30º CONGRESO SETH

22-24 octubre 2025
Auditorio de la Diputación de Alicante, ADDA

SOCIEDAD ESPAÑOLA DE TRASPLANTE HEPÁTICO

ORGANIZAN

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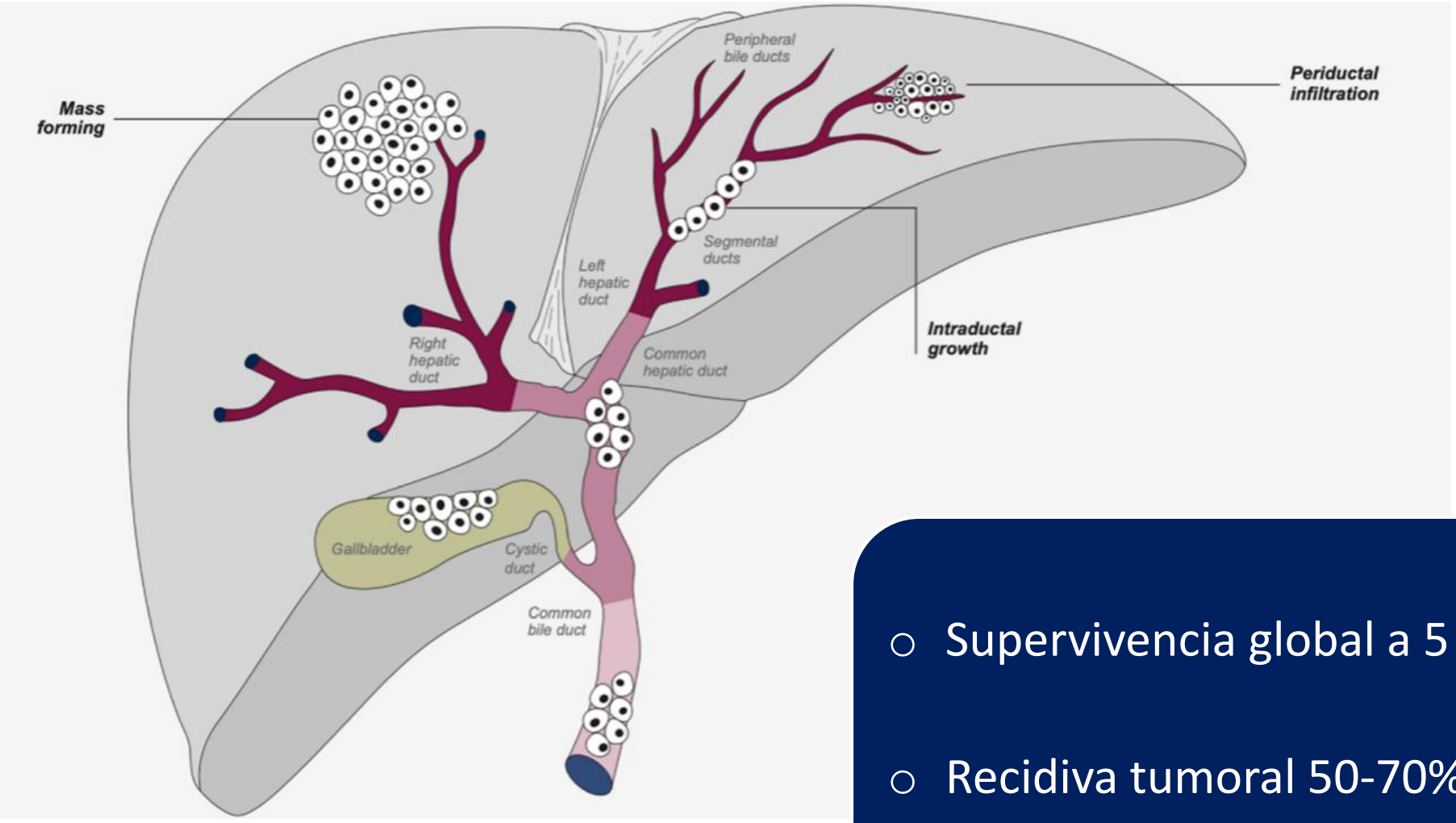
Hospital General Universitario Dr. Balmis

GENERALITAT VALENCIANA

www.sethepatico.org
@SETHepatico

SELECCIÓN PARA TRASPLANTE HEPÁTICO EN PACIENTES CON COLANGIOCARCINOMA. ¿DÓNDE ESTAMOS?

Cristina Dopazo, MD/PhD
Unidad de Cirugía HBP y Trasplantes
Servicio de Cirugía General y del Aparato Digestivo
Hospital Universitario Vall d´Hebron (Barcelona)



10-40% son resecables

- Supervivencia global a 5 años 25-40%
- Recidiva tumoral 50-70%

D Zhang et al. Eur J Cancer 2024; 203: 114046

EASL-ILCA Guidelines. J Hepatol 2023 79:181-208

La resección es el único tratamiento curativo

01

Factores relacionados con el paciente:

ECOG, performance status

02

Factores técnicos y anatómicos:

Tumor resecable

Suficiente remanente hepático (función y volumen)

03

Factores Oncológicos:

Tumores múltiples

Grandes lesiones

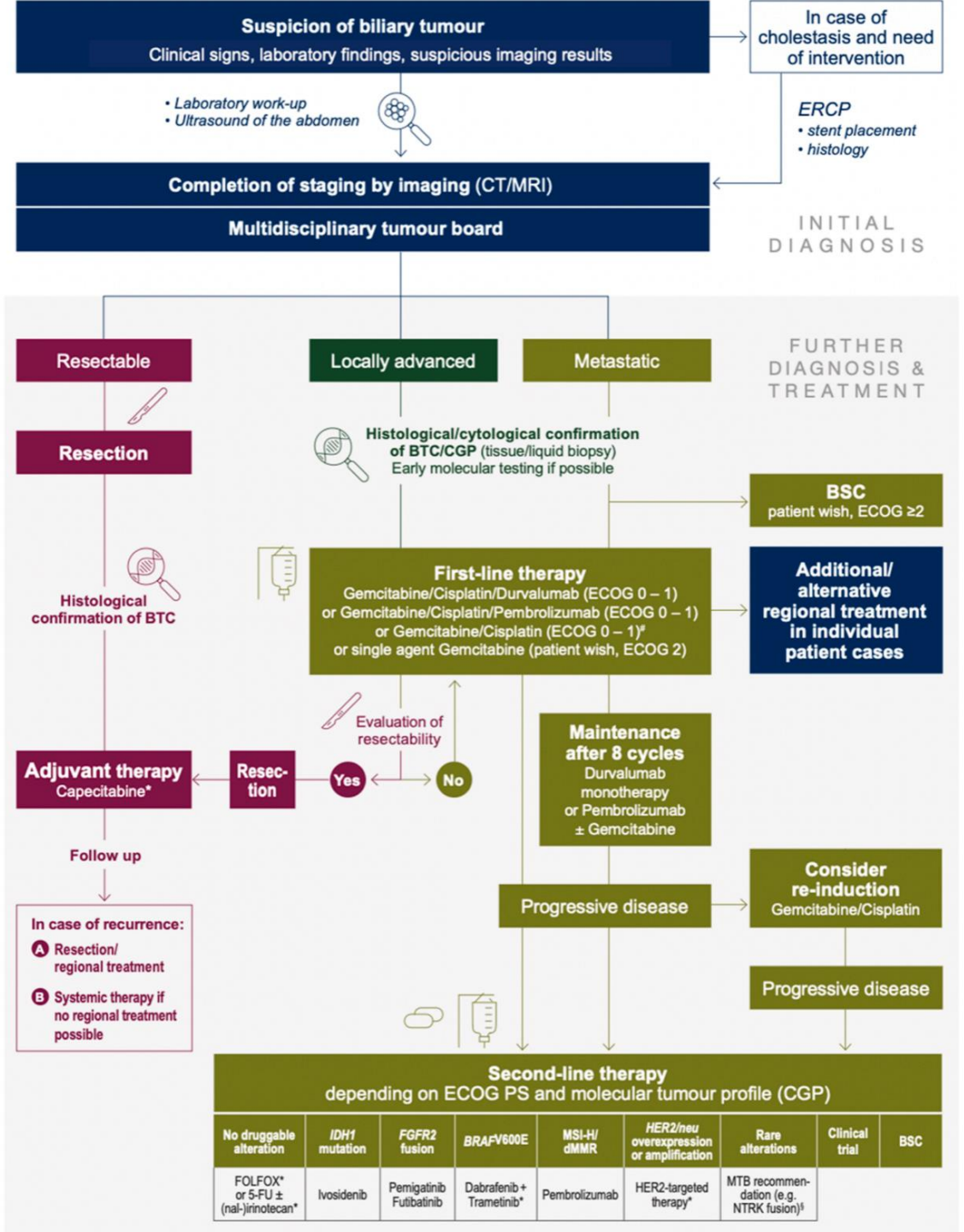
Invasión micro/macrovascular

Afectación linfática

Diferenciación tumoral

Biomarcadores

EASL-ILCA Guidelines. J Hepatol 2023 79:181-208



D Zhang et al. Eur J Cancer 2024; 203: 114046

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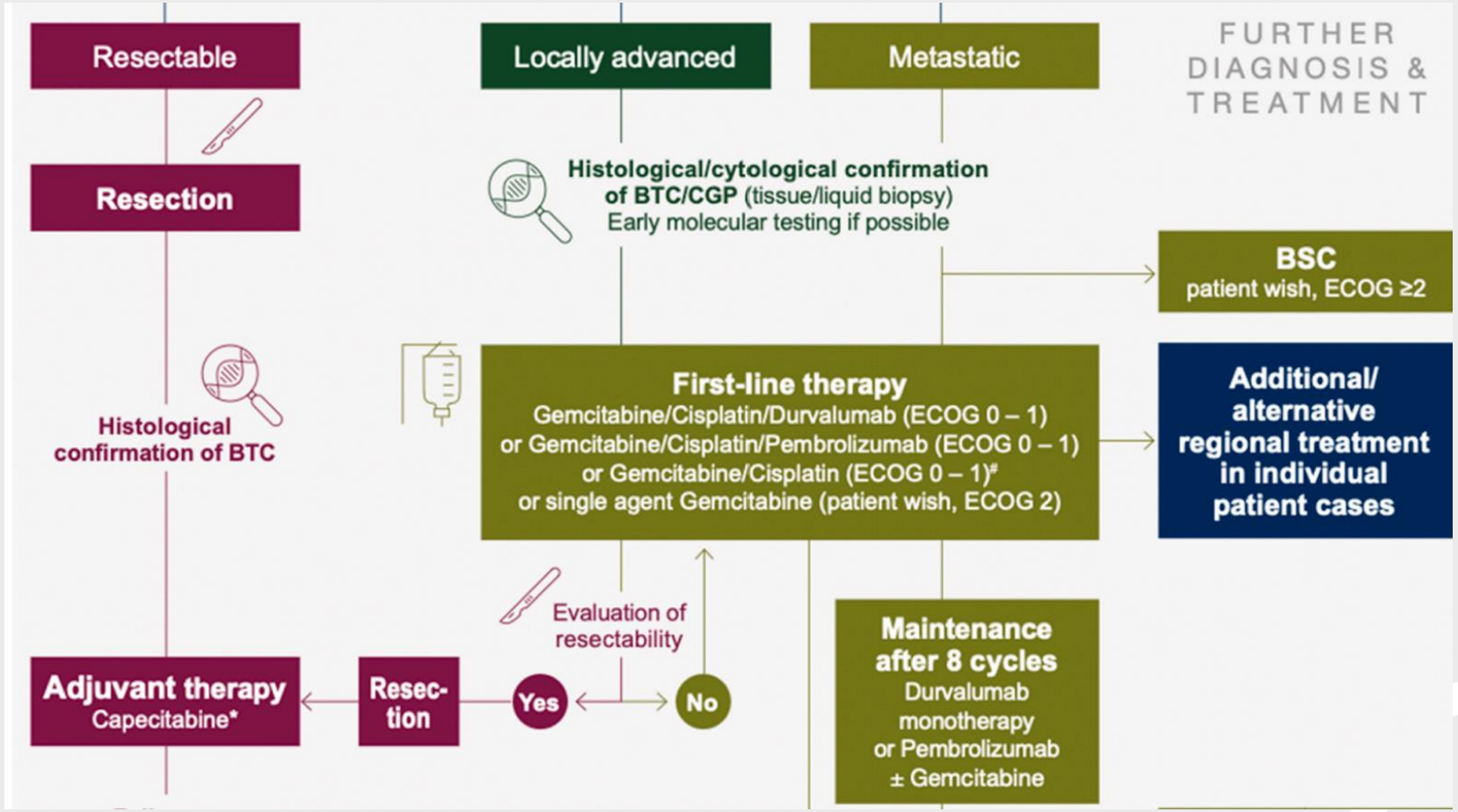


LIVER TRANSPLANT

QUÉ ES COLANGIOCARCINOMA LOCALMENTE AVANZADO O IRRESECABLE?

