XIX JORNADA DE ACTUALIZACIÓN ASCO GI 2025

5 de marzo de 2025

¿Qué hay de nuevo en los tumores hepato-bilio-pancreáticos?

Dr. Carlos López López

Hospital Universitario Marqués de Valdecilla, Santander

“Mis COIs…”

- Consultant or Advisory Role: Amgen, Roche, Lilly, Pfizer, Ipsen, Sanofi, Merck, EISAI, Bayer, Servier, Astra-Zeneca, Takeda.
- Research Funding: Amgen, Roche, MSD, Astra-Zeneca, Bayer, Ipsen, EISAI, Celgene, Sanofi, Merck, EXELISIS, Servier, GSK.
- Speaking: Roche, Pfizer, Novartis, Ipsen, Sanofi, Merck, EISAI, Bayer, Astra-Zeneca, Servier.
- Travel, Accommodations, Expenses: Roche, Lilly, Pfizer, Ipsen, Merck, Servier, Amgen, Triple AAA. Novartis.

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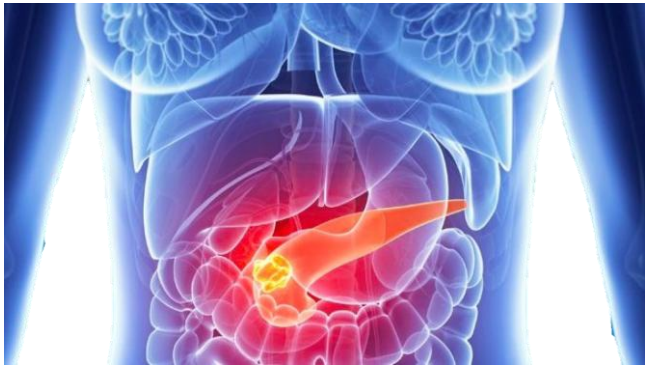
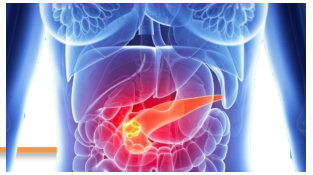


Cáncer de Páncreas Avanzado



Pamrevlumab plus nab-paclitaxel/gemcitabine (Pam + GA) as first- and second-line therapy in metastatic pancreatic cancer (mPDAC): Results from Precision Promise (PrP) Bayesian platform trial

Vincent Picozzi, MD – Abstract #673, *on behalf of the Precision Promise Consortium*

LAPIS: Randomized Phase 3 trial of chemotherapy with and without pamrevlumab for locally advanced pancreatic cancer

Vincent Picozzi, MD Abstract #675

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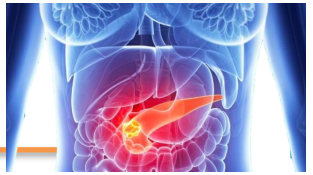
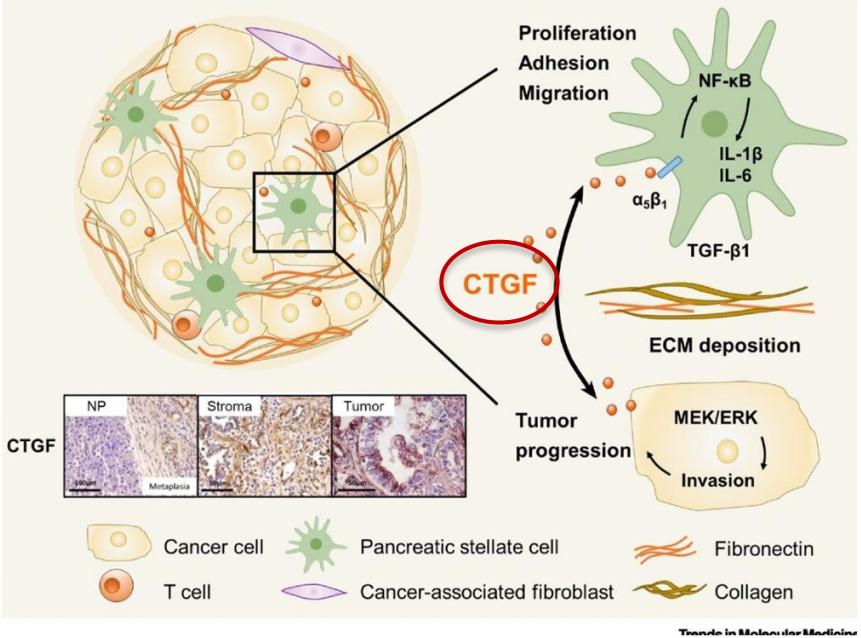


