



¿Qué técnicas innovadoras existen para el abordaje locorregional del cáncer de páncreas?

Jorge Adeva

Hospital Universitario 12 de Octubre



Disclosure information

- Consultant or Advisory Role: Servier, Incyte, Taiho, Astra-Zeneca.
- Speaking: Incyte, Astra-Zeneca, Jazz
- Other: Travel / accommodation: Merck, Servier, OncoSil Medical Limited.



PDAC

R0/R1

R

BL

LA (UR)

M1

Adjuvant

Neoadjuvant

1L

2L

Surgery

Radiotherapy?

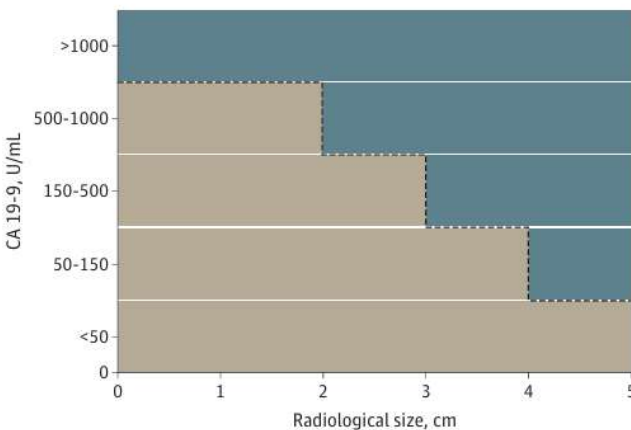
Systemic treatment (Chemotherapy)



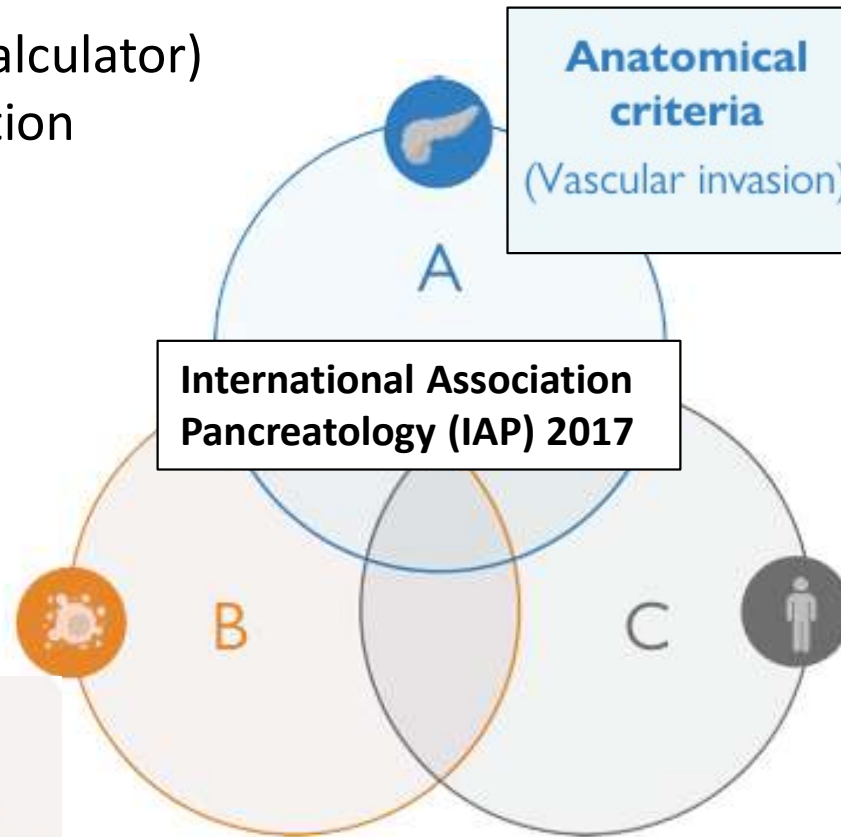
SURGERY in PDAC

MetroPancreas (online calculator) Futility for upfront resection

B Dichotomous criteria



Tumour biology
(CEA 19-9 and lymph node metastasis)



	Superior mesenteric artery	Coeliac axis	Common hepatic artery	Portomesenteric venous axis
Resectable	No involvement	No involvement	No involvement	≤180° contact without vein contour irregularity
Borderline resectable	≤180° contact	≤180° contact	Any contact without extension to CA or hepatic artery bifurcation*	≤180° contact with vein contour irregularity OR >180° contact without vein contour irregularity or thrombosis, but reconstructable OR Any contact with inferior vena cava
Locally advanced	>180° contact	>180° contact OR any contact of the CA with aortic involvement	Any contact with extension to CA and/or hepatic artery bifurcation	No reconstructable involvement due to tumour contact or occlusion (either due to tumour or bland thrombus)
Metastatic	Distant metastatic disease, regardless of vascular involvement of the primary tumour			

- Artery First Approach
- Vascular Resection / Reconstruction
- Arterial Divestment
- TME

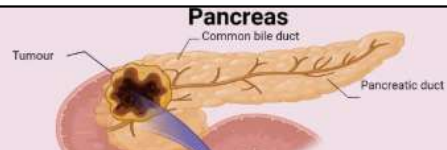
Patient and center conditions
(ECOG PS, center volume, surgeon experience)



PDAC

What is our goal?

- Downstaging for radical resection (ORR)?
- Just palliative (OS/QoL)?



Irr
Elec

Isolated Upper
Abdominal
Perfusion

Ablation (RFA)

(MWA)

Focused Ultrasound
Ablation (HIFU)

Cryoblation

LA (UR)