Colangiocarcinoma intrahepático CCAi

No hay "Criterios de Milan":

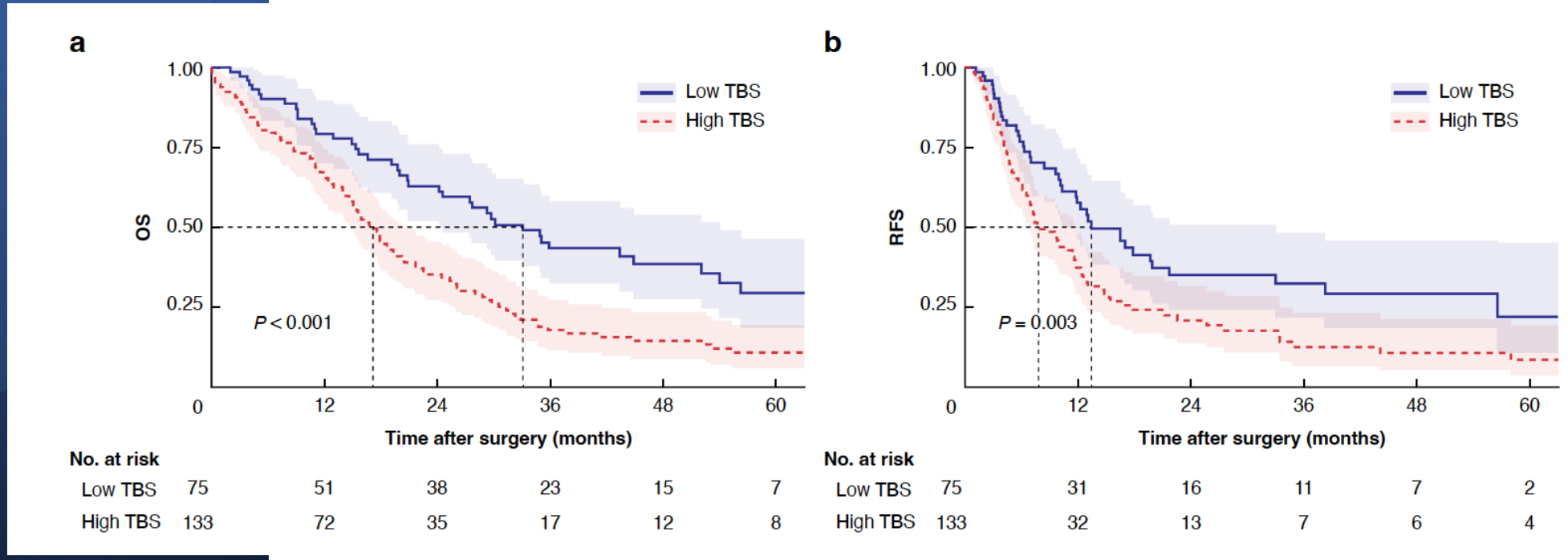
Lesiones múltiples

Gran tamaño y riesgo de margen positivo

Cirrosis hepática

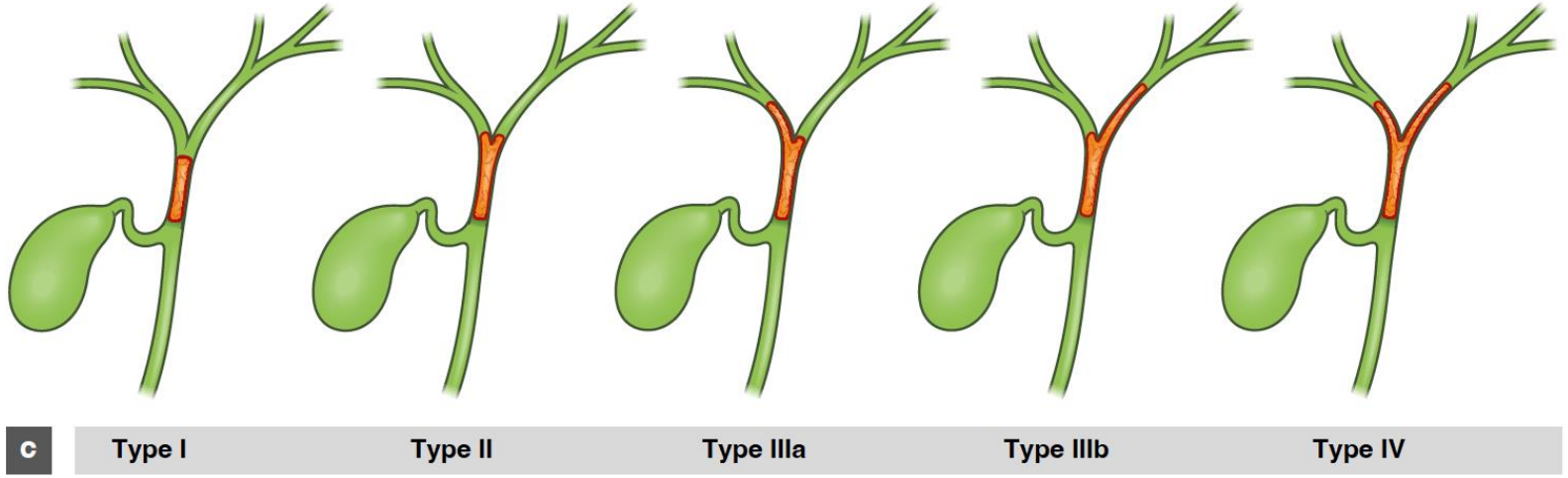
Afectación linfática

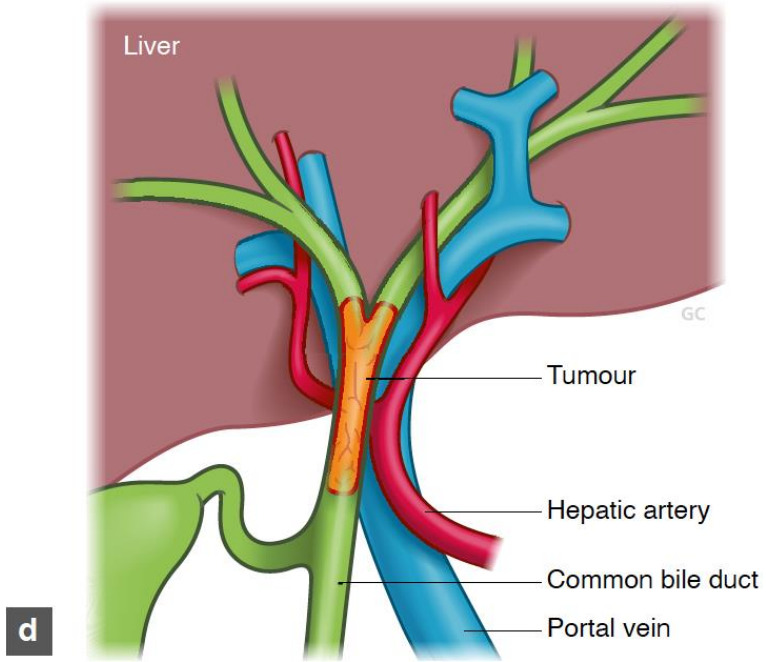
Estado mutacional de mal pronóstico (BRAF, K-Ras)



Jun Kawashima et al. *BJS*, 2025, znaf050

Colangiocarcinoma perihiliar CCAp





Margen positivo
Insuficiente remanente hepático
Afectación vascular contralateral
Afectación linfática

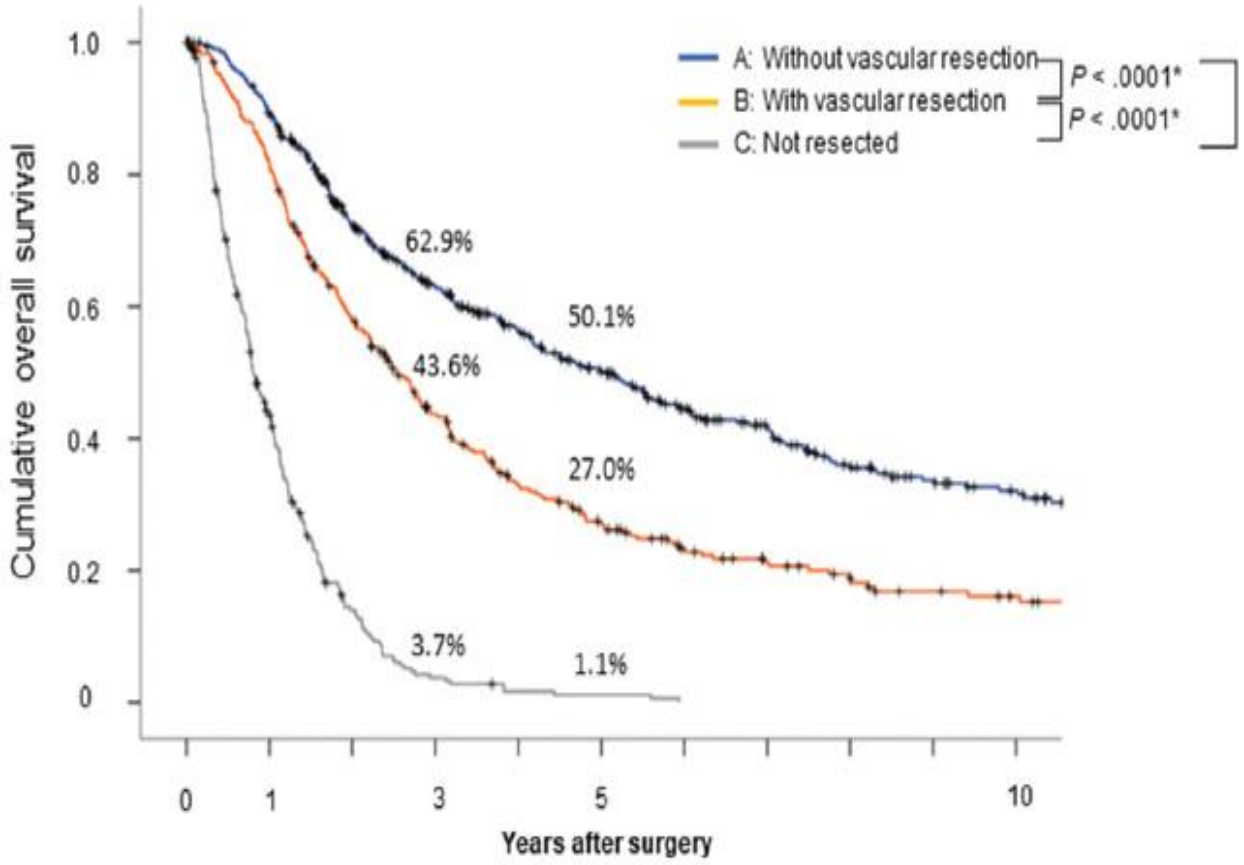
C Sturesson et al. *BJS*, 2025, znae329

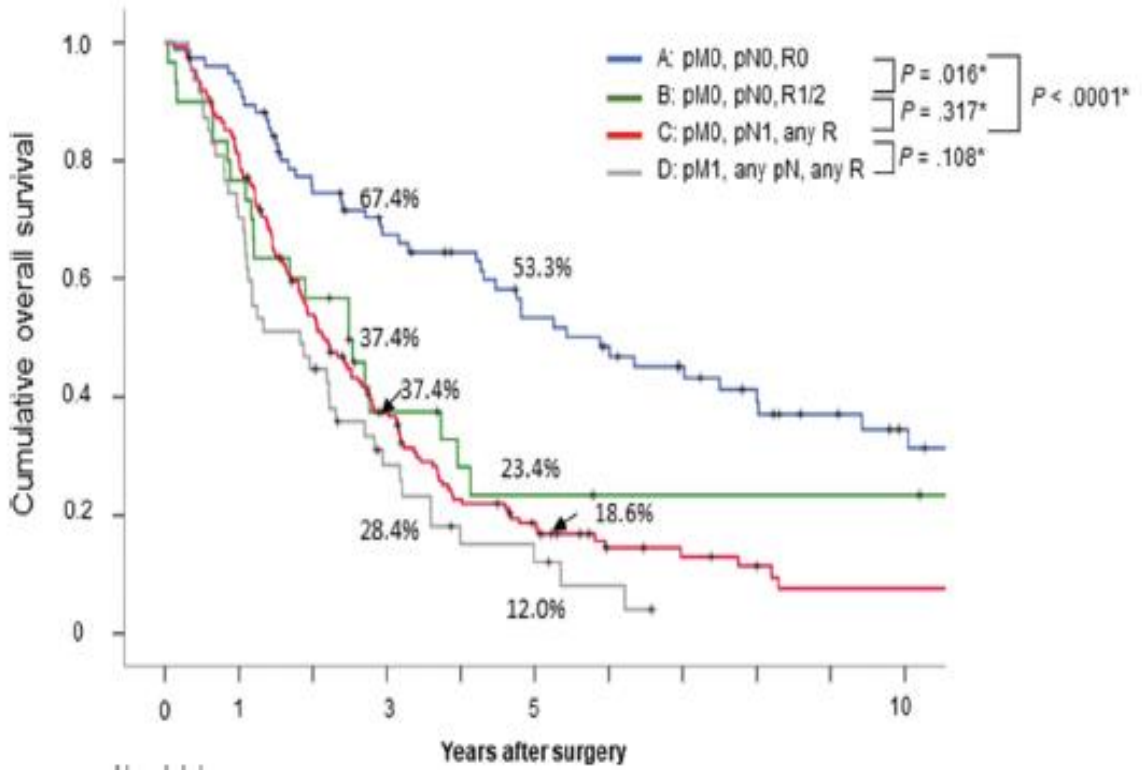
Ann Surg 2022; 275: 382-390

Combined Vascular Resection for Locally Advanced Perihilar Cholangiocarcinoma

Takashi Mizuno, MD, Tomoki Ebata, MD,* Yukihiro Yokoyama, MD,* Tsuyoshi Igami, MD,* Junpei Yamaguchi, MD,* Shunsuke Onoe, MD,* Nobuyuki Watanabe, MD,* Yuzuru Kamei, MD,† and Masato Nagino, MD*✉*

Resección vascular





¿Qué es claramente **NO** resecable?