Pamrevlumab

- Connective tissue growth factor antibody
- Prevents extra-cellular matrix deposition
- Phase 1/2 study: median OS 19.3 m in locally advanced pancreas cancer



Shen et.al., Tr in Mol Med Volume 26, Issue 12, 1064 – 1067
Picozzi et.al., ESMO Open. 2020 Aug;5(4):e000668.

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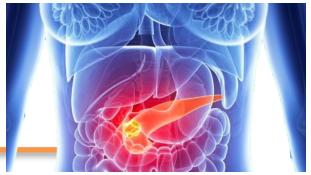

Precision Promise: Study Design

"Hasta 40 Pacs/mes…" (24 centroS en EEUU)

Key Eligibility
- mPDAC
- 0-1 lines of prior systemic therapy
- Measurable disease
- ECOG PS 0-1

Pre-treatment Core Bx
- WGS/RNAseq

Research blood
- WGS matched normal sample
- Serum
- Plasma
- ctDNA

Randomization
70 Investigational:30 Control

- Pam + GA — 70%
- Other Investigational Arms — SM-88 Arm*
- GA — 15%
- mFOLFIRINOX — 15%

Progression, Toxicity

Co-treatment bx @ 8 wks
Tumor imaging, research blood and PROs every 8 wks

Screening for Line 2 if Progression on Line 1

Endpoints:
Primary: OS
Key Secondary: PFS, ORR, TEAEs

Follow-up visits every 3 months for survival

PANCREATIC CANCER ACTION NETWORK

Clinicaltrials.gov: NCT04229004

"Análisis interino de futilidad a los **50 pacs**…"
Adelante si análisis Bayesiano **P éxito Brazo Exp ≥35%**

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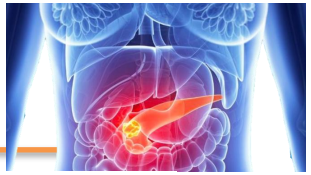

Patient Characteristics

mITT population receiving GA backbone (283 patients)

	First Line		Second Line	
	GA N = 34	Pam + GA N = 102	GA N = 36	Pam + GA N = 111
Age at Study Entry (years)				
Median (Range)	67.5 (38, 81)	63 (37, 85)	63 (44, 75)	62 (43, 78)
Sex, n (%)				
Female	18 (52.9)	55 (53.9)	18 (50.0)	52 (46.8)
Baseline ECOG Performance Status*, n (%)				
0	15 (44.1)	43 (42.2)	11 (30.6)	36 (32.4)
1	18 (52.9)	58 (56.9)	25 (69.4)	75 (67.6)
Stage at Initial Diagnosis, n (%)				
Stage IV	28 (82.4)	89 (87.3)	31 (86.1)	73 (65.8)
Liver Metastases				
Yes	25 (73.5)	72 (70.6)	27 (75.0)	80 (72.1)
Prior Pancreatic Cancer-related Surgery, n (%)				
Yes	3 (8.8)	14 (13.7)	2 (5.6)	22 (19.8)

Table reflects a subset of the primary analysis population – mFOLFIRINOX is not summarized
Table reflects non-concurrently and concurrently randomized GA participants
*One ECOG 2 participant in first line GA and first line Pam + GA groups

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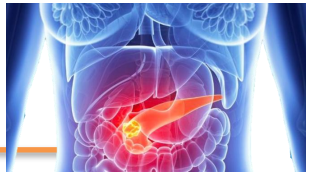

PFS and ORR Outcomes

mITT population receiving concurrent GA backbone (258 patients)

PFS and ORR are in a subset of the primary analysis population that only included concurrently randomized GA controls