M1

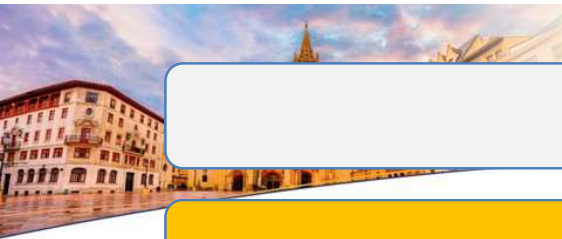
1L

2L

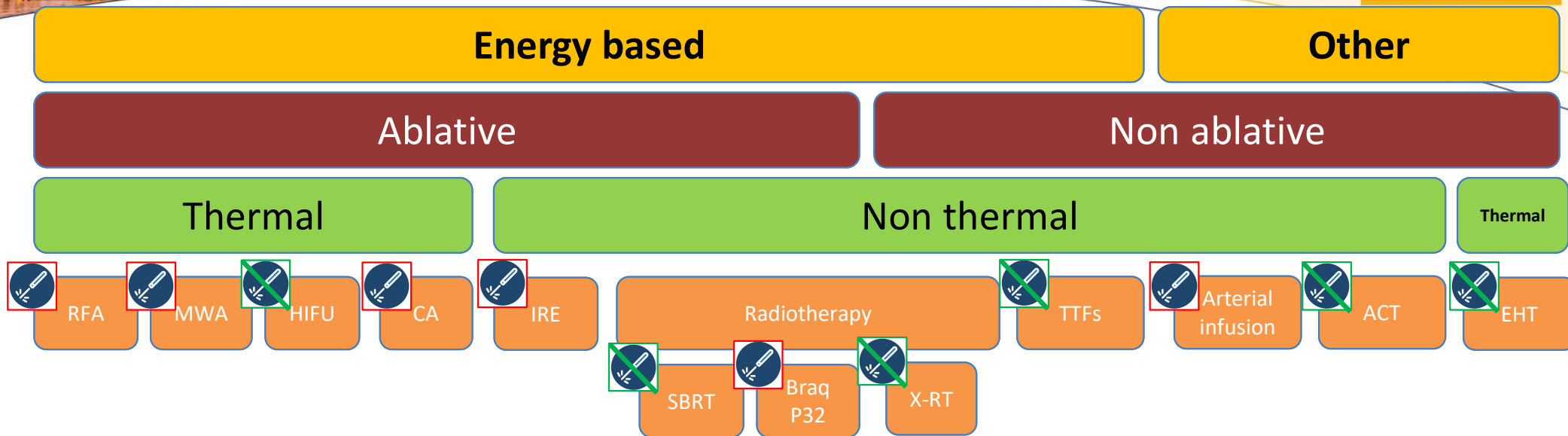
LRT

by

Chemotherapy)



Locoregional therapies for PDAC



Locoregional therapies for PDAC

Energy based

Other

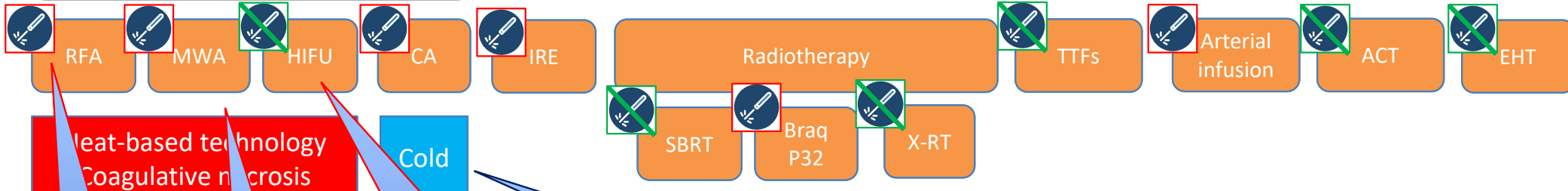
Ablative

Non ablative

Thermal

Non thermal

Thermal



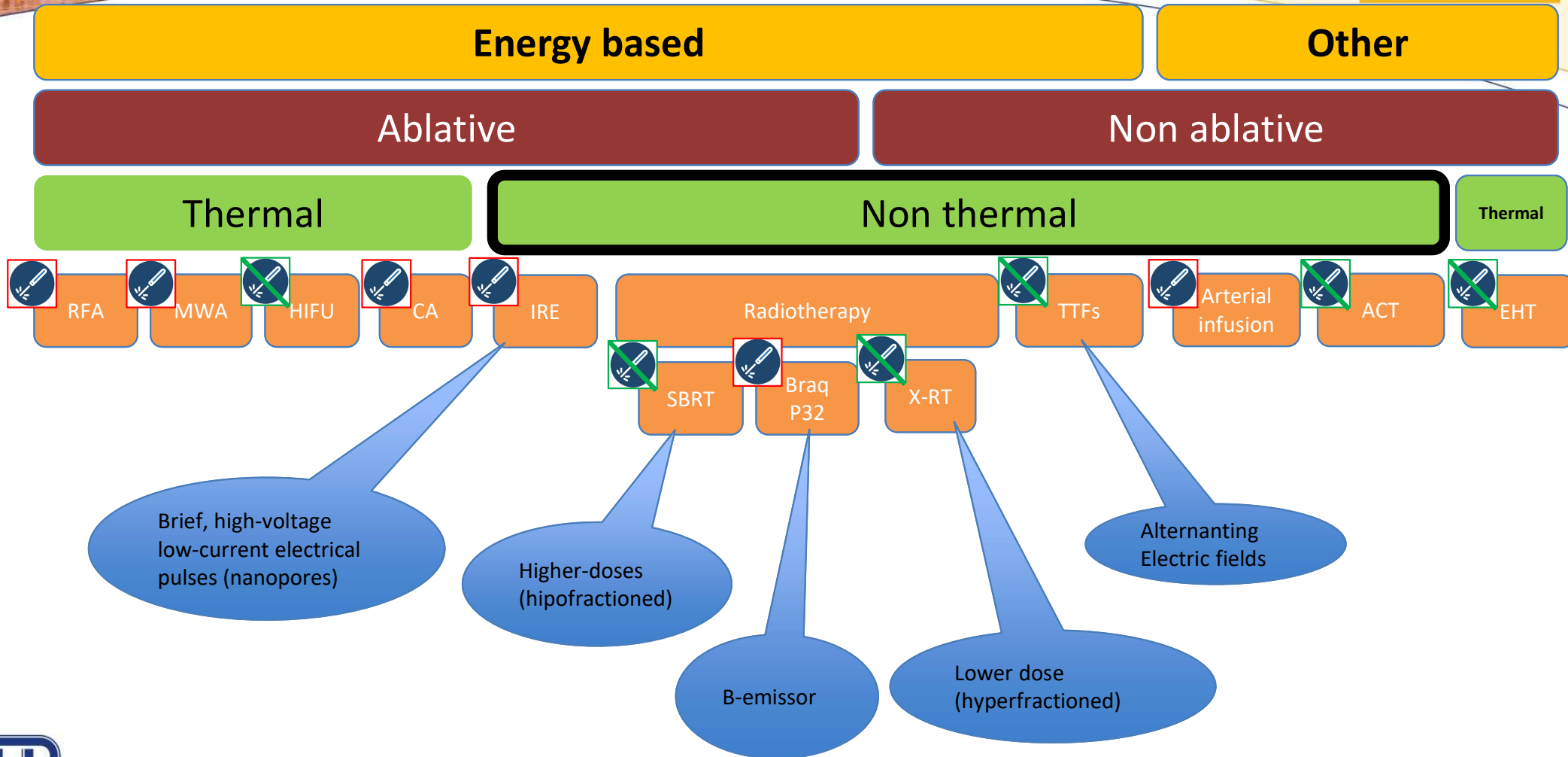
High-frequency
alternating
electrical current
(heating tissue
by friction)