Pacientes con enfermedad metastásica

o afectación linfática a distancia

Tratamiento sistémico → 12meses

Enfermedad limitada al hígado SIN afectación linfática:

- Cirrosis hepática avanzada
- Lesiones múltiples bilaterales (≥ 4)
- Afectación vascular
- Insuficiente remanente hepático +/-elevada probabilidad de margen positivo

Podemos ofrecer una alternativa

Podemos mejorar la supervivencia

?

Trasplante hepático es una opción factible si...

Si mejora la supervivencia del paciente
(al menos similar a aquellos resecables)

⬇

Beneficio individual para el paciente

Si no impacta en la lista de espera para otras indicaciones con supervivencia claramente establecida

⬇

Beneficio colectivo para la población trasplantada

Si podemos mejorar la selección del paciente

Sapisochin G et al. Ann Surg 2021; 273: 483-493

Trasplante hepático es una opción factible si...

Si mejora la supervivencia del paciente
(al menos similar a aquellos resecables)

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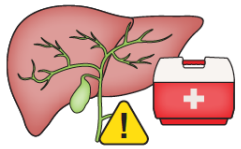
Sapisochin G et al. Ann Surg 2021; 273: 483-493

CCAi



Currently not a standard therapy!

Liver transplant (LT)

Retrospective studies are now being conducted with more stringent selection criteria. One major study found a 5-year overall survival of 65% after transplantation for single tumors ≤2 cm.

Selection

Use of LT in iCCA and selection criteria for these patients is under active study. LT is considered for patients that are unresectable due to location, liver dysfunction, or bilobar disease

Indications

- Unresectable (ex. cirrhotic FLR)
- Early stage iCCA (Single tumor ≤2 cm)
- Locally advanced iCCA
  - Response to neoadjuvant
  - Favorable tumor biology

Contraindications

- Vascular invasion
- Extrahepatic disease
- Lymph node spread
- Locally advanced iCCA
  - No response to neoadjuvant
  - Unfavorable tumor biology

Surgery

Consider the source of a donor liver and pre-transplant lymph node procurement

Living donor liver transplant *vs.* Deceased donor liver transplant

Portal lymphadenectomy — Staging and prognosis

EASL-ILCA Guidelines. J Hepatol 2023 79:181-208

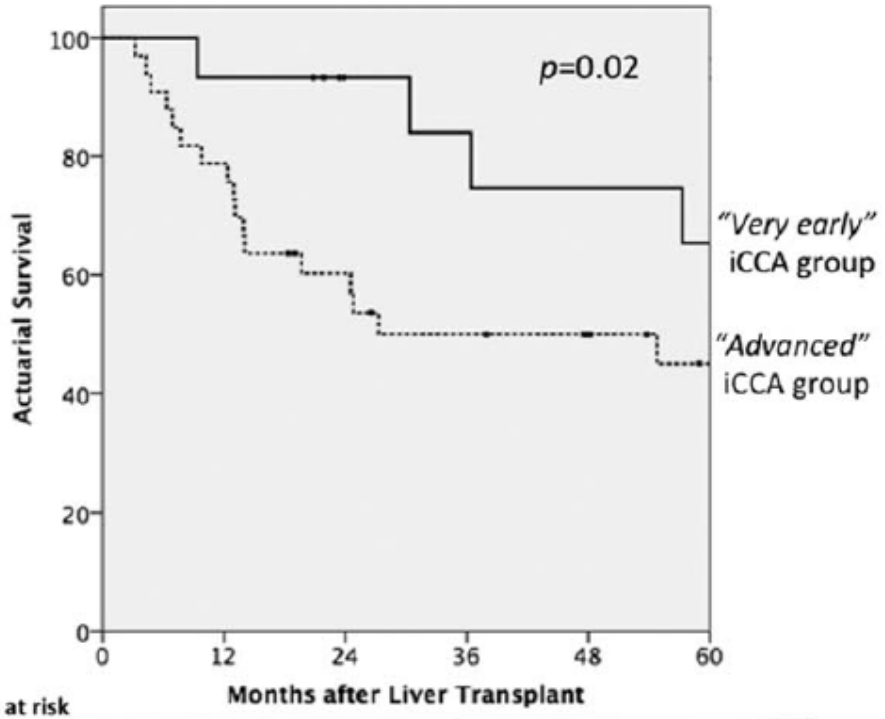
Tumor único ≤2cm en pacientes cirróticos
Estudios retrospectivos

SG 65% a 5 años

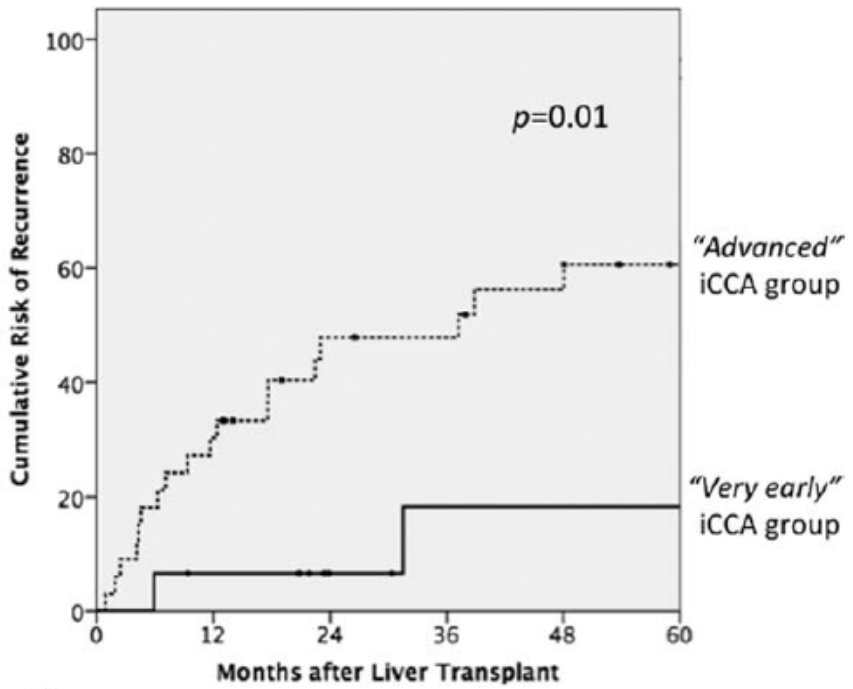
Liver Transplantation for "Very Early" Intrahepatic Cholangiocarcinoma: International Retrospective Study Supporting a Prospective Assessment

Hepatology 2016; 64: 1178

G. Sapisochin,[1] M. Facciuto,[2] L. Rubbia-Brandt,[3] J. Marti,[2] N. Mehta,[4] F.Y. Yao,[4] E. Vibert,[5] D. Cherqui,[5] D.R. Grant,[1] R. Hernandez-Alejandro,[6] C.H. Dale,[6] A. Cucchetti,[7] A. Pinna,[7] S. Hwang,[8] S.G. Lee,[8] V.G. Agopian,[9] R.W. Busuttil,[9] S. Rizvi,[10] J.K. Heimbach,[10] M. Montenovo,[11] J. Reyes,[11] M. Cesaretti,[12] O. Soubrane,[12] T. Reichman,[13] J. Seal,[13] P.T.W. Kim,[14] G. Klintmalm,[14] C. Sposito,[15] V. Mazzaferro,[15] P. Dutkowski,[16] P.A. Clavien,[16] C. Toso,[17] P. Majno,[17] N. Kneteman,[18] C. Saunders,[18] and J. Bruix[19]; on behalf of the iCCA International Consortium



Patients at risk						
"Very Early"	15	14	10	9	8	7
"Advanced"	33	26	18	14	12	8



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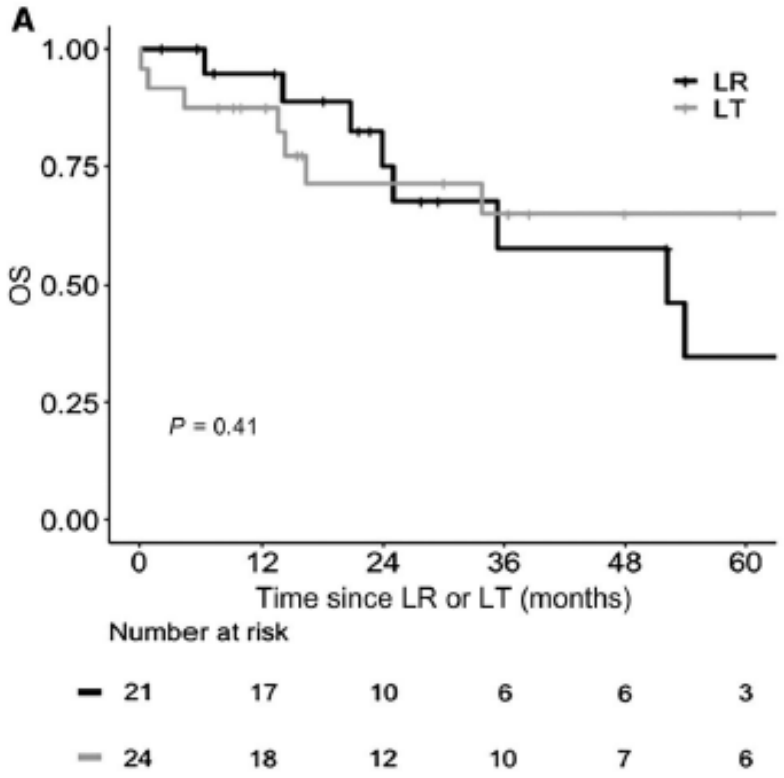
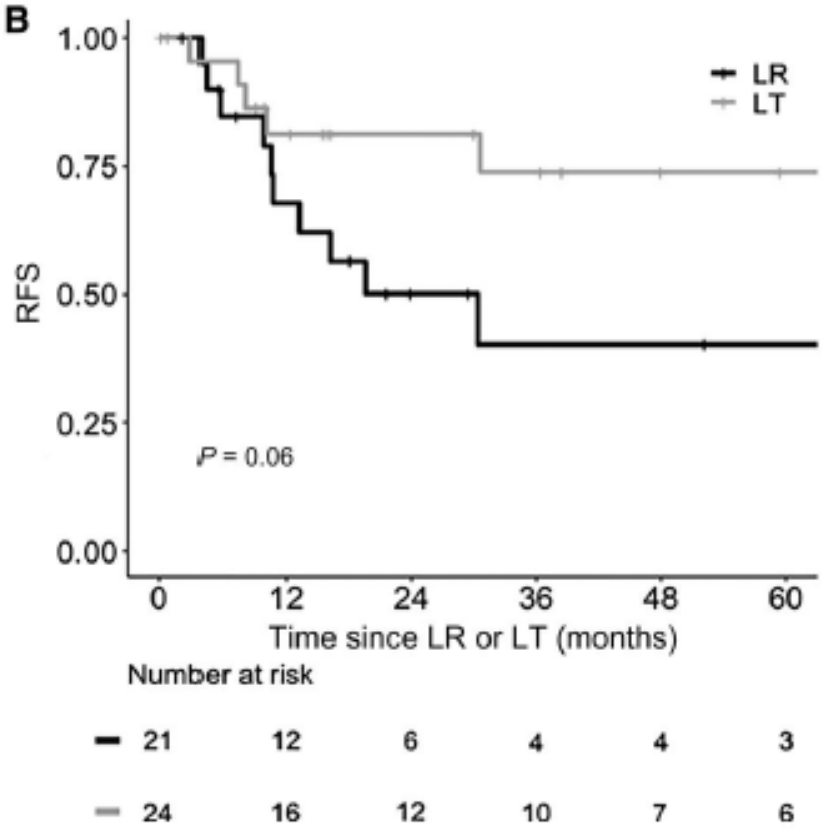
"Advanced"	33	23	14	13	10	6

Analysis of Liver Resection Versus Liver Transplantation on Outcome of Small Intrahepatic Cholangiocarcinoma and Combined Hepatocellular-Cholangiocarcinoma in the Setting of Cirrhosis

E de Martin, et al. Liver Transpl 2020; 26: 785





Tumors >2cm but ≤ 5cm

ORIGINAL CLINICAL SCIENCE—LIVER

Expanding Indications of Liver Transplantation in Spain: Consensus Statement and Recommendations by the Spanish Society of Liver Transplantation

Rodríguez-Perálvarez, Manuel MD, PhD[1]; Gómez-Bravo, Miguel Ángel MD, PhD[2]; Sánchez-Antolín, Gloria MD, PhD[3]; De la Rosa, Gloria MD[4]; Bilbao, Itxarone MD, PhD[5]; Colmenero, Jordi MD, PhD[6]

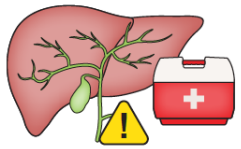
Author Information

Transplantation 105(3):p 602-607, March 2021. | *DOI:* 10.1097/TP.0000000000003281

6. Intrahepatic cholangiocarcinoma in patients with liver cirrhosis

6.1	In selected patients with portal hypertension and intrahepatic cholangiocarcinoma, LT could be considered only in the context of well-designed randomized trials	2B	53,54
6.2	The diameter of the tumor is tightly associated with post-LT recurrence. Only single-nodule tumors ≤2 cm without vascular invasion would be acceptable.	1B	53,55
6.3	Management of patients within the waiting list concerning prioritization and surveillance should mirror established protocols for hepatocellular carcinoma.	2C	N/A
6.4	Tumor progression (an increase of diameter beyond 2 cm, new nodules, vascular invasion, and significant elevation of Ca19.9 or extrahepatic spread) should motivate exclusion from the waiting list.	1C	N/A
6.5	Retransplantation is contraindicated in patients with tumor recurrence.	1C	N/A