	First Line		Second Line	
	Concurrent GA N = 23	Pam + GA N = 102	Concurrent GA N = 22	Pam + GA N = 111
Progression Free Survival				
Median PFS (mos)	5.3	5.9	7.0	3.9
Hazard Ratio (95% Confidence Interval)	0.64 (0.36,1.14)		1.35 (0.78,2.33)	
Disease Response				
Confirmed ORR, n (%)	6 (26.1)	36 (35.3)	1 (4.5)	10 (9.0)
Partial Response, n (%)	6 (26.1)	36 (35.3)	1 (4.5)	10 (9.0)
Stable Disease, n (%)	12 (52.2)	49 (48.0)	11 (50.0)	62 (55.9)
Progressive Disease, n (%)	2 (8.7)	5 (4.9)	4 (18.2)	31 (27.9)
Not Evaluable, n (%)	3 (13.0)	12 (11.8)	6 (27.3)	8 (7.2)

"Toxicidad fundamentalmente hematológica similar en ambas ramas (ligero incremento de astenia)…"

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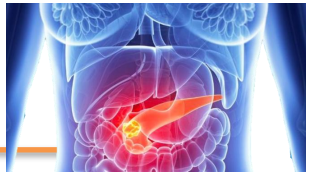
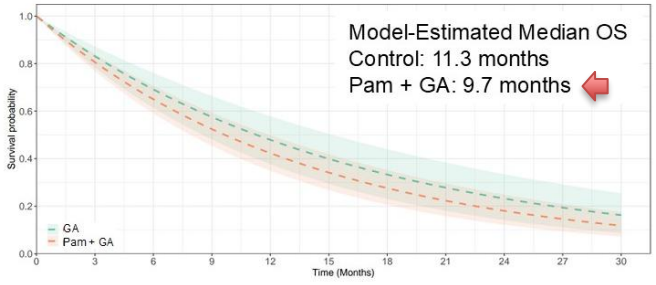


Primary Efficacy Analysis: Model-Estimated OS

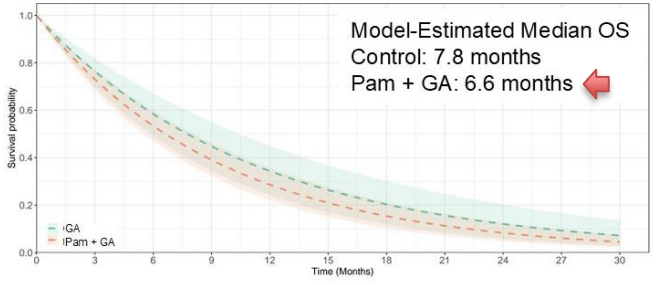
mITT population uses all dosed patients before and during Pam + GA enrollment

Model-estimated survival curves for Line 1 and Line 2 mITT participants in Pam + GA and Control. The dashed curves represent the posterior means, and the shaded areas correspond to the 95% credible intervals.

Line 1 mITT Population



Line 2 mITT Population



Model-Estimated Mean Hazard Ratio across Line 1 and Line 2	1.18
(95% Credible Interval)	(0.88, 1.56)
Posterior Pr(HR < 1)	0.14

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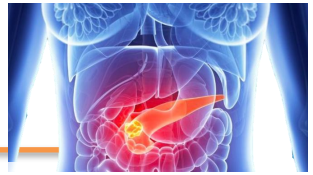

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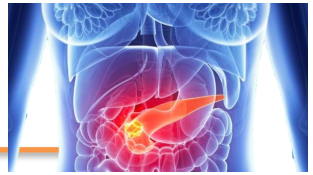

- 284 Pacs. LAPC
  - Rand 1:1 a QT (GA o mFOLFIRINOX) +/- Pamrevlumab (Máx. 6 ciclos)
  - Obj 1º: OS / Obj. 2º: EFS, PFS & ORR
- Resultados:
  - Aprox. 2/3 completan 6 ciclos de tto.
  - 15 *vs* 20% exploración Qx → 8,8 *vs* 8,6% "resección alcanzada"

FAIL

	CTX + pamrevlumab	CTX + placebo	HR (95% CI)
Overall survival, months	17.3	18.0	1.08 (0.83–1.41) P=.5487
Event-free survival, months	5.7	5.8	1.05 (0.78–1.39)
Progression-free survival, months	9.4	9.4	1.01 (0.65–1.56)
Objective response rate[a]	30.1%	45.4%	0.50 (0.31–0.82)