Focused ultrasound waves
(heating and mechanical
damage (cavitation))

Repeated freezing and
thawing cycles to cause
cell death (Argon gas)

High frequency microwaves
(dielectric heating of polar
water molecules)

Locoregional therapies for PDAC



Locoregional therapies for PDAC

Energy based

Ablative

Thermal



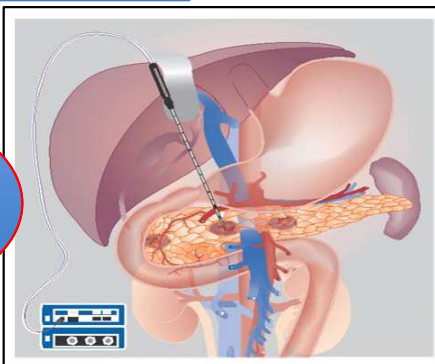
RFA

- Laparotomía
- Endoscópico/EUS
- Percutáneo

Heat-based technology
Coagulative necrosis

Heat sink
effect

High-frequency
alternating
electrical current
(heating tissue
by friction)



Not yet recruiting ⓘ

Pilot Study of EUS-Guided Radiofrequency and FOLFIRINOX in Advanced Pancreatic Cancer (RadioFAP) (RadioFAP)

ClinicalTrials.gov ID ⓘ NCT06743386

Sponsor ⓘ French Society of Digestive Endoscopy

Recruiting ⓘ

EUS-RFA PANCARDINAL-1 Trial

ClinicalTrials.gov ID ⓘ NCT04990609

Sponsor ⓘ The University of Texas Health Science Center, Houston

Radiofrequency ablation

Seelen, Pando, HBP 2024, FP07-1

Locoregional therapies for PDAC

Energy based

Ablative

Thermal



HIFU

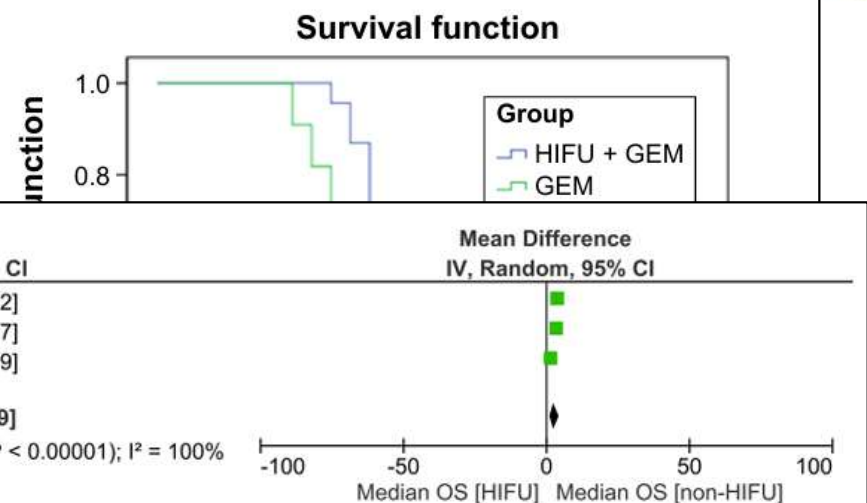
Heat-based technology
Coagulative necrosis



15/10/2024

Focused ultrasound waves
(heating and mechanical
damage (cavitation))

Study or Subgroup	Weight	Mean Difference	
		IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Li X 2016	33.4%	3.70 [3.68, 3.72]	
LV 2016	33.1%	3.38 [3.09, 3.67]	
Ning 2019	33.4%	1.40 [1.31, 1.49]	
Total (95% CI)	100.0%	2.83 [1.06, 4.59]	
Heterogeneity: Tau ² = 2.41; Chi ² = 2380.76, df = 2 (P < 0.00001); I ² = 100% Test for overall effect: Z = 3.14 (P = 0.002)			



0.00 2.5

Metanalysis, N=939 (19 articles)

- 8 Retro, 10 Props, 1RCT
- 12mOS (p < 0.05)
- Pain level (p < 0.05)
- Decrease Ca 19.9 (p < 0.05)

Locoregional therapies for PDAC

Energy based

Ablative

Thermal

USE
Laparoscopy



CA

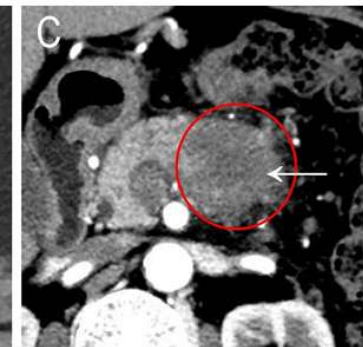
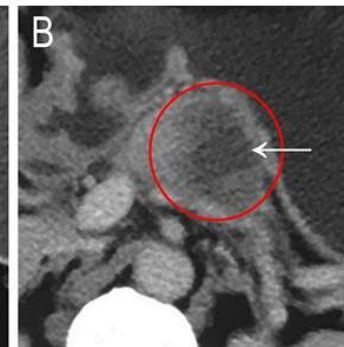
Cold



Repeated freezing and
thawing cycles to cause
cell death (Argon gas)

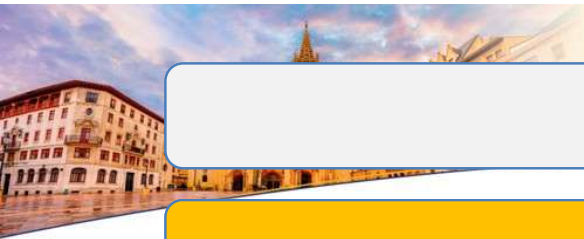
N=10

- No major complications were observed after the operation
- Tumor diameter 49mm → 46mm (3m)
- CA19-9 levels 347.5 → 165 (3m)
- Average pain scores 6.9 → 1.3 (1w)



Cryoablation

Wu Y, Jpn J Radiol. 2022



Locoregional therapies for PDAC

Energy based

Ablative

Non thermal



IRE

Radiotherapy



SBRT



Braq
P32

Locoregional therapies for PDAC

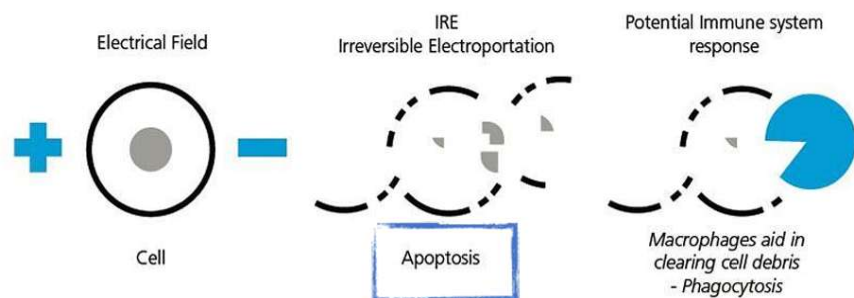
Energy based

Ablative

Laparotomía
Percutáneo



IRE



Mínimo efecto sobre estructuras circundantes fuera del radio de acción.