CCAi



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Tumor único ≤2cm en pacientes cirróticos
Estudios retrospectivos

SG 65% a 5 años

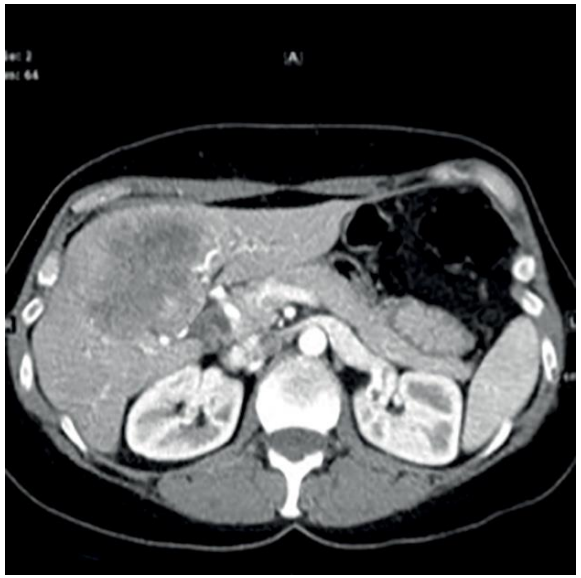
Tumores localmente avanzados sobre hígado sano
Estabilidad de respuesta tras 6 meses de quimioterapia

SG 57% a 5 años

Liver transplantation for locally advanced intrahepatic cholangiocarcinoma treated with neoadjuvant therapy: a prospective case-series

Lunsford KE, et al. Lancet Gastroenterol Hepatol 2018; 3:337-48

2010-2015
N=6
No limited in size or number
Without vascular invasion, positive regional lymph nodes or extrahepatic disease



Intrahepatic cholangiocarcinoma

Tumour characteristics

- Biopsy-proven cholangiocarcinoma
- Intrahepatic rather than periductal location
- Not amenable to surgical therapy
- No evidence of extrahepatic disease

Diagnostic criteria

- Triple-phase CT of the chest, abdomen, and pelvis
- MRI bone scan
- FDG-PET scan if serum cancer antigen 19-9 elevated
- Endoscopic ultrasound-guided biopsy of enlarged nodes

↓

Neoadjuvant chemotherapy

- First-line platinum-based therapy and gemcitabine
- Second-line chemotherapy for progression or intolerance
- Addition of targeted biologics on case-by-case basis

↓

Disease stability for at least 6 months on given regimen

- Repeat imaging every 3 months
- Stable or regressing disease
- No extrahepatic disease

↓

Liver transplantation

- Post-transplant adjuvant therapy for 4–6 months depending on explant pathology

LOCALLY ADVANCED DISEASE

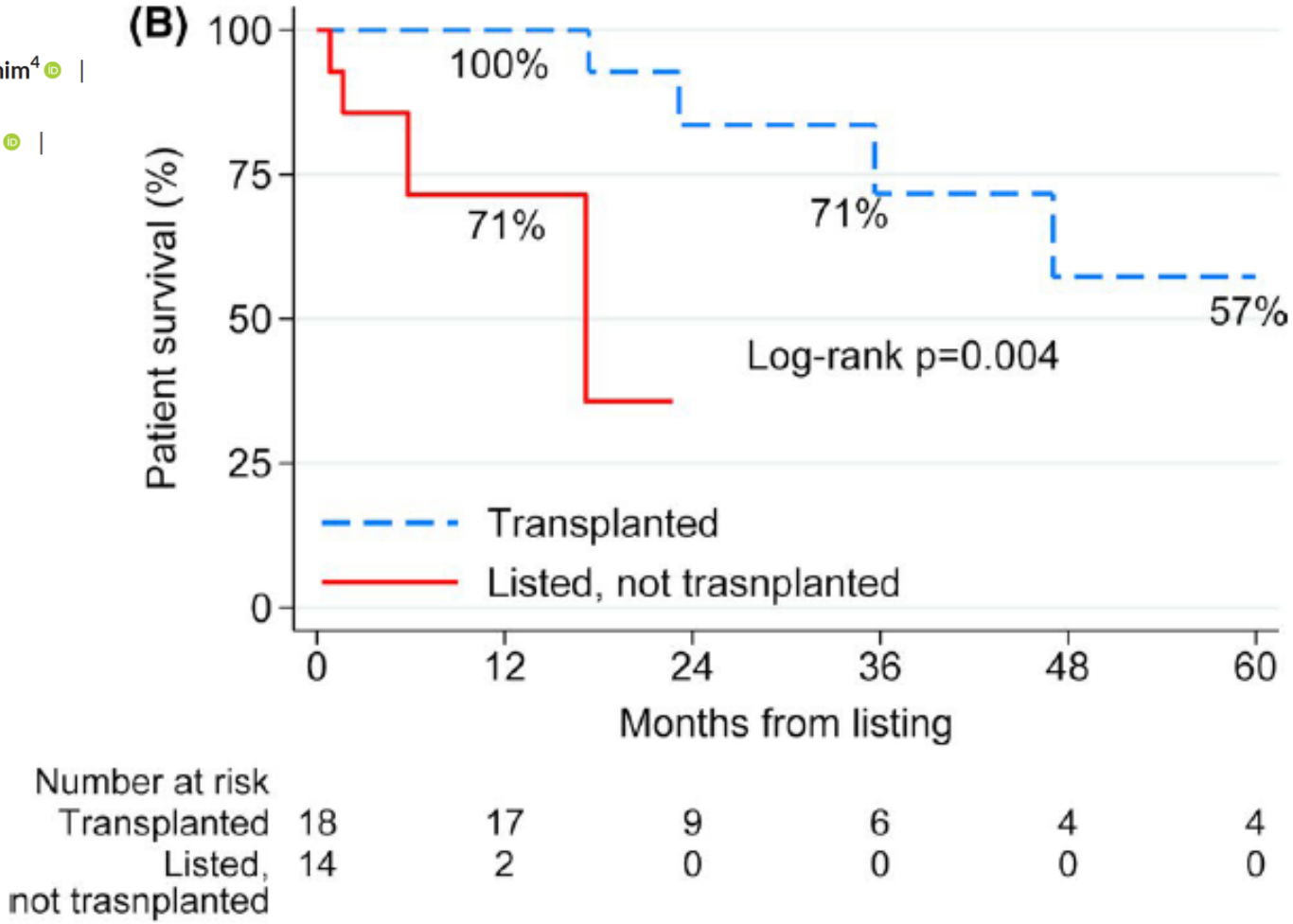
Survival following liver transplantation for locally advanced, unresectable intrahepatic cholangiocarcinoma

Robert R. McMillan[1] | Milind Javle[2] | Sudha Kodali[3] | Ashish Saharia[1] | Constance Mobley[1] | Kirk Heyne[4] | Mark J. Hobeika[1] | Keri E. Lunsford[5] | David W. Victor III[3] | Akshay Shetty[3] | Robert S. McFadden[3] | Maen Abdelrahim[4] | Ahmed Kaseb[2] | Mukul Divatia[6] | Nam Yu[7] | Joy Nolte Fong[1] | Linda W. Moore[1] | Duc T. Nguyen[6] | Edward A. Graviss[6] | A. Osama Gaber[1] | Jean-Nicolas Vauthey[8] | R. Mark Ghobrial[1]

Am J Transplant 2022;22: 823-832

Median number of lesions 2 (1-10)
Median size 8.5cm (2.9-20)
Median follow-up 26 months
38.9% of recurrence

FGFR y DNA damage repair pathways



CCAi

Liver biopsy should be considered mandatory.

Molecular profiling is important but not recommended for patient selection.

Indications:

1. Decompensated cirrhotic patients with iCCA after a period of observation and stability with no extrahepatic metastases and a lesion $\leq$ 3cm.
2. In non-cirrhotic patients, for those unresectable iCCA with no vascular invasion and no extrahepatic metastasis whose disease has at least 6 months of stability only under clinical protocols or clinical trials. Limitations in ion tumor size and number should be explored in prospective clinical trials.

S Khodali et al. Liver Transpl 2025; 31:815-831

28º Congreso
SETH SOCIEDAD ESPAÑOLA DE TRASPLANTE HEPÁTICO
SANTANDER

Estudio COLIN_TRANSPLANT
Colangiocarcinoma intrahepático localmente avanzado y trasplante hepático.
Estudio Nacional prospectivo multicéntrico.

Cristina Dopazo, PhD/MD

Servicio de Cirugía HBP y Trasplantes. Hospital Universitario Vall d´Hebron

@SETHepatico

CCAp

The Mayo Clinic Protocol

Inclusion Criteria

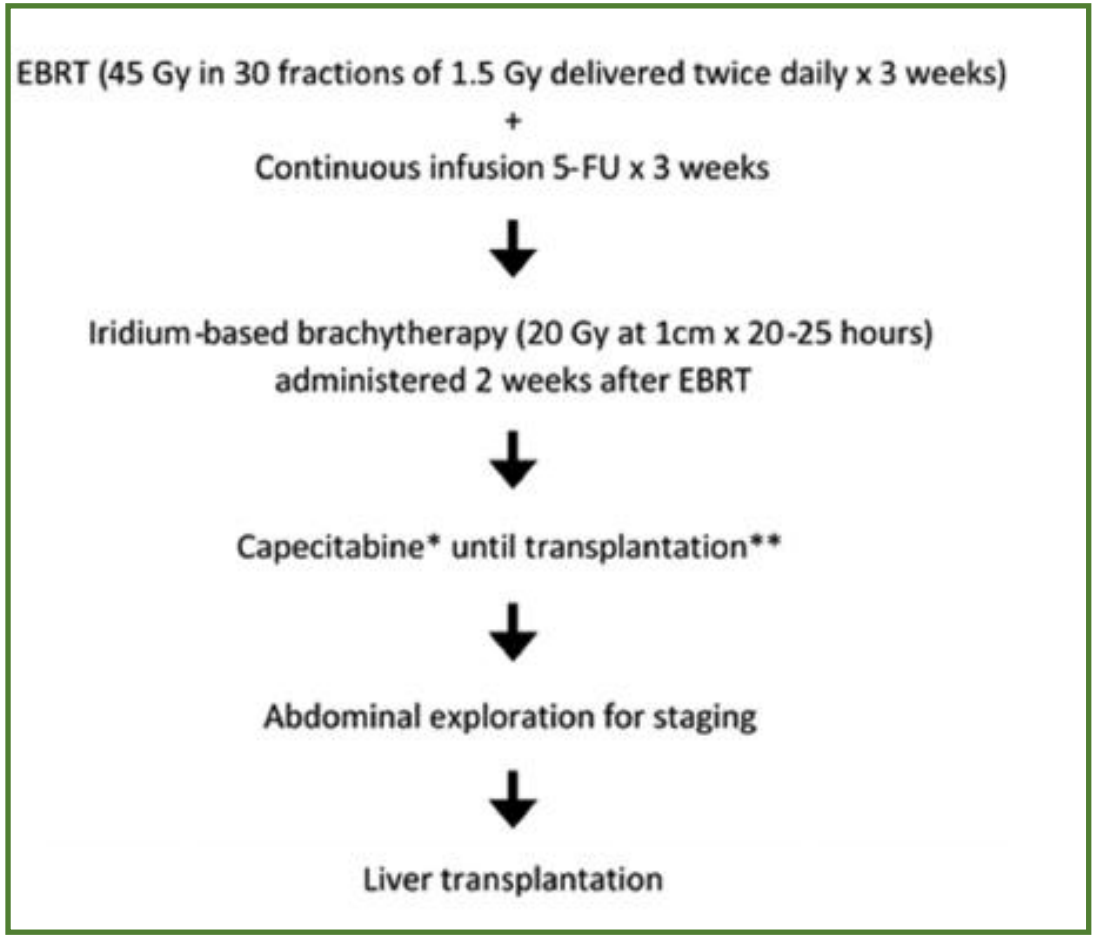
Diagnosis of cholangiocarcinoma (1 of following criteria):

- Transcatheter biopsy or brush cytology
- CA 19–9 > 100 mg/ml and/or mass on cross-sectional imaging with a malignant-appearing stricture on cholangiography
- Biliary ploidy by FISH with a malignant-appearing stricture on cholangiography

Unresectable tumor above the cystic duct

Resectable cholangiocarcinoma in patient with PSC
Candidate for liver transplantation