"Toxicidad & Morbimortalidad Qx similar en ambos brazos…"

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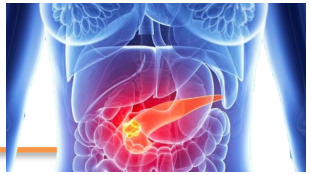
Cáncer de Páncreas Avanzado (Ancianos)



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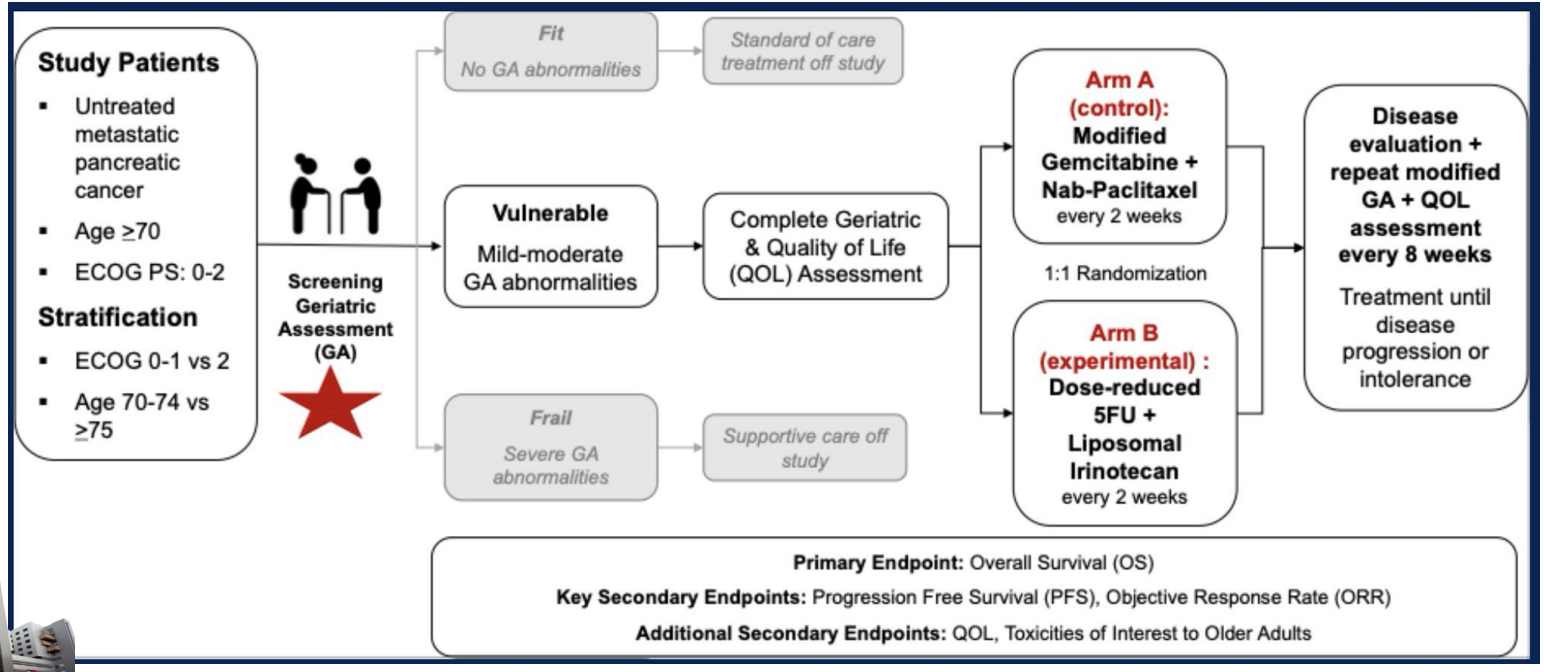

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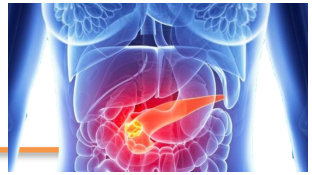