Active, not recruiting

A Pivotal Study of Safety and Effectiveness of NanoKnife IRE for Stage 3 Pancreatic Cancer (DIRECT)

ClinicalTrials.gov ID [NCT03899636](#)

Sponsor [Angiodynamics, Inc.](#)

Not yet recruiting

AG Plus Nimotuzumab Sequential Irreversible Electroporation Ablation for Locally Advanced Pancreatic Cancer

ClinicalTrials.gov ID [NCT06938503](#)

Sponsor [Tianjin Medical University Cancer Institute and Hospital](#)

Recruiting

Intra-tumoral Mitazalimab (CD40 Antibody) With Irreversible Electroporation (IRE) in Locally Advanced Pancreas Cancer

ClinicalTrials.gov ID [NCT06205849](#)

Sponsor [University of California, San Diego](#)

Not yet recruiting

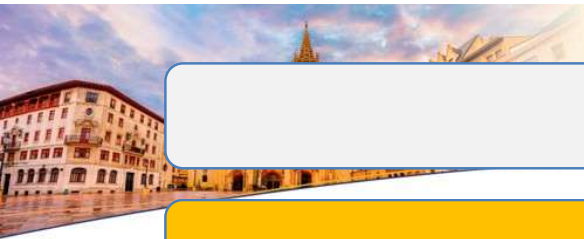
Irreversible Electroporation Ablation Combined With Anti-PD(L)1 Therapy for Locally Advanced Pancreatic Cancer

ClinicalTrials.gov ID [NCT06677762](#)

Sponsor [Ruijin Hospital](#)

Marcellier, Clin Trans GE 2025

Irreversible electroporation



Locoregional therapies for PDAC

Energy based

Ablative

Non thermal

Radiotherapy



SBRT



Braq
P32



PDAC

R0/R1

R

BL

LA (UR)

M1

Adjuvant

Neoadjuvant

1L

2L

RTOG 0848

Preopanc

Conko-007

LAP-07

Preopanc-2

ESPAC 5FU

A021501

EBRT 36 Gy (15 x 2,4)
+ Gem 1000mg/m2 d1,8,15

SBRT 33-40Gy (5 sessions) HIGRT
25Gy (5x5) "fiducial"
Hypofractionated image guided

IMRT o 3DRT 50,4Gy (28x1,8)
+ Gem 300 mg/m2 d1,8,15,22,29

EBRT 50,4Gy (28x1,8)
+ Cape 830mg/m2/12h

EBRT 54Gy (30x1,8)
+ Cape 800mg/m2/12h

Locoregional therapies for PDAC

Energy based

Ablative

X-RT

Magnetic resonance image guided RT (MRg



Stereotactic Magnetic resonance image Adaptive
guided RT (SMART)

SMART (Ph2NR)

50 Gy in 5 fractions (BED10 = 100Gy)
N=136 (77 LA, 59 BL) After CT
Acute GI TRAEs GI 0%
2yOS 40.5% (Sx) vs 27% (Non Sx)

- N=68 LAPC → mFFN x8
→ SABR (n=34) vs IRE (n=34)
- mOS 16.1m vs 12.5m (nes)
 - Stop for futility.
 - G3-4 AEs 16% vs 25% (nes)

SBRT

CROSSFIRE (Ph2R)

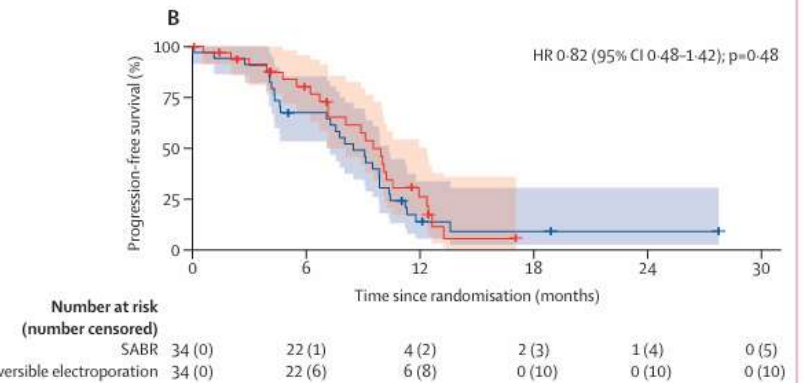
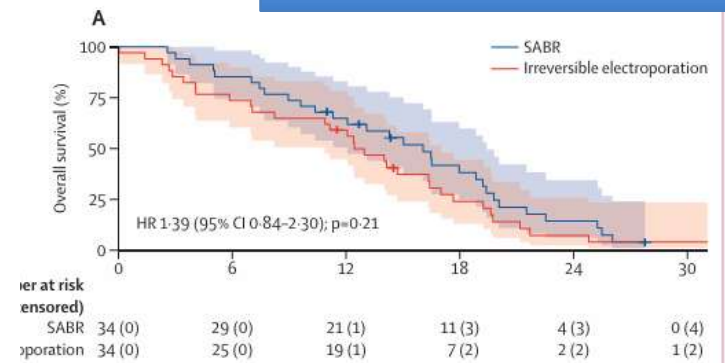


Figure 2: Kaplan-Meier curves for overall survival (A) and progression-free survival (B)
SABR=stereotactic ablative body radiotherapy. HR=hazard ratio.

Timmer, Lancet Gastroenterol Hepatol 2024

Locoregional therapies for PDAC

• **CE Marking and MDR:** OncoSil™ received CE Marking approval based on the EU Medical Device Regulation (MDR) in January 2025, providing marketing authorization across the EU and UK.



