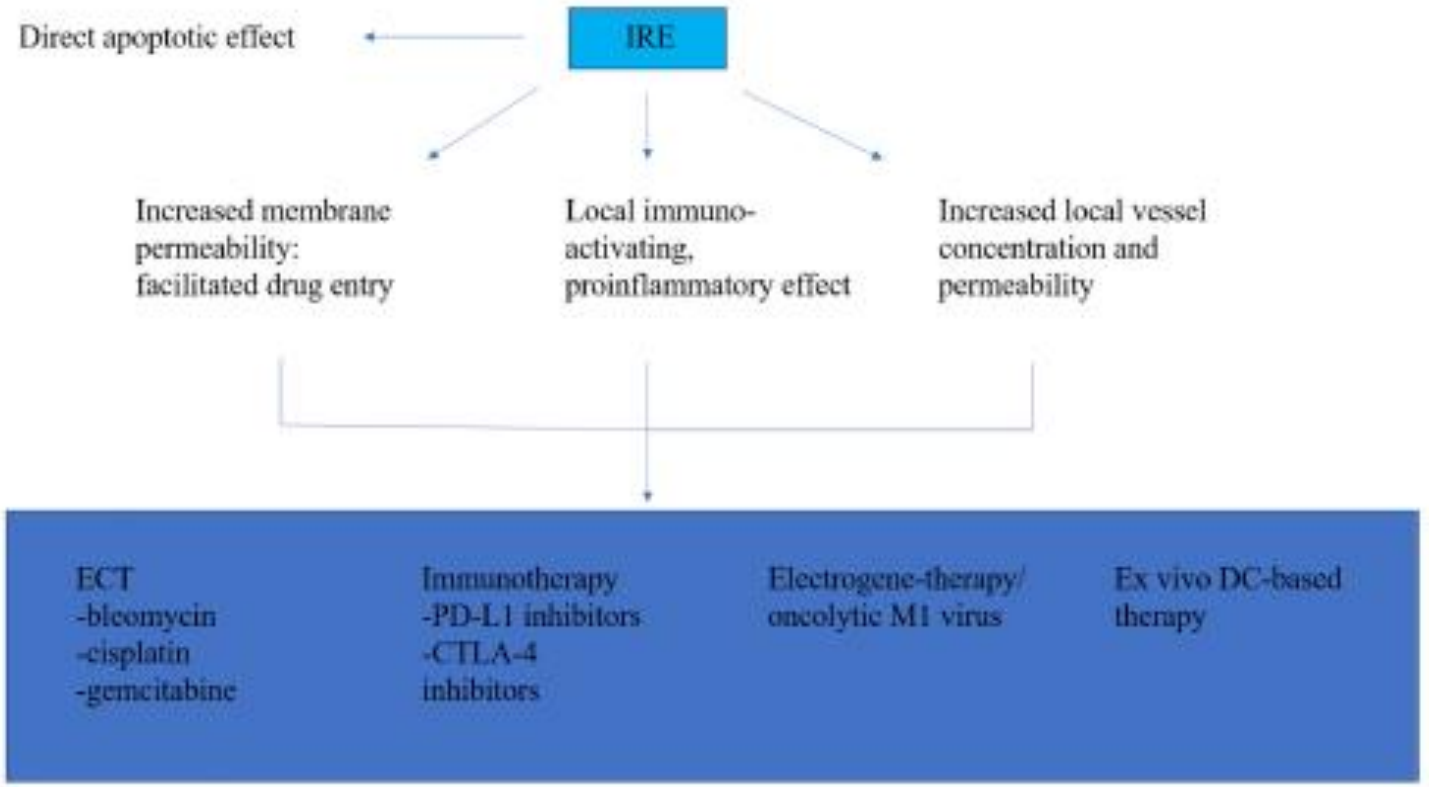
	IRE (N = 20)	Non-IRE (N = 91)	P value
Type of operation			**<0.001**
Classic Whipple	20 (100%)	51 (56.0%)	
Pylorus preserving PD	0 (0.0%)	40 (44.0%)	
Positive frozen section	3 (15.8%)	10 (11.1%)	0.696
PV/SMV resection	8 (40.0%)	19 (20.9%)	0.071
Completion total pancreatectomy	2 (10.0%)	6 (6.6%)	0.461
Immediate post-op outcomes			
Bleeding	1 (5.0%)	3 (3.3%)	0.711
Pancreatitis	0 (0.0%)	0 (0.0%)	–
Pancreatic leak	4 (21.0%)	10 (11.1%)	0.262
Delayed gastric emptying	1 (5.0%)	10 (11.0%)	0.449
Chyle leak	3 (15.0%)	19 (20.9%)	0.550
Post-op PVT	1 (5.0%)	1 (1.1%)	0.235
Clavien-Dindo complications			0.451
No complications	11 (55.0%)	46 (50.5%)	
Grade 1	6 (30.0%)	20 (22.0%)	
Grade 2	3 (15.0%)	22 (24.2%)	
Grade 3a	0 (0.0%)	2 (2.2%)	
Grade 3b	0 (0.0%)	1 (1.1%)	
Grade 4a/4b/5	0 (0.0%)	0 (0.0%)	
Length of stay (days)	12.5 (8–18)	10 (8–14)	0.352
Adjuvant chemotherapy	18 (90.0%)	78 (87.6%)	0.769
Margin involved (R1)	7 (35.0%)	47 (51.6%)	0.177
Which margin was involved?			
SMV margin	3 (15.0%)	28 (30.8%)	0.155
SMA margin	3 (15.0%)	20 (22.0%)	0.486
Posterior pancreatic margin	1 (5.0%)	23 (25.3%)	**0.046**
Pancreatic resection margin	0 (0.0%)	4 (4.4%)	0.340
Lymphovascular invasion	19 (95.0%)	83 (91.2%)	0.574
Perineural invasion	17 (85.0%)	81 (89.0%)	0.613
Total no. of lymph nodes	20 (16–23)	20 (16–25)	0.639
No. of positive lymph nodes	2 (0–5)	3 (0–5)	0.496
Lymph node ratio	0.10 (0.01–0.22)	0.15 (0.00–0.25)	0.704