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	Gemcitabine+ Nab-Paclitaxel (N=88)	5FU+ Liposomal Irinotecan (N=88)	Total (N=176)	P-value
Performance Status, n (%)				0.974
0	20 (22.7%)	22 (25.0%)	42 (23.9%)	
1	57 (64.8%)	55 (62.5%)	112 (63.6%)	
2	11 (12.5%)	11 (12.5%)	22 (12.5%)	
Screening vulnerability, n (%)				
Age	32 (36.4%)	33 (36.4%)	64 (36.4%)	
Co-Morbidity	25 (28.4%)	32 (36.4%)	57 (32.4%)	
Cognition	36 (41.4%)	43 (49.4%)	79 (45.4%)	
Function (ADL)	5 (5.7%)	7 (8.0%)	12 (6.9%)	
Function (IADL)	18 (20.7%)	16 (18.4%)	34 (19.5%)	
# of Vulnerability Domains, n(%)				
1	53 (60.9%)	43 (49.4%)	96 (55.2%)	
2	20 (23.0%)	25 (28.7%)	45 (25.9%)	
≥3	6 (6.9%)	10 (11.5%)	16 (9.2%)	

Geriatric Assessment at baseline

Median (Range)	Gemcitabine+ Nab-Paclitaxel (N=88)	5FU+ Liposomal Irinotecan (N=88)	Total (N=176)	P-value
Co-morbidities: CIRS-G score	8 (1-18)	9 (1-16)	8 (1-18)	0.362
Cognition: BOMC Score	4 (0-16)	6 (0-15)	4 (0-16)	0.305
Depression: GDS Score	3 (0-12)	2 (0-13)	2 (0-13)	0.924
Nutrition: Pre-TX BMI	25.9 (17.9-44.1)	24.7 (15.7- 43.8)	25.6 (15.7 - 44.1)	0.046
Weight Loss (Lb)	14.5 (0- 62)	12.6 (0 - 95)	14.0 (0 - 95)	0.812
MNA score	9.0 (5 - 13)	9.0 (3 - 13)	9.0 (3 - 13)	0.058
Functional status: Falls	0 (0-3)	0 (0-3)	0 (0-3)	0.905
ADL	6 (5-6)	6 (4-6)	6 (4-6)	0.303
IADL	8 (4-8)	8 (2-8)	8 (2-8)	0.374
Quality of Life Assessment:				
FACT-G (0-108)	84.5 (39-105)	83.0 (47-108)	83.0 (39 -108)	0.880
FACT-Trial Outcome Index (TOI) (0-128)	90 (48-123)	91.5 (37-123)	90.0 (37 -123)	0.653
FACT-HEP (0-180)	129.5 (74- 172)	132.5 (77- 175)	130.5 (74 - 175)	0.892

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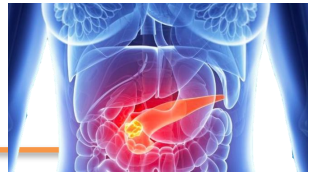

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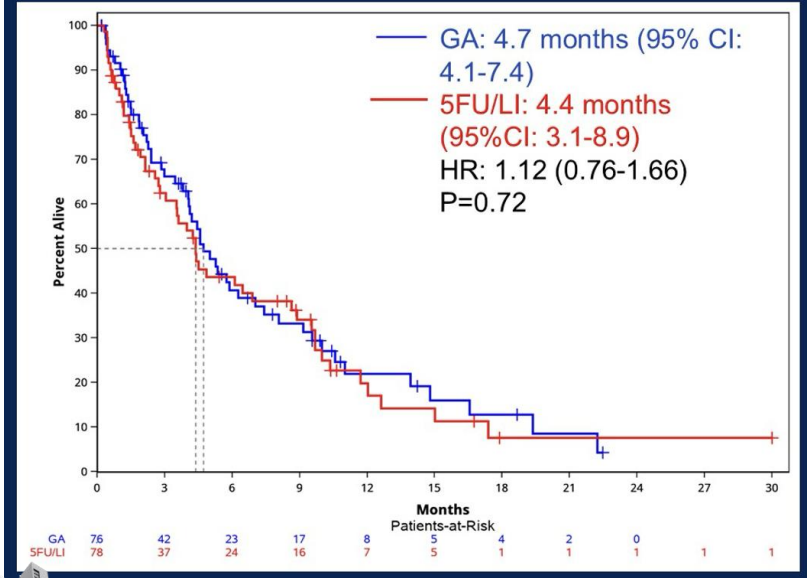