MDR Certification - Regulation
(EU) 2017/745 on Medical Devices

2025 ASCO
ANNUAL MEETING

Non thermal

Radiotherapy



Braq
P32

N=25 LAPC (March 2022-January 2025)

- Gemcitabine (± nab-paclitaxel) + OncoSil
- Tumour size 31.5 mm
- mFU=17.2 months
- 2 AE (G1 abdominal pain, G2 asthenia)
- 4/25 (16%) Surgery (3 R0 + 1 R1)
- mPFS= 8.4
- mOS= 13.8 months
- 12/25 (48%) patients alive after this FU period

GASTROINTESTINAL CANCER—GASTROESOPHAGEAL, PANCREATIC, AND HEPATOBIILIARY

e16455

Publication Only

Experience of 25 patients treated with echoendoscopically implanted ^{32}P micro-particles associated with chemotherapy in locally advanced pancreatic adenocarcinoma.

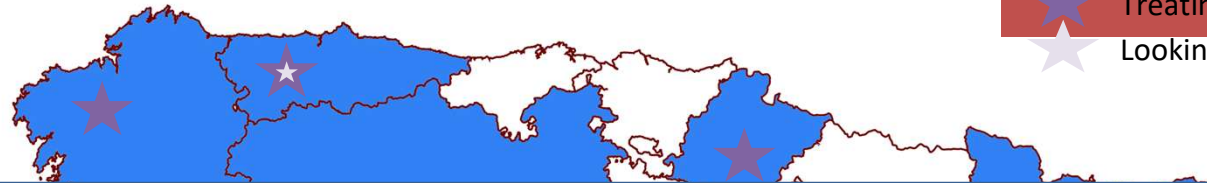
Carmen Guillen-Ponce, Ignacio Juez, Victoria Lopez-Gomez, Sonia Candamio Folgar, Ignacio Navales, Rebeca Chulvi, Marisol Huerta, Alejandra Giménez, Fayna Armas, Jorge Adeva, Maria Purificacion Rodriguez Cernuda, Mariano Ponz-Sarvisé, Rafael Álvarez, Ana Garcia Garcia De Paredes, Javier Zamora; Medical Oncology Department, Ramón y Cajal University Hospital. IRYCIS, Madrid, Spain; Hospital Universitario de Fuenlabrada, Madrid, Spain; Hospital Universitario Ramón y Cajal, Madrid, Spain; Complejo Hospitalario Universitario de Santiago, Santiago De Compostela, Spain; Vall d'Hebron University Hospital, Barcelona, Spain; Medical Oncology Service, Doctor Peset University Hospital, FISABIO, Valencia, Spain; Department of Medical Oncology, INCLIVA Biomedical Research Institute, University of Valencia, CIBERONC, Instituto de Salud Carlos III, Valencia, Spain; Department of Medical Oncology, University Hospital La Fe, Valencia, Spain; Hospital Universitario Insular de Gran Canaria, Las Palmas De Gran Canaria, Spain; Department of Medical Oncology Hospital 12 de Octubre, Madrid, Spain; Hospital Clínico Universitario de Valladolid, Valladolid, Spain; Clínica Universidad de Navarra, Pamplona, Spain; CIOCC HM Sanchinarro Hospital, Madrid, Spain; Gastroenterology Department, Hospital Universitario Ramón y Cajal, IRYCIS, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain; Unidad de Bioestadística, Hospital Universitario Ramón y Cajal, IRYCIS, Madrid, MADRID, Spain



Current Spanish situation : 75 treated patients

XXXIII SIMPOSIO
INTERNACIONAL
INTERNATIONAL
SYMPOSIUM

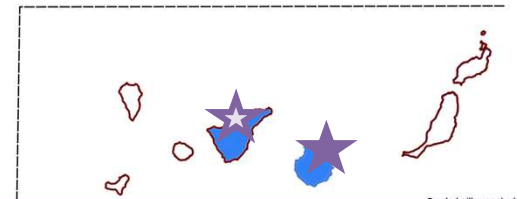
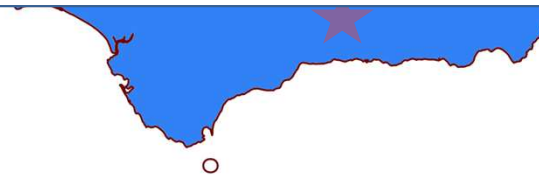
- HU Santiago de Compostela
- HU Fuenlabrada
- HU Doctor Peset



★ Treating hospitals
★ Looking for 1st patient

- Fase **II aleatorizada** (Reclutamiento finalizado HUVH)
 - **TRIPP-FFX / NCT05466799 (Fase II):**
 - FOLFIRINOX $\pm$ **OncoSil** en LAPC irresecable.
 - Objetivo: **seguridad/eficacia** adicional del P-32 sobre FOLFIRINOX. Resultados aún no publicados

- HU Nuestra Señora de la Candelaria
- HU Toledo
- HUCA
- HU Virgen de la Arrixaca
- HU Reina Sofía





Varón 68a. DM2 (mal control metabólico). HTA. DL.

- **Nov 24: Epigastralgia y síndrome constitucional**
- **Neoplasia caput pancreas infiltra AHC (>180°) y CEPm, N+/-**
- **Estenosis infranqueable de apex bulbar.**
- **Dic 24 CdT: Irresecable. Se desestima cirugía.**
- **USE-PAAF: ADC.**



Dic/24: Cx gastroenteroanastomosis (20/12/24).