Tumor < 3 cm
No involved lymph nodes on staging diagnostics



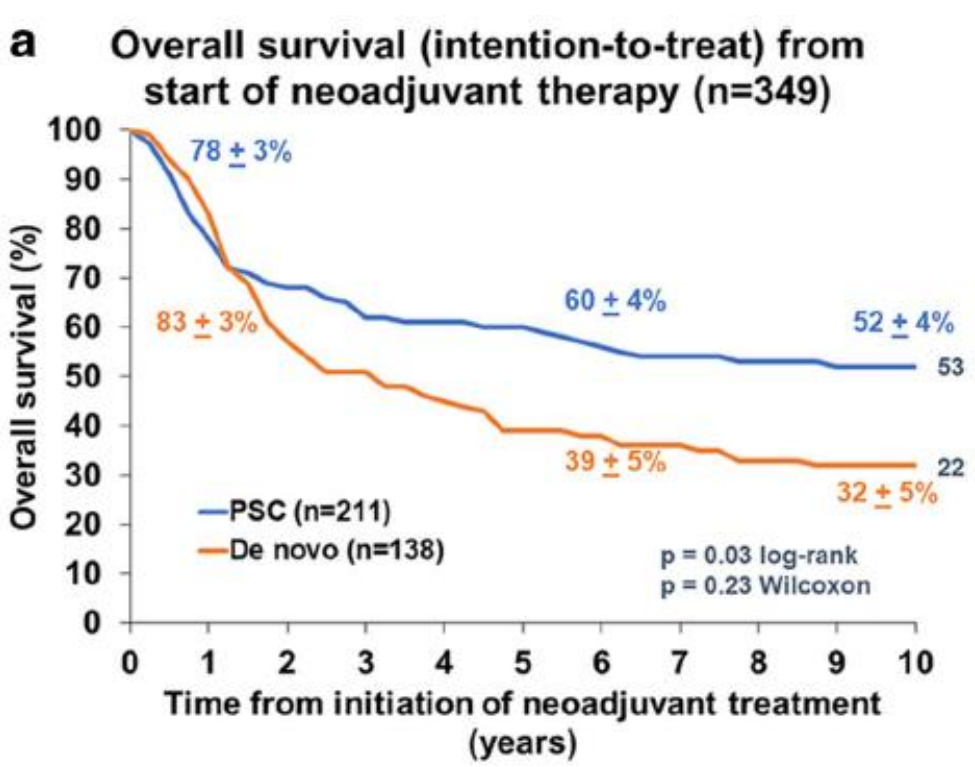
Legend: *In earlier versions of the protocol, patients received intravenous infusion 5-FU rather than oral 5-FU (capecitabine);

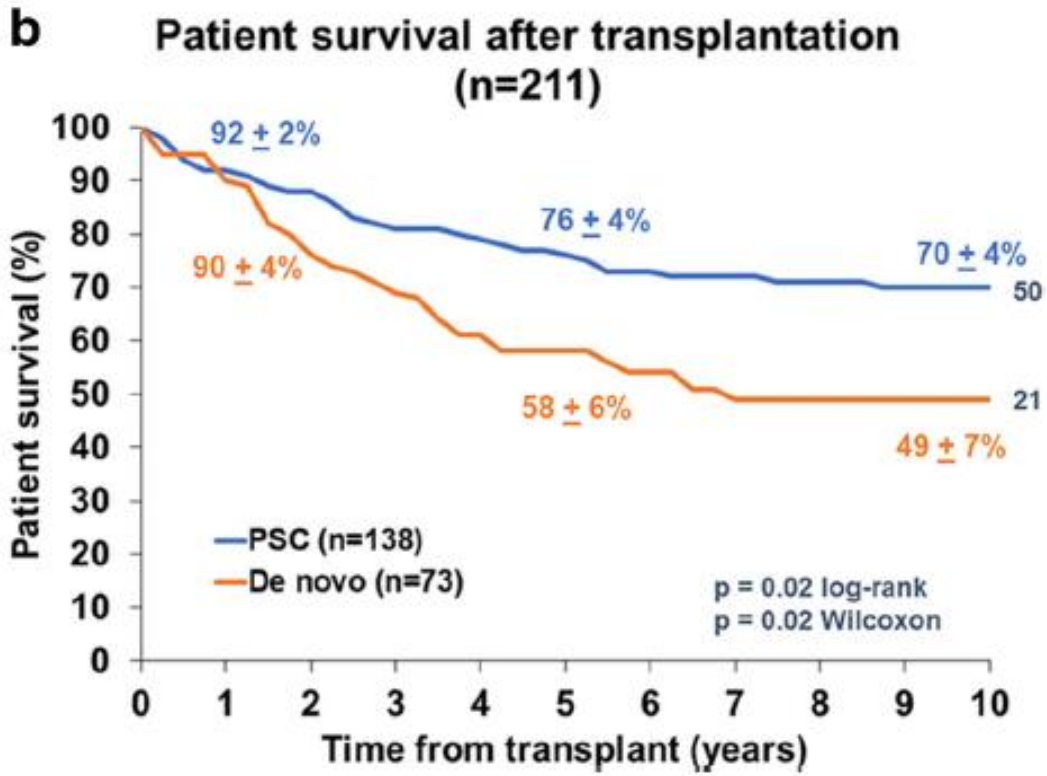
Acher AW, et al. Exp Rev Gastroenterol&Hepatol 2021; 15: 555-566

Pfister M et al. Ann Surg 2025 (in press)

The Mayo Clinic Protocol

Results from 1993-2018

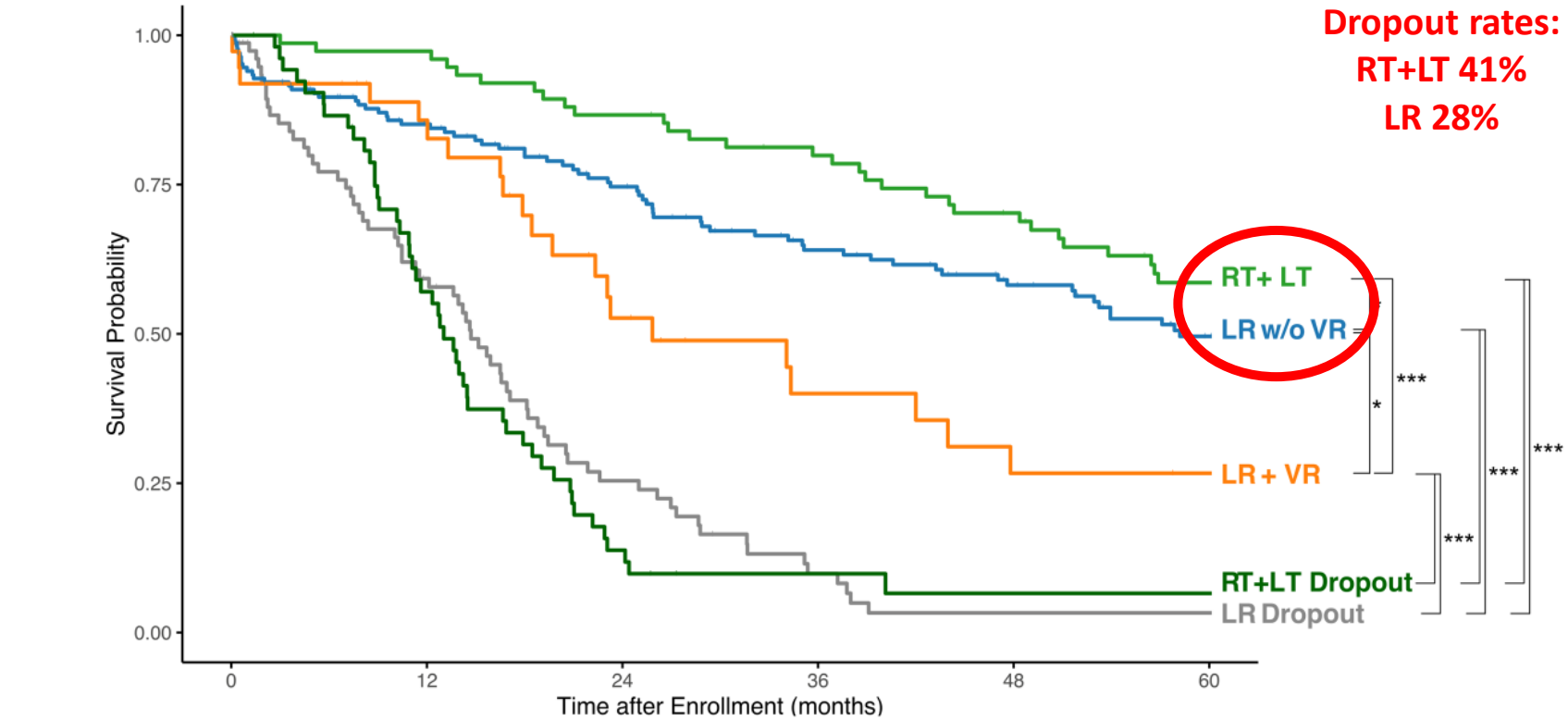




EK Tan, et al. J Gastrointestinal Surg 2020; 24: 2679

The Mayo Clinic Protocol

Results from 1993-2023



Dropout rates:
RT+LT 41%
LR 28%

Number at risk

RT+ LT	75	73	65	58	50	39
LR w/o VR	170	128	104	79	65	49
LR + VR	37	28	15	9	6	5
RT+LT Dropout	52	29	7	3	2	2
LR Dropout	81	42	17	6	2	2

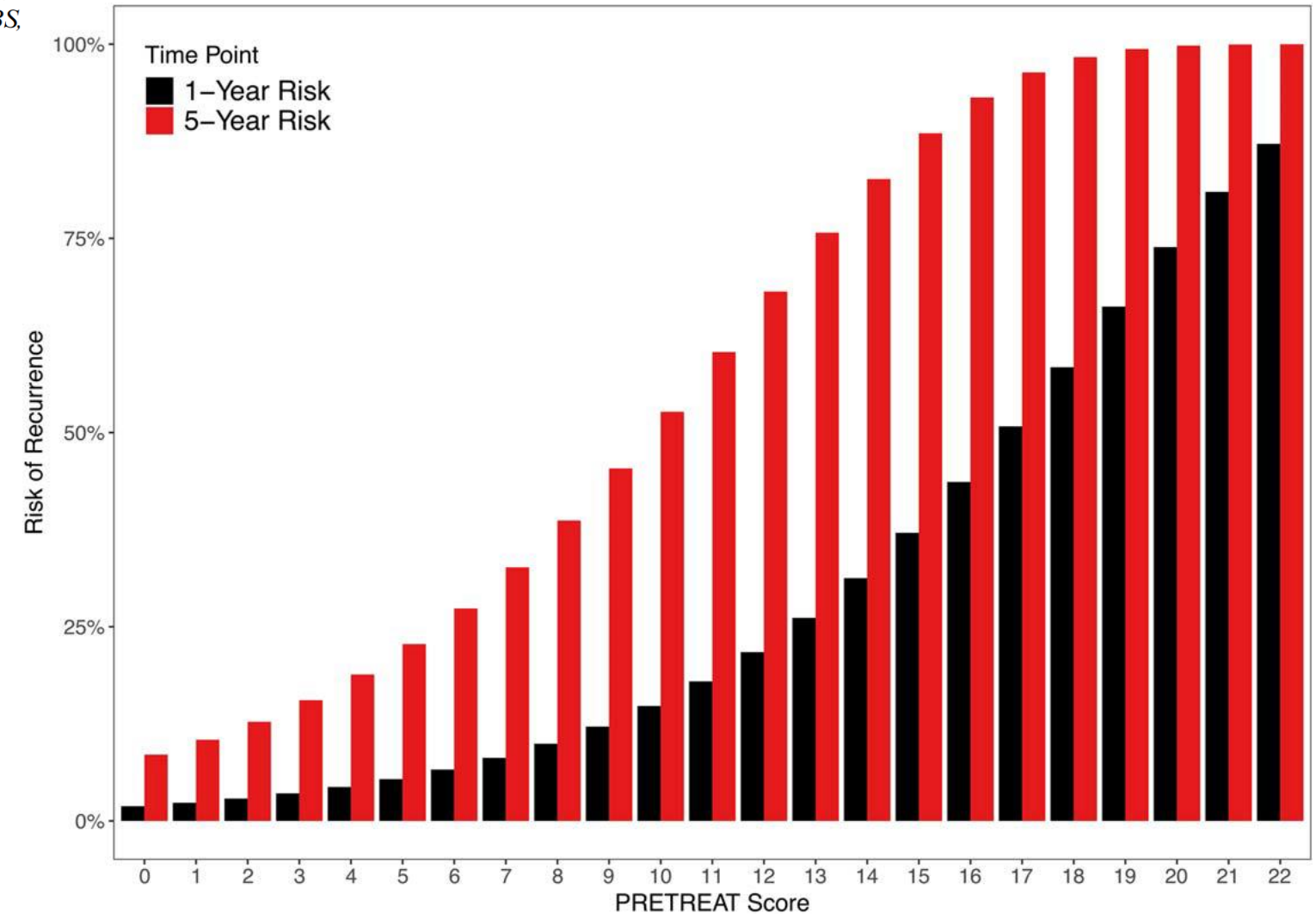
Y Dong, et al. Hepatology 2025 (in press)

Development of the Perihilar Cholangiocarcinoma Risk Estimation of Tumor Recurrence After Transplant (PRETREAT) Score

Zhihao Li, MD, Timucin Taner, MD, PhD,* John E. Eaton, MD,† Byron H. Smith, MS,‡ Sumera I. Ilyas, MBBS,†§ Chris L. Hallemeier, MD,‖ Nguyen H. Tran, MD,¶ Tayyab S. Diwan, MD,* Amit K. Mathur, MD,# Blanca C. Lizaola-Mayo, MD,** Dana K. Perry, MD,†† Liu Yang, MBBS, Gregory J. Gores, MD,† and Julie K. Heimbach, MD*✉*

Ann Surg 2025; 282:503-514

- ✓ Macroscopic residual tumour on explant (HR:12.4)
- ✓ Vascular encasement (HR: 2.18)
- ✓ Lymphovascular invasion (HR: 2.04)
- ✓ Radial tumor diameter (HR: 1.02/mm).