Impact of margin accentuation with intraoperative irreversible electroporation on local recurrence in resected pancreatic cancer

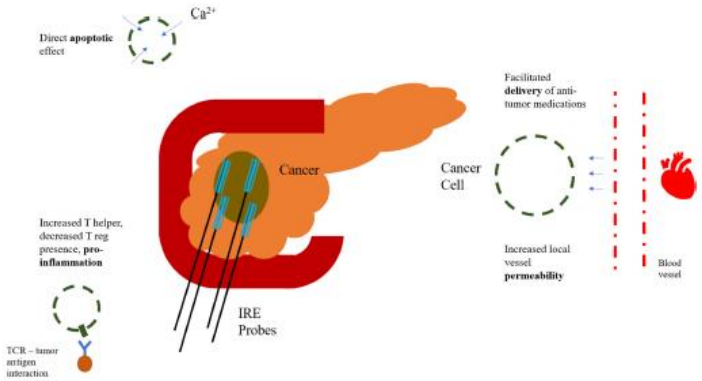
Robert C.G. Martin II, MD, PhD[a,*], Eric C. Schoen, BS[a], Prejesh Philips, MBBS[a], Michael E. Egger, MD, MPH[a], Kelly M. McMasters, MD, PhD[a], Charles R. Scoggins, MD, MBA[a]

Recurrence locations and recurrence outcome after pancreatectomy for stages IIB and III patients without and with irreversible electroporation–margin accentuation