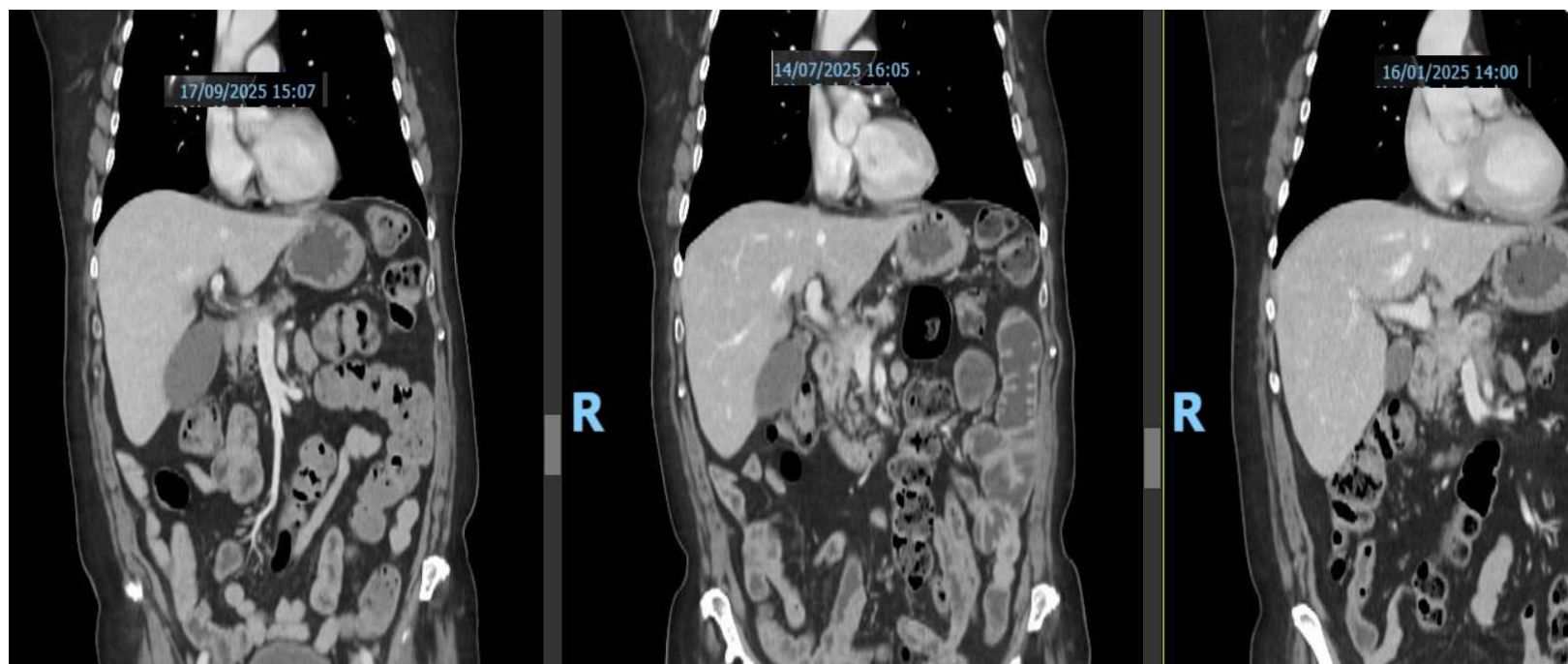
Ene/25-Jul/25: 1L EC Oncosil: mFFN (rama experimental) x 12.

- **Feb25 P32.**

Mar 25 EE. Posible trombosis asociada a picc (HBPM)

- **Jul/25 2ª P32.**

Jul/25-Sep/25: W/W.





Sep/25: EE. Exploración sin cambios significativos con respecto a estudio previo. Enfermedad estable.

- **CdT HBP 07/10/2025: Lesion pancreatica tiene menos realce y se delimita mejor, sin claro plano sepracion del estomago, calibre de VMS normal, persiste rodete de HA comun. Persiste la adenopatía del tronco celiaco. Impresiona de mejoría venosa pero persiste rodete peri arteria hepática común. Explorar en quirófano.**

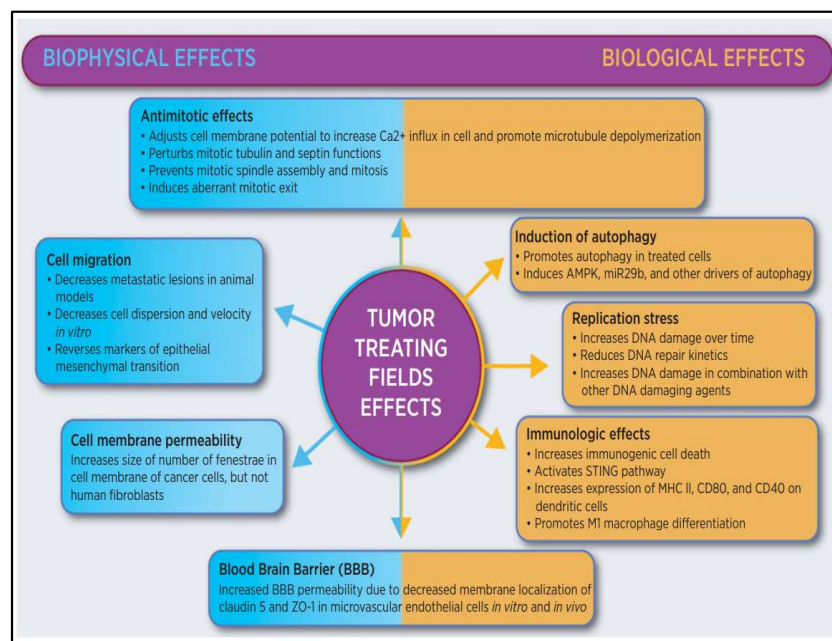
04/11/2025: Cx, se expora hilio hepático y zona de manguito a arteria hepática. No se considera que infiltre la arteria, se decide proceder con la cirugia. DPC. AP pendiente.

Locoregional therapies for PDAC

Energy based

Non ablative

Non thermal



TTFs

TTFs

Alternating
Electric fields

Locoregional therapies for PDAC

TTFs

Energy based

Non thermal

Non ablative

XXXIII SIMPOSIO
INTERNACIONAL
INTERNATIONAL
SYMPOSIUM
11 - 12 DE DICIEMBRE DE 2025
OVIEDO

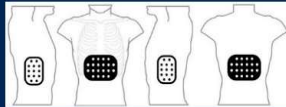


Day Layouts – continued

E) Left lumbar-shifted to the left with the superior discs row at the inferior border of the 10th costal cartilage



G) Large epigastric- centered with the superior discs row at the level of the xiphoid



F) Right lumbar-shifted to the right with the superior discs row at the inferior border of the 10th costal cartilage



H) Large umbilical- centered with the inferior discs row below the umbilicus



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ASCO AMERICAN SOCIETY OF
CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER



• Vincent Picozzi

PANOVA-3

Key Takeaway Points/Conclusions

LBA3

PANOVA-3: Pain and quality of life (QoL) outcomes with Tumor Treating Fields (TTFields) therapy in patients with locally advanced pancreatic adenocarcinoma (LAPC)

T. Macarulla Mercade¹, V.J. Picozzi², S. Chandana³, B. Melichar⁴, A. Kasi⁵, J. Gang⁶, J. Gallego Plazas⁷, C. de la Fouchardiere⁸, A. Bullock⁹, C. Hao¹⁰, L.S. Wyrwicz¹¹, A. Osipov¹², T. Dragovich¹³, W. Lee¹⁴, K. Feeney¹⁵, P. Philip¹⁶, M. Ueno¹⁷, E. Van Cutsem¹⁸, T. Seufferlein¹⁹, H. Babiker²⁰

PANOVA-3 establishes TTFields with GnP as a potential new standard paradigm for unresectable LA-PAC

*as the time to a ≥ 20 -point increase from baseline on a patient-reported visual analogue scale for pain or death.
GnP, gemcitabine/nab-paclitaxel; LA-PAC, locally advanced pancreatic adenocarcinoma; OS, overall survival; TTFields, Tumor Treating Fields.