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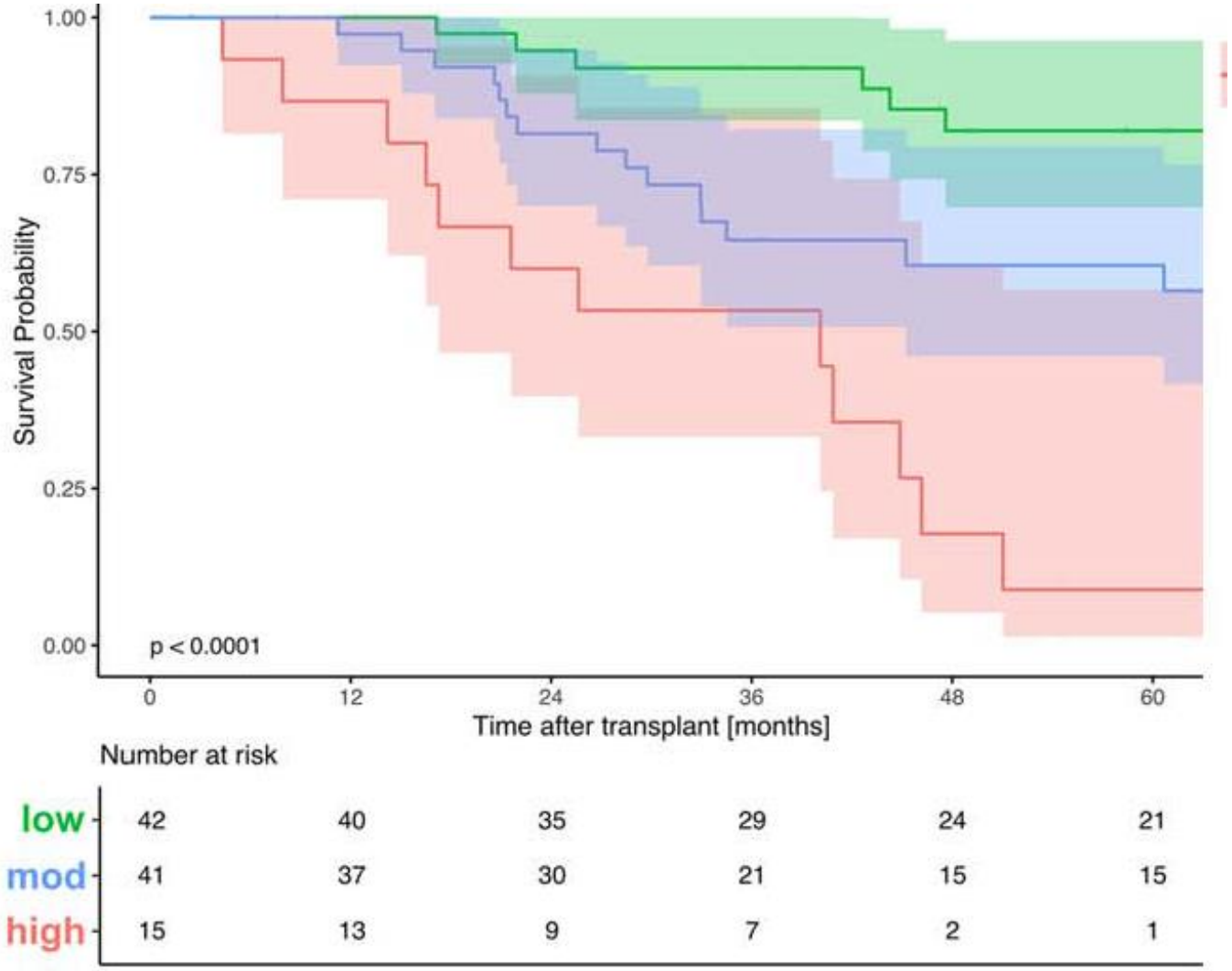

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Si no impacta en la lista de espera para otras indicaciones con supervivencia claramente establecida

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Beneficio colectivo para la población trasplantada

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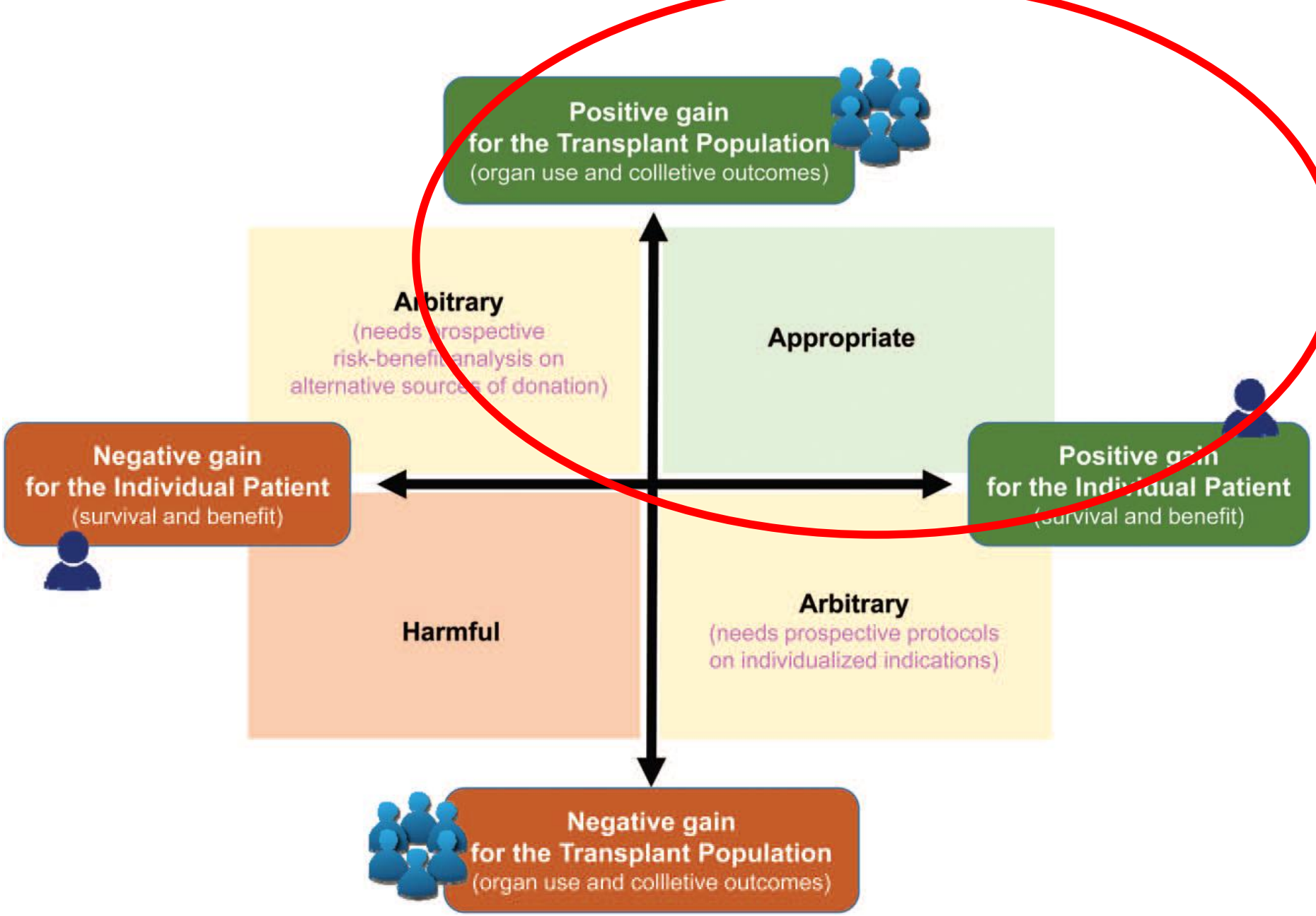
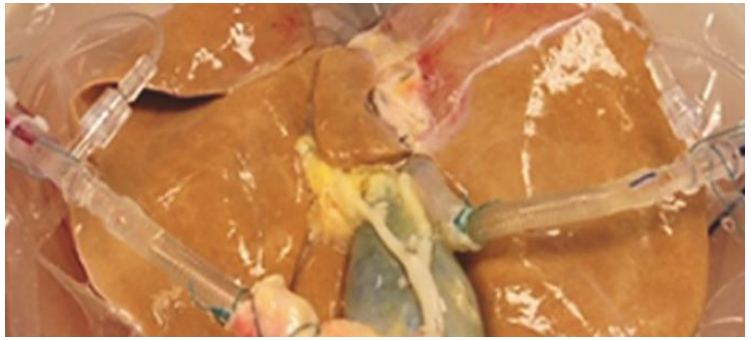


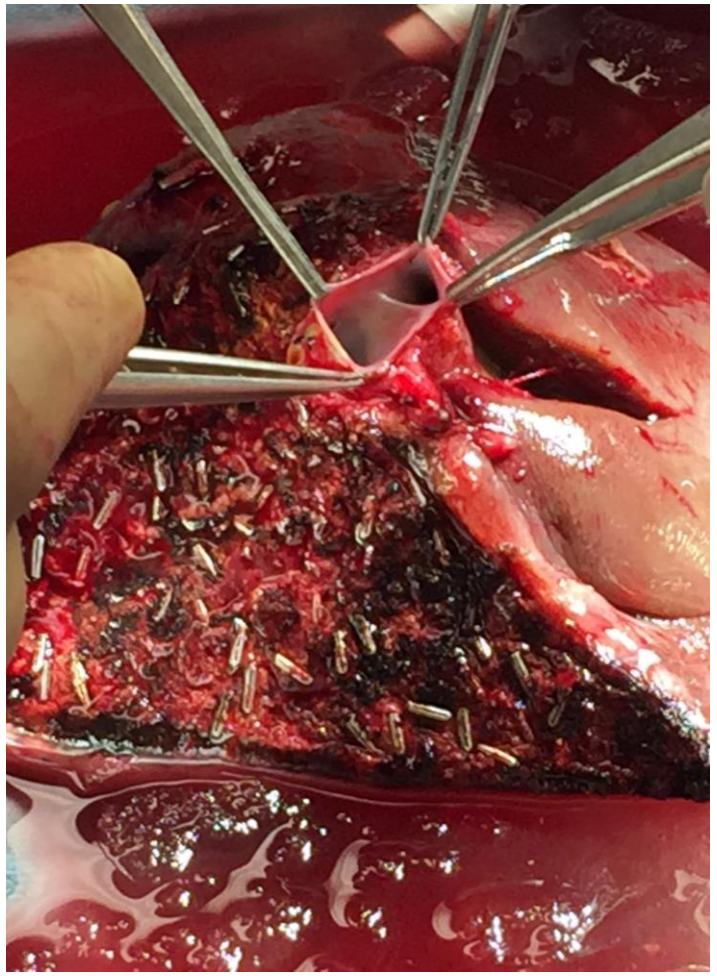
Sapisochin G, et al. Ann Surg 2021; 273: 483-493

Extended donor criteria

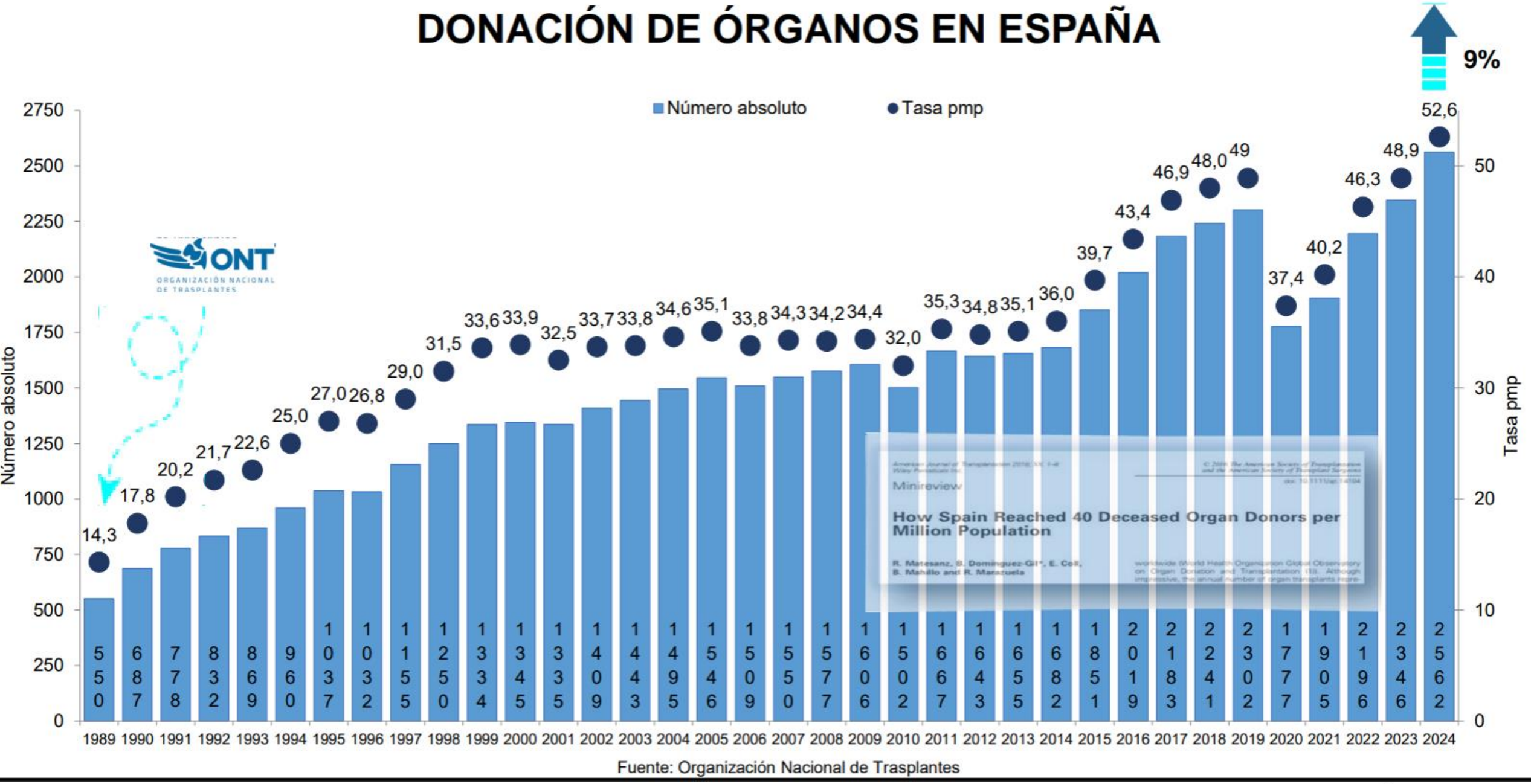


Ex-situ machine perfusion

Living donor



DONACIÓN DE ÓRGANOS EN ESPAÑA



Fuente: Organización Nacional de Trasplantes

ONT
ORGANIZACIÓN NACIONAL DE TRASPLANTES

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Si mejora la supervivencia del paciente
(al menos similar a aquellos resecables)

⬇

Beneficio individual para el paciente

Si no impacta en la lista de espera para otras indicaciones con supervivencia claramente establecida

⬇

Beneficio colectivo para la población trasplantada

Si podemos mejorar la selección del paciente

Sapisochin G et al. Ann Surg 2021; 273: 483-493

¿Es el tamaño y el número de lesiones (morfología) el mejor factor de selección?