Variable	Pancreatectomy alone ($n = 71$)	Pancreatic resection with IRE margin ($n = 75$)	*P* value
Recurrence any type, *n* (%)	30 (42)	49 (65)	0.06
Local only	13 (18)	13 (17)	
Regional (lymph node) only	0 (0)	6 (12)	
Distant only	24 (33)	26 (34)	
Location of distant progression, *n* (%)	34	29	NS
Peritoneum	10 (29)	7 (24)	
Lymph node	4 (12)	1 (3)	
Lung	4 (12)	6 (21)	
Bone	0 (0)	1 (3)	
Time to local recurrence from diagnosis (mo), mean	16.5	15.8	NS
Time to local recurrence from procedure (mo), mean	10.5	9.4	NS
Time to any recurrence from diagnosis (mo), mean	24.9	27.3	NS
Time to any recurrence from procedure (mo), mean	17.3	17.4	NS
OS from diagnosis (mo), mean	27.9	34.2	0.04
OS from procedure (mo), mean	20.3	24.4	0.08



Abbreviations: IRE = Irreversible Electroporation; ECT = Electrochemotherapy; PD-L1 = Programmed Death Ligand 1; CTLA4 = Cytotoxic T – Lymphocyte Associated protein 4; DC = Dendritic Cell



Abbreviations: IRE = Irreversible Electroporation; TCR = T-cell Receptor.

Minimale invasieve pancreaschirurgie

Ons uitgangspunt voor kwalitatieve pancreasheelkunde:

- Oncologisch correct verwijderen van het letsel
  - Zo veel mogelijk gezond weefsel als marge rondom
  - Correcte hoeveelheid lymfeklieren uit de directe omgeving en ook op afstand, volgens strikte criteria van zowel RIZIV, Guidelines als Pathologen….
  - Patiënten voldoende vlot en goed laten herstellen dat op tijd de chemotherapie kan worden gestart of hervat…..
- Zo vlot mogelijk herstel door het lichaam op verschillende vlakken te ondersteunen:
  - Goede calorie intake, liefst via de mond, anders via infuus (onder begeleiding van de diëtisten)
  - Goede opvolging van eventuele suikerziekte
  - Goede mobilisatie door kinesitherapie
  - Goede psychologische begeleiding

Fast track protocol

- **Dag 1 op kamer**: Opstarten Infuus voeding.
- **Dag 2 op kamer**: Laterale drain rechts verwijderen, MS 10 cm terugtrekken en slokje H20, PCEA en blaassonde verwijderen. Indien laag risico: start voeding via de maagsonde.
- **Dag 3 op kamer**: MS verwijderen. Lipase op penrose en drain bepalen. Indien lipase negatief: Drain rechts mediaal uit en penrose mobiliseren. Indien lipase positief: Penrose herfixeren en sandostatine LAR 30 mg toedienen. Start met H20 en yoghurt.
- **Dag 4 op kamer**: Start opklimmende voeding. Start Primperan 3 x 1 ampulle per dag (tenzij contra indicatie).
- **Dag 5 op kamer**: Verder opklimmende voeding. Indien mogelijk afbouwen infuusvoeding.
- **Dag 6 en verder**: Patiënt verder mobiliseren en verder opklimmende voeding tot ontslag.

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journal homepage: www.elsevier.com/locate/ijso

Research Paper

Evaluation of an enhanced recovery program for outcome improvement after pancreaticoduodenectomy: A retrospective cohort study

Ann-Sophie Hufkens, Stijn van Cleven, Luis Abreu de Carvalho, Aude Vanlander, Frederik Berrevoet*

Department of General and HPB Surgery and Liver Transplantation,Ghent University Hospital, Corneel Heymanslaan 10, 9000, Ghent, Belgium

Opnameduur

- Gemiddeld rond de 10-12 dagen (tussen 6 en 14 dagen)
- Afhankelijk van complicaties of vertraging bij herstel van transit
- Belangrijkste problemen:
  - Vermoeidheid
  - Verzwakking
  - Geen eetlust
  - Vertraagde maaglediging
  - Steatorrea
  - Diabetes

- Aanbeveling:
  - Calorie-inname is belangrijker dan type voeding, uitz. DM type II
  - High energy drinks
  - Alles wat vlot binnen gaat…..