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Locoregional therapies for PDAC

Transarterial microperfusion

Other

Non ablative

Non thermal

Thermal



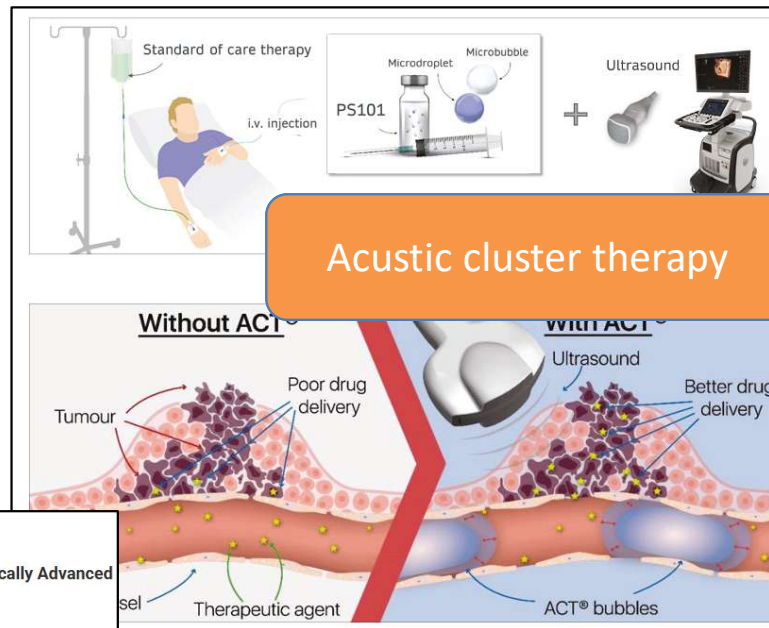
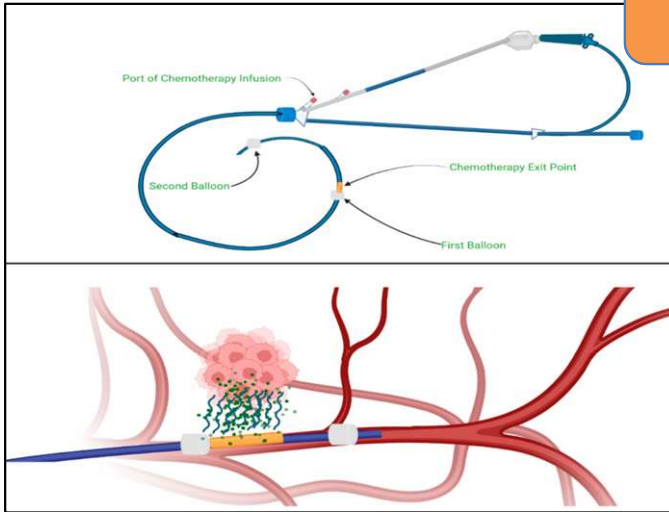
Arterial infusion



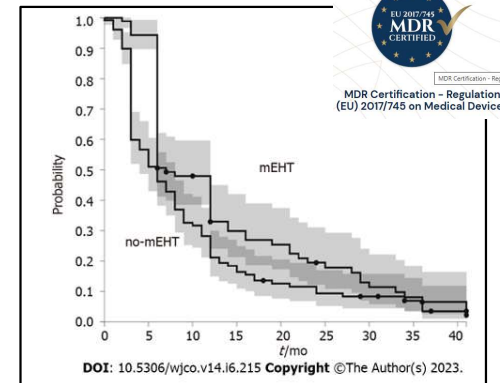
ACT



EHT



Acoustic cluster therapy



OncothermiaTM

Loco-regional modulated electro-hyperthermia (mEHT) device

Recruiting 1
Intra-arterial Gemcitabine vs. IV Gemcitabine and Nab-Paclitaxel Following Radiotherapy for LAPC (TIGeR-PaC)
ClinicalTrials.gov ID NCT03257033
Sponsor RenovorRx

Recruiting 1
Acoustic Cluster Therapy (ACT) With Chemotherapy for the Treatment of Locally Advanced Pancreatic Cancer (ENACT)
ClinicalTrials.gov ID NCT06850623
Sponsor EXACT Therapeutics AS

Locoregional therapies for PDAC

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Energy based

Other

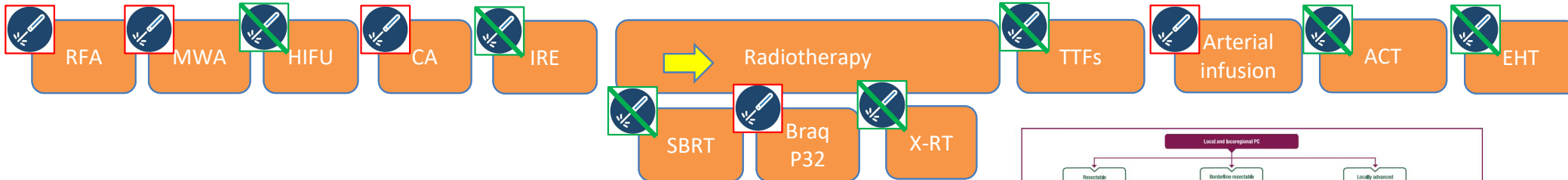
Ablative

Non ablative

Thermal

Non thermal

Thermal



ESMO guidelines PDAC 2023

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

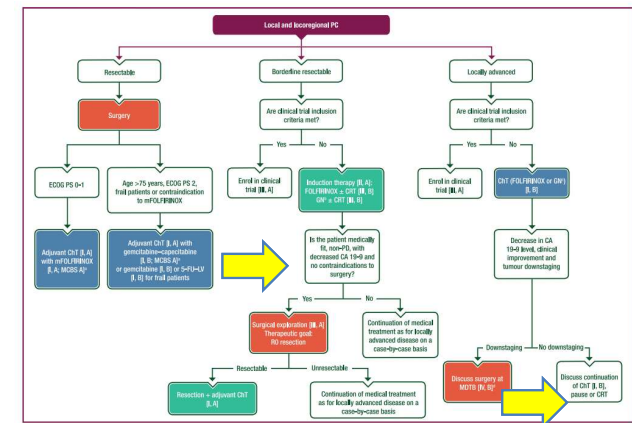
ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Pancreatic cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up*