RESPUESTA AL TRATAMIENTO NEOADYUVANTE (**BIOLOGÍA**)

NO PROGRESIÓN EN EL TIEMPO (**CRONOLOGÍA**)

Durvalumab plus chemotherapy in advanced biliary tract cancer: 3-year overall survival update from the phase III TOPAZ-1 study

14% localmente avanzado. 9% CCAp

685 adult participants with advanced BTC (previously untreated or recurrent post-surgery)

→ Randomised

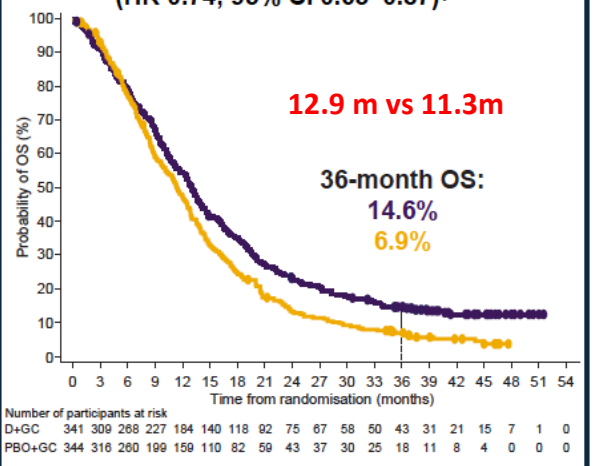
- Durvalumab + GemCis (n=341)
- Placebo + GemCis (N=344)

→ Participants followed for ≥3 years after randomisation

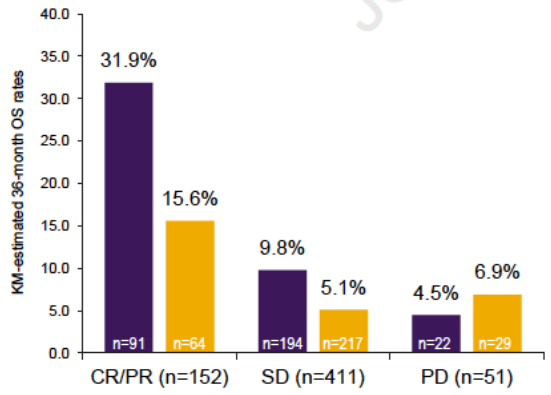
→ **Endpoints**

- Overall survival
- SAEs
- Extended long-term survivors (alive ≥30 months) described
- SAT use

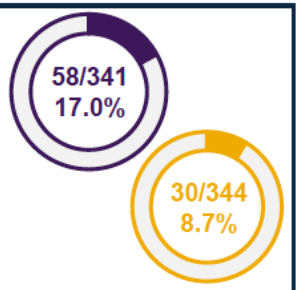
OS in the FAS:
durvalumab + GemCis (n=341)
***vs.* placebo + GemCis (n=344)**
(HR 0.74; 95% CI 0.63–0.87)†



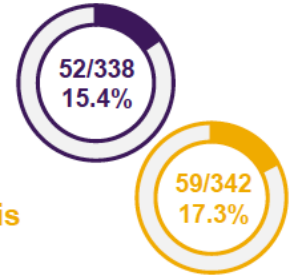
36-month OS rates by BOR:
durvalumab + GemCis *vs.* placebo + GemCis



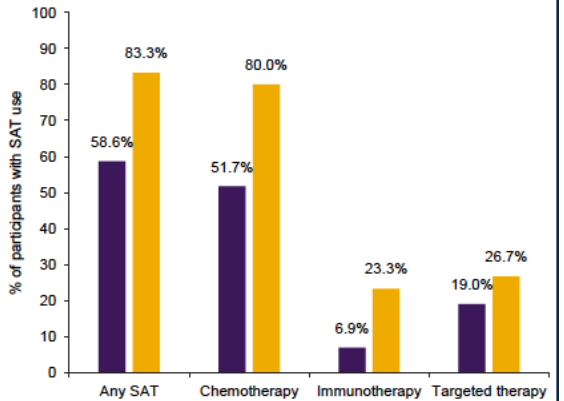
More extended long-term survivors in durvalumab + GemCis *vs.* placebo + GemCis



Serious TRAE rates in durvalumab + GemCis and placebo + GemCis

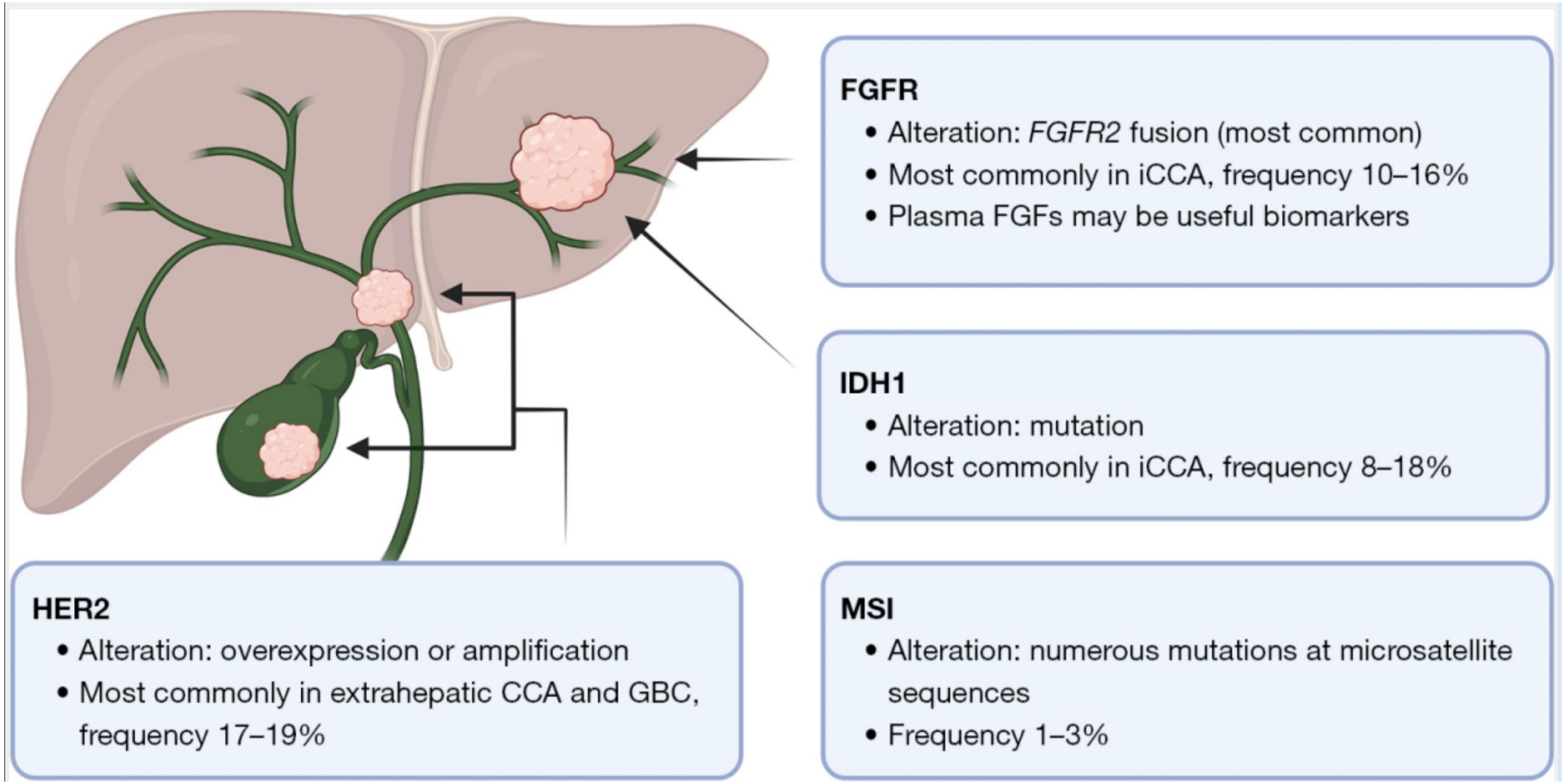


SAT use in eLTS:
durvalumab + GemCis (n=58)
***vs.* placebo + GemCis (n=30)**



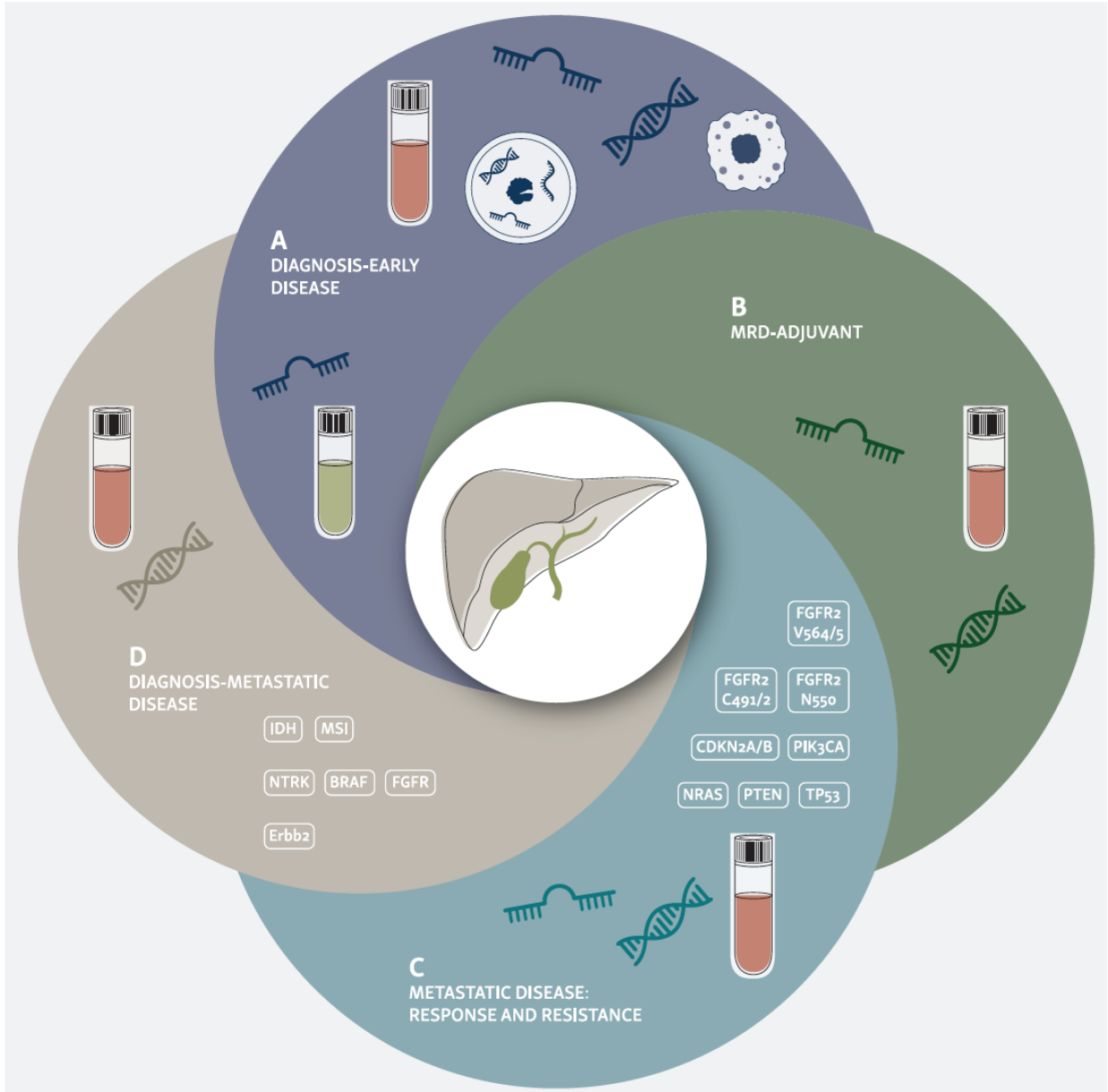
Do-Youn Oh et al. J Hepatol 2025; S0168-8278(25)02201-9

Mutaciones diana



E Warren et al. HBSN 2024; 13: 29-38

ctDNA



M de Scordilli et al. ESMO Open. 2025;10:105079.