De brug naar de minimaal invasieve chirurgie

- Meestal spreken we over oncologische chirurgie….
- Chemotherapie na de operatie is een van de bouwstenen van de behandeling…..
- Er is een belangrijke leercurve, dus grote aantallen van dezelfde ingreep is belangrijk……
- Het herstel van de heelkunde wordt voor een groot deel bepaald door het inwendig herstel, niet door het litteken……
- Een chirurg brengt zijn/haar patiënt niet graag van de regen i de drop……

"Eat when you can,

Sleep when you can

Don't mess with pancreas"

Anderzijds….

- Innovatie MOET er zijn….
- Geleidelijk aan komt er meer bewijs dat voor de lichaam- en staartresecties de uiteindelijke overleving alsook de frequentie en ernst van complicaties ongeveer gelijk is…..
- De ernst van de complicaties bij een linkszijdige resectie is lager…..
- De rol van de laparoscopie en de robot neemt daardoor toe……

Minimaal invasieve chirurgie

Laparoscopische pancreasresecties

Robotic (assisted) pancreaschirurgie

- In meerdere centra wordt een distale pancreatectomie MI uitgevoerd
  - Feasible and safe
  - Licht verminderde opnameduur
  - Licht verminderde morbiditeit (vnl. thv de incisie)

- Pancreaticoduodenectomie wordt soms al MI uitgevoerd
  - Hoge morbiditeit
  - Meer complicaties
  - Weinig voordeel op ligdagen
  - Beperkt bewijs rond duidelijke voordelen (zelfs in ervaren handen…)

ORIGINAL SCIENTIFIC ARTICLE

Laparoscopic Pancreaticoduodenectomy Should Not Be Routine for Resection of Periampullary Tumors

Dokmak, Safi MD[a,*]; Ftériche, Fadhel Samir MD[a]; Aussilhou, Béatrice MD[a]; Bensafta, Yacine MD[a]; Lévy, Philippe MD[b]; Ruszniewski, Philippe MD[b]; Belghiti, Jacques MD[a]; Sauvanet, Alain MD[a]

Author Information

Journal of the American College of Surgeons: May 2015 - Volume 220 - Issue 5 - p 831-838
doi: 10.1016/j.jamcollsurg.2014.12.052

CONCLUSIONS:

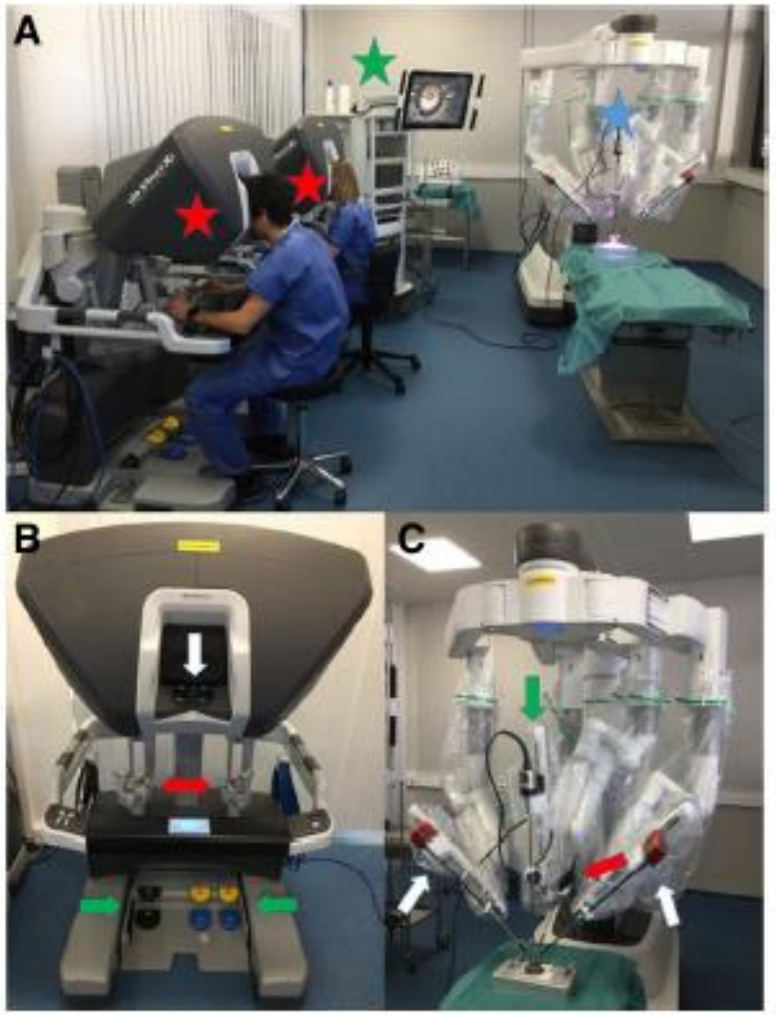
This study found that LPD is associated with higher morbidity, mainly due to more severe PF. Laparoscopic pancreaticoduodenectomy should be considered only in the subgroup of patients with a low risk of PF.

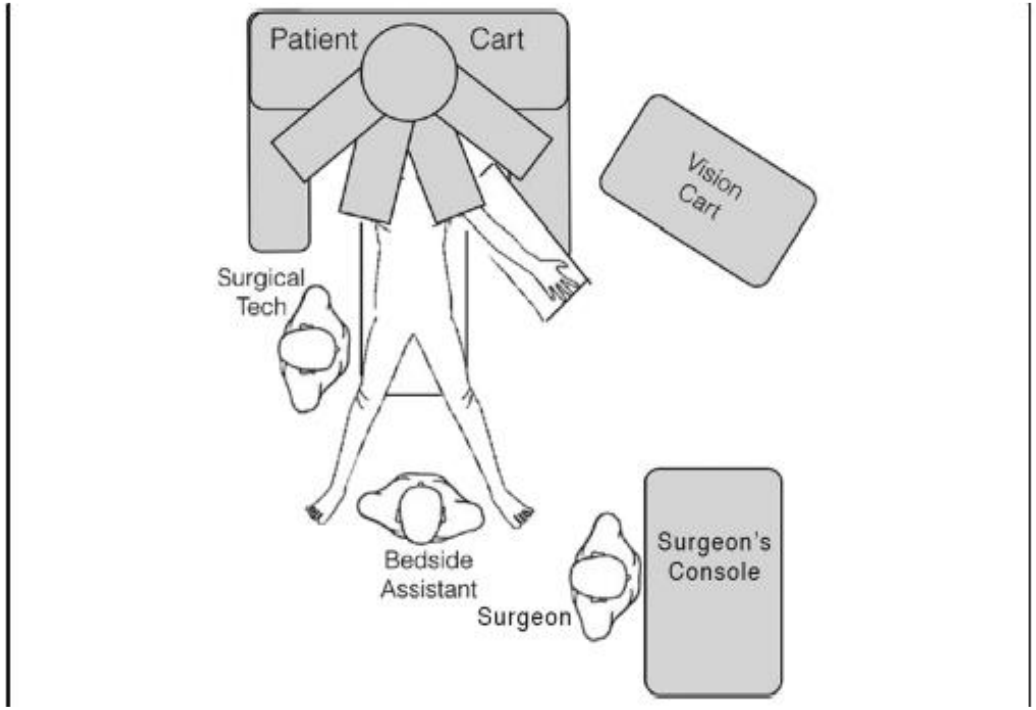
Wanneer robot en wanneer laparoscopie?