T. Conroy^{1,2}, P. Pfeiffer³, V. Vilgrain^{4,5}, A. Lamarca⁶, T. Seufferlein⁷, E. M. O'Reilly⁸, T. Hackert⁹, T. Golan¹⁰, G. Prager¹¹, K. Haustermans¹², A. Vogel¹³ & M. Ducreux¹⁴, on behalf of the ESMO Guidelines Committee*

*Department of Medical Oncology, Institut de Cancérologie de Lorraine, Vandœuvre-lès-Nancy; ²APÉMAC, Équipe MICs, Université de Lorraine, Nancy, France; ³Department of Oncology, Odense University Hospital, Odense, Denmark; ⁴Centre de Recherche sur l'Inflammation U1149, Université Paris Cité, Paris; ⁵Department of Radiology, Beaulieu Hospital, APHP Nord, Clichy, France; ⁶Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK; ⁷Department of Internal Medicine I, Ulm University Hospital, Ulm, Germany; ⁸Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, USA; ⁹Department of General, Visceral and Thoracic Surgery, University Hospital Hamburg-Eppendorf, Hamburg, Germany; ¹⁰Gastrointestinal Unit, Oncology Institute, Sheba Medical Center, Tel Aviv University, Tel Aviv, Israel; ¹¹Department of Medicine I, Division of Oncology, Medical University of Vienna, Vienna, Austria; ¹²Department of Radiation Oncology, University Hospitals Leuven, Leuven, Belgium; ¹³Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany; ¹⁴Université Paris-Saclay, Gustave Roussy, Inserm Unité Dynamique des Cellules Tumorales, Villejuif, France



Conroy, Ann Onc 2023

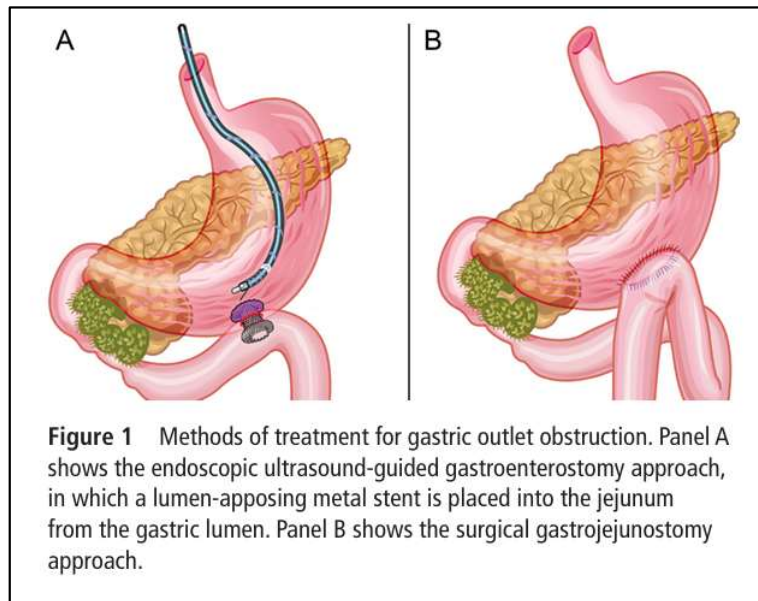


Approval regulation for medical devices

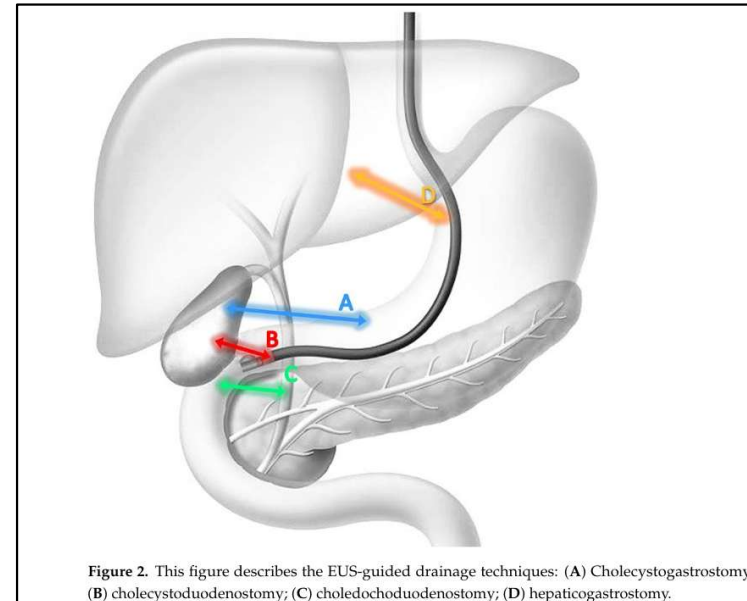
Medical Device Approval Regulation

Feature 	US Food and Drug Administration (FDA)	European Medicines Agency (EMA)
Regulatory Framework	Regulated by the FDA (specifically the Center for Devices and Radiological Health, CDRH) through different pathways (e.g., Premarket Approval (PMA), 510(k) clearance) depending on risk. Requires a clear set of uniform standards and evidence.	Devices are regulated differently than drugs and historically involved various "Notified Bodies" with less uniform standards across the EU. The new Medical Device Regulation (MDR) has strengthened requirements and conformity assessments.
Clinical Data	Clinical trial data requirements are generally limited for most devices, with data often submitted from lab tests, literature reviews and small studies. Breakthrough Device Designation can accelerate the path for novel devices like the OncoSil device for pancreatic cancer.	Requires devices to prove they are safe and perform as intended, but historically had no uniform standards or evidence requirements across Notified Bodies. The new MDR aims for more stringent clinical evidence requirements.

Paliative procedures



Gastric outlet



Biliary obstruction



Take home messages

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- Surgery and Radiotherapy remains SoC
- TTFs improves OS in LAPC
- Novel ways of RT, such as Oncosil, looks promising (TRIPP-FFX!)
- Indirect effect of these therapies may synergize with systemic treatments such as immunotherapy
- Always look for balance risks / benefits and resources.
- Oncologists should be opened-minded but also critical.
- Regulatory approval mechanisms for medical devices differ from drugs and between FDA and Europe (CE).