What is next?

1. Cómo mejorar el control sistémico de la enfermedad pretrasplante

- Es importante el balance entre la eficacia y la toxicidad.
- Gemcitabina-cisplatino como tratamiento quimioterápico de elección.
- Considerar añadir inmunoterapia. 40-50 días período de washout.
- Recomendable su manejo en centros de experiencia y alto volumen con disponibilidad de trasplante hepático.
- Las colangitis de repetición son un hándicap. Estudio TESLA S Franssen , JHEP Reports 2025 (in press)

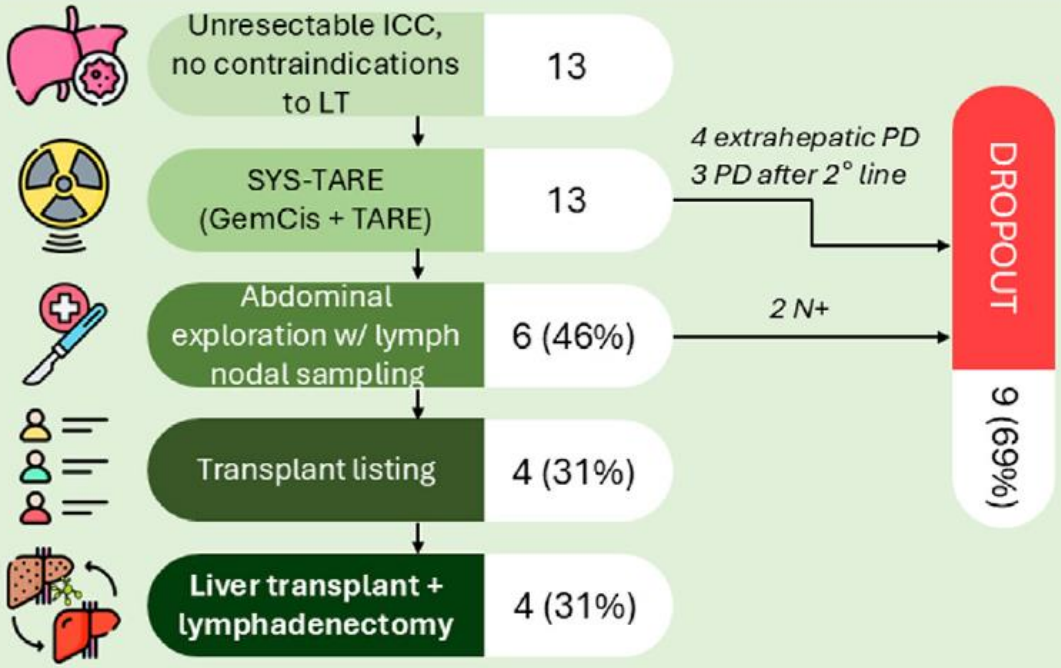
TESLA

PRIMARY PERCUTANEOUS STENTING

2. Control local de la enfermedad

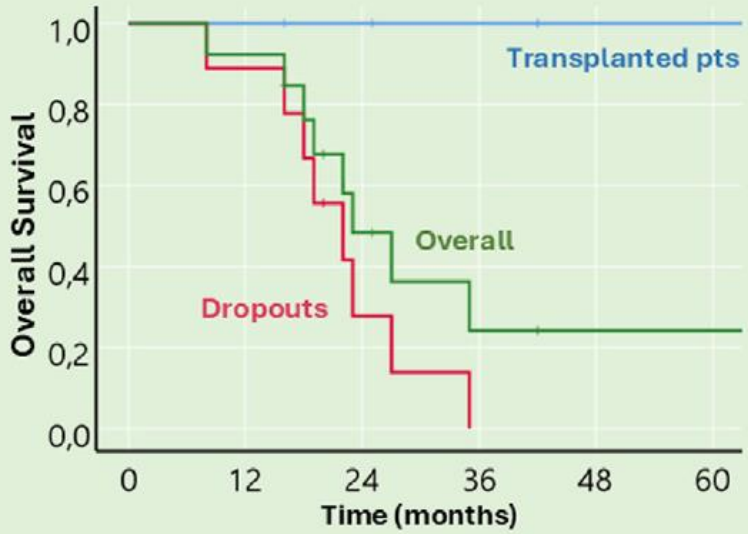
Liver Transplantation for Intrahepatic Cholangiocarcinoma after Chemotherapy and Radioembolization: an Intention-to-Treat Study

DOWNSTAGING PROTOCOL & INCLUDED PATIENTS



ONCOLOGICAL OUTCOMES

All transplanted patients are alive and disease-free at 73, 40, 12 and 8 months from transplant



Transplant for iCC after downstaging with SYS-TARE is safe and feasible, with remarkable oncological outcomes

Maspero, et al. *Transpl. Int.* 2024
doi: 10.3389/ti.2024. 13641

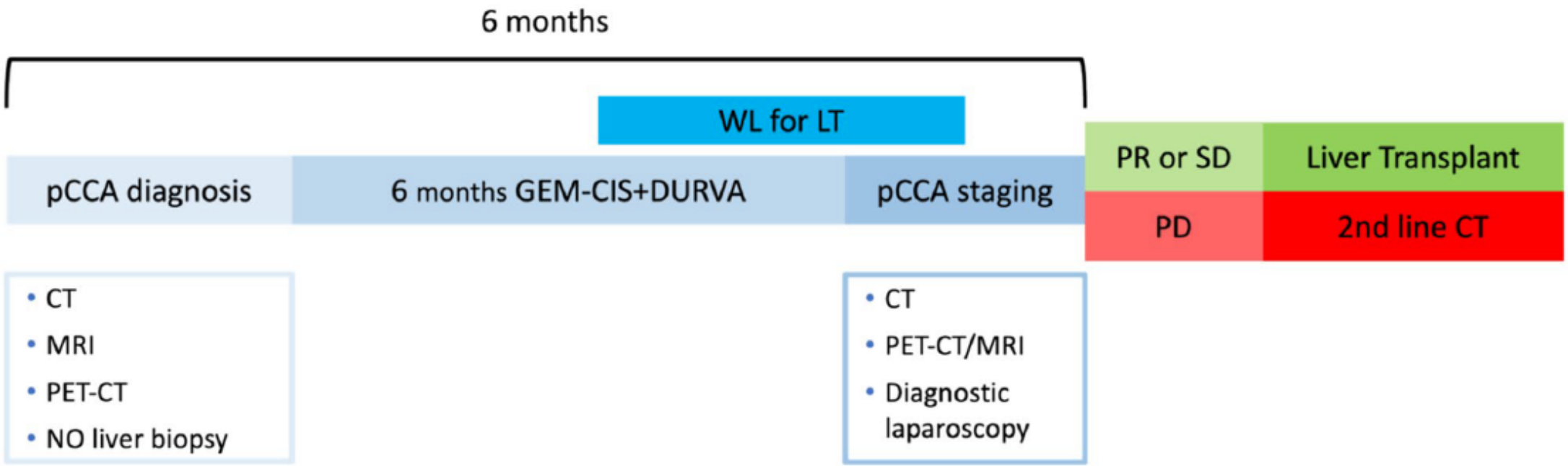
2. Control local de la enfermedad

- **CCAp y la radioterapia**: Lista de espera < 3 meses, disponibilidad de quimioterapia más eficaz y morbilidad asociada durante el proceso quirúrgico del trasplante (complicaciones vasculares) → **¿SE PUEDE EVITAR?**

Author	Institution	Year	N	Main results
Soliman	Houston, Tx	2024	27	There was no significant difference in OS and RFS when stratified by regimen (radiotherapy vs. no radiotherapy). RT impact in RFS multivariant analyses
Gringeri	Italy	2024	53	5-year OS for chemo without RT 35% vs. chemo with RT 50% (p=0.13)
Wu	UCLA, Ca	2023	8	44.4% achieved pCR with SBRT; pCR had a significantly better survival in pCCA patients

*Presentado por Working Group 2: Surgery Committee. Cholangiocarcinoma Foundation. Salt Lake City. 9 Abril 2025

LIver TrAnspLantation for non-resectable peri-HIlar cholangioCArcinoma (LITALHICA)



Gringeri E, et al. Updates Surg 2024; 76: 2505-2413

Aplicabilidad del Trasplante Hepático en el Colangiocarcinoma Perihiliar Irresecable.

Estudio prospectivo multicéntrico.

Estudio Colangiotrans V5. PR(AG) 223-2019.

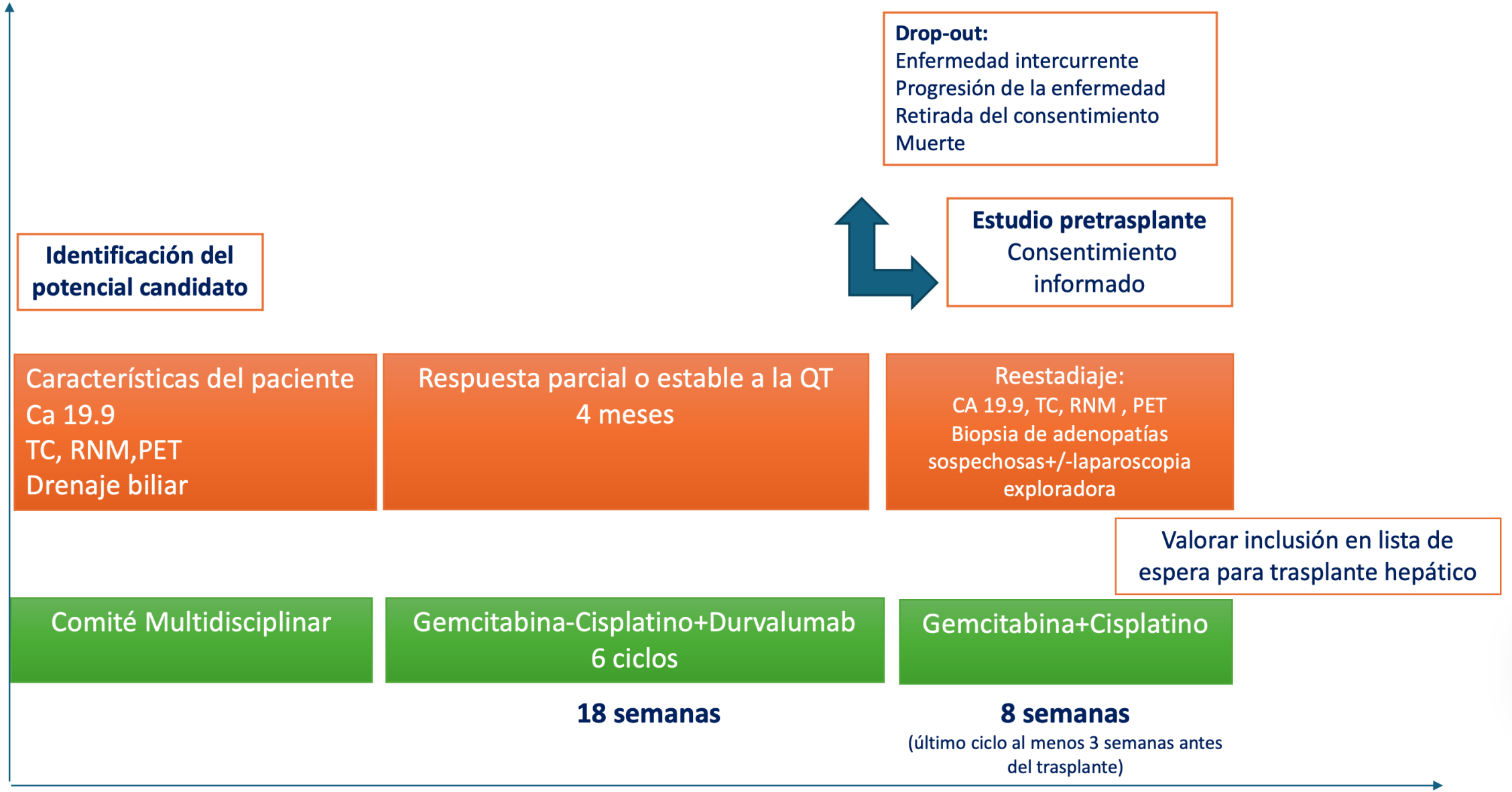
ClinicalTrials.gov ID: NCT04378023

16/21 Trasplantados	Aplicabilidad del procedimiento **76%**
10/16 Vivos	Supervivencia global **62%**
6/16 Exitus post-trasplante	Mortalidad post-operatoria (5/16) **31%**
5/16 Complicaciones vasculares	**31%** (estenosis arterial, trombosis arterial,trombosis portal, trombosis portal y arterial y dificultad del drenaje venoso)
Una recidiva precoz	
11/27 No llegan a trasplantarse	Drop-out **40%**

C Dopazo. Revisión Julio 2025. Datos no publicados

Aplicabilidad del Trasplante Hepático en el Colangiocarcinoma Perihiliar Irresecable.

Propuesta no aprobada



En resumen…

Trasplante hepático en CCAp irresecable ≤ 3cm sin adenopatías ni enfermedad extrahepática es factible tras quimio-radioterapia.

¿Es el momento de reevaluar el protocolo de neoadyuvancia?

Trasplante hepático en CCAi localmente avanzado.

¿Es el momento para un ensayo clínico nacional?

Cristina.dopazo@vallhebron.cat

@cdopazo1