- Verminderde beschikbaarheid van de robot in een operatiekwartier
- Meeste voordeel indien de chirurg een of meerdere nieuwe verbindingen moet maken en de rol van een 3D zicht belangrijker wordt….
- Hierdoor: laparoscopie en robot-assisted chirurgie voor linkszijdige chirurgie van de pancreas als evenwaardig te beschouwen.
- Voor een Whipple operatie lijkt robot de meest aangewezen techniek….

Gebruik van de robot

- De chirurgische techniek blijft hetzelfde…
- De chirurg blijft hetzelfde……
- Het “speelgoed” is geheel iets anders





- Geen ‘gevoel’ van behandeling/aanraking van de weefsels…..
- Pancreas is een zeer zacht orgaan, dat gemakkelijk beschadigd wordt, met veel ontsteking tot gevolg…..
- Maar: in vergelijking met laparoscopie veel beter ‘hechtingsmogelijkheden’

Pancreaticojejunostomy

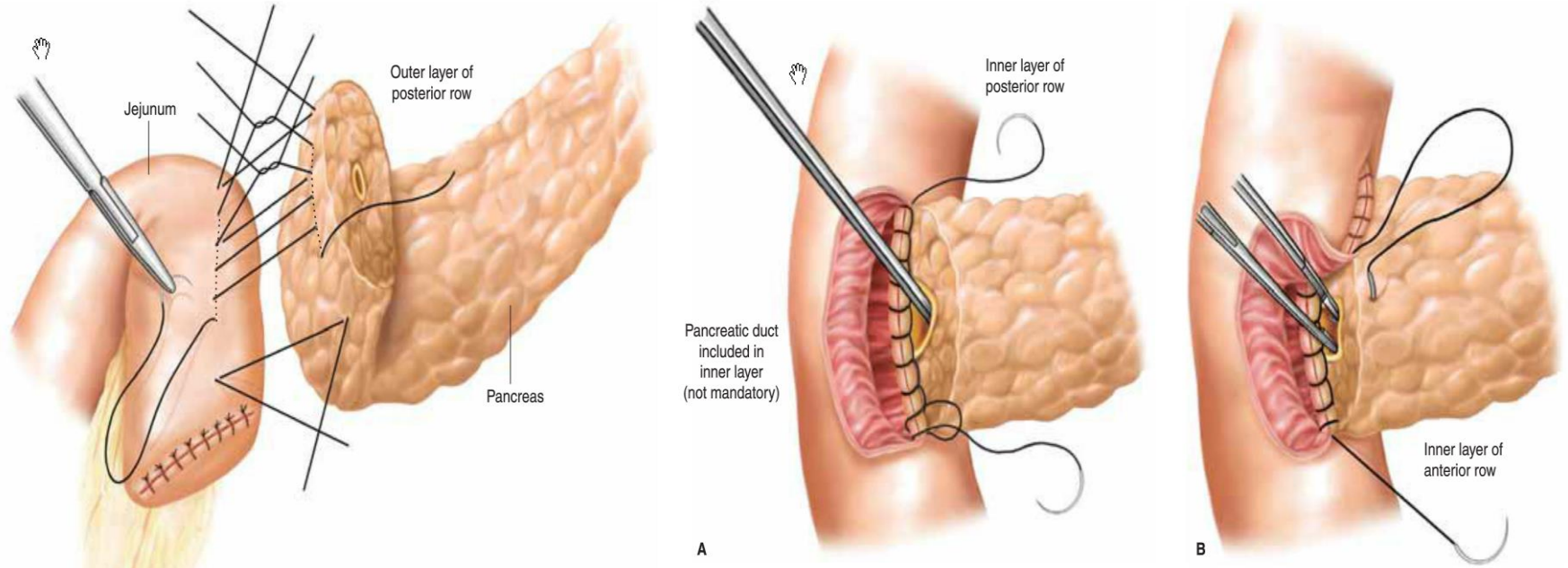
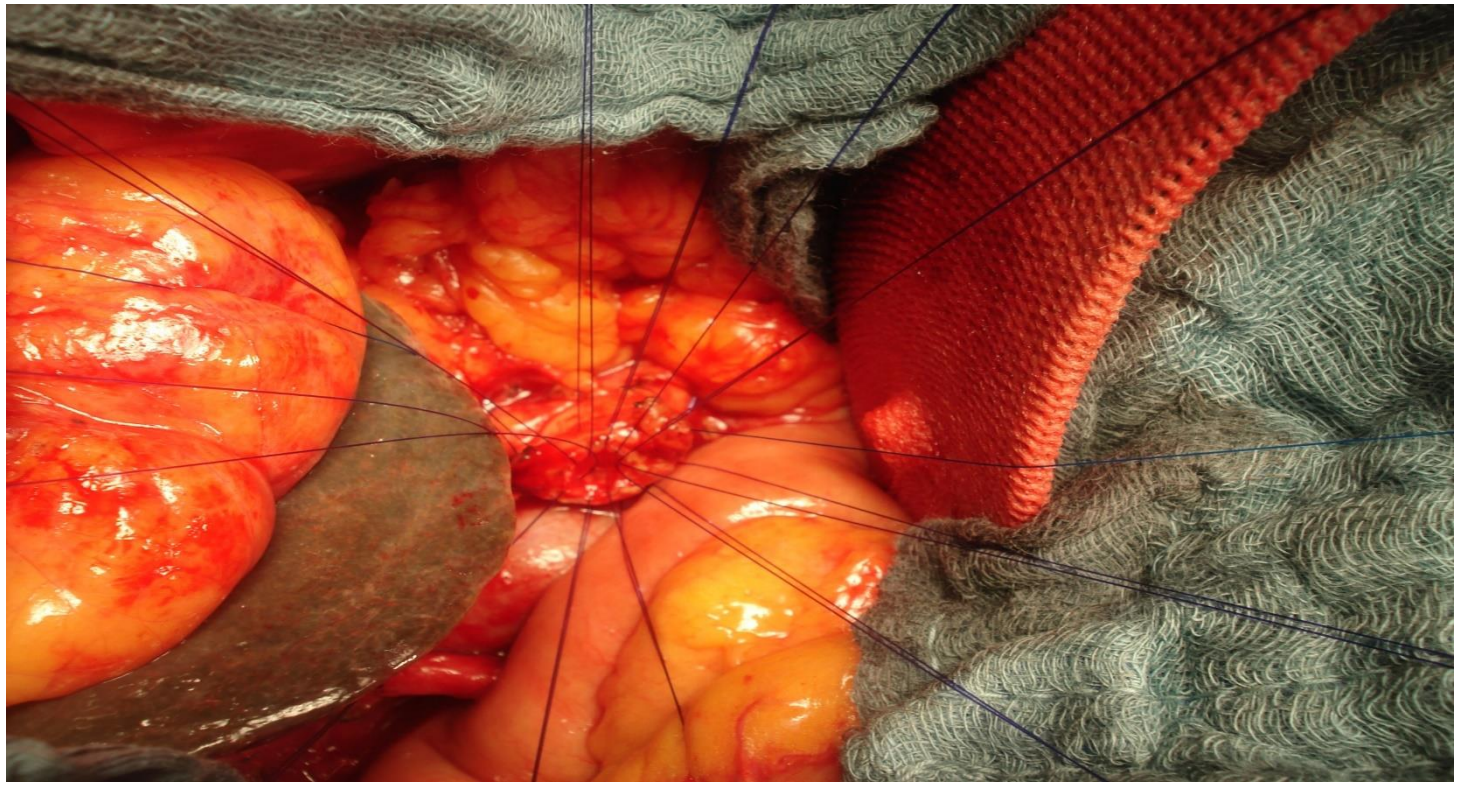


Figure 2.12 The inner layer of continuous 3-0 polyglactin suture is placed in a locking fashion on the posterior aspect of the anastomosis **(left)** and converted to a simple running suture for the inner anterior layer **(right)**.



Ons nabije toekomst doel in UZ Gent

- Progressieve implementatie van deze technieken

- Step by step aanpak
  - Linkszijdige verwijdering
  - Wegname rechtszijdig
  - Reconstructie rechtszijdig
  - Volledige ingreep robotisch geassisteerd

- Belangrijke patiënten selectie
  - Standaard procedures
  - Geen ‘speciallekes’
  - Laagdrempelig om een bijkomende insnede te maken

- Implementatie over een periode van 1 à 2 jaar (begin 2022 gestart)

Conclusie:

- Neoadjuvante therapie heeft de toekomst, vermoedelijk voor zowel resecabele als borderline of lokaal gevorderde resecabele letsels.

- Electroporatie biedt, samen met de chemotherapie een extra optie tot verkrijgen van R0 resectie en potentieel verbeteren van de overleving.

- Immunotherapie is momenteel niet behulpzaam in geval van pancreas adenocarcinomen.

- Zoals voor andere chirurgische procedures wint de minimaal invasieve (robot) techniek ook licht terrein voor pancreasresecties, maar gezien veel oncologische indicaties en het belang van goede adjuvante therapie wordt dit behoudend uitgebouwd.

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Dr Hasan Eker
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Nieuwe collega's:

Dr.Ann Verena Lerut
Fellow (8/2022)

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IA
T1 N0 M0
The cancer is confined to the pancreas and is no bigger than 2 cm (0.8 inch) across (T1). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).

IB
T2 N0 M0
The cancer is confined to the pancreas and is larger than 2 cm (0.8 inch) but no more than 4cm (1.6 inches) across (T2). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).

IIA
T3 N0 M0
The cancer is confined to the pancreas and is bigger than 4 cm (1.6 inches) across (T3). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).

IIB
T1 N1 M0
The cancer is confined to the pancreas and is no bigger than 2 cm (0.8 inch) across (T1) AND it has spread to no more than 3 nearby lymph nodes (N1).
It has not spread to distant sites (M0).

T2 N1 M0
The cancer is confined to the pancreas and is larger than 2 cm (0.8 inch) but no more than 4cm (1.6 inches) across (T2) AND it has spread to no more than 3 nearby lymph nodes (N1). It has not spread to distant sites (M0).

T3 N1 M0
The cancer is confined to the pancreas and is bigger than 4 cm (1.6 inches) across (T3) AND it has spread to no more than 3 nearby lymph nodes (N1).
It has not spread to distant sites (M0).

III
T1 N2 M0
The cancer is confined to the pancreas and is no bigger than 2 cm (0.8 inch) across (T1) AND it has spread to 4 or more nearby lymph nodes (N2).
It has not spread to distant sites (M0).

T2 N2 M0
The cancer is confined to the pancreas and is larger than 2 cm (0.8 inch) but no more than 4cm (1.6 inches) across (T2) AND it has spread to 4 or more nearby lymph nodes (N2). It has not spread to distant sites (M0).

T3 N2 M0
The cancer is confined to the pancreas and is bigger than 4 cm (1.6 inches) across (T3) AND it has spread to 4 or more nearby lymph nodes (N2).
It has not spread to distant sites (M0).

T4 Any N M0
The cancer is growing outside the pancreas and into nearby major blood vessels (T4). The cancer may or may not have spread to nearby lymph nodes (Any N).
It has not spread to distant sites (M0).

IV

Any T Any N M1

The cancer has spread to distant sites such as the liver, peritoneum (the lining of the abdominal cavity), lungs or bones (M1). It can be any size (Any T) and might or might not have spread to nearby lymph nodes (Any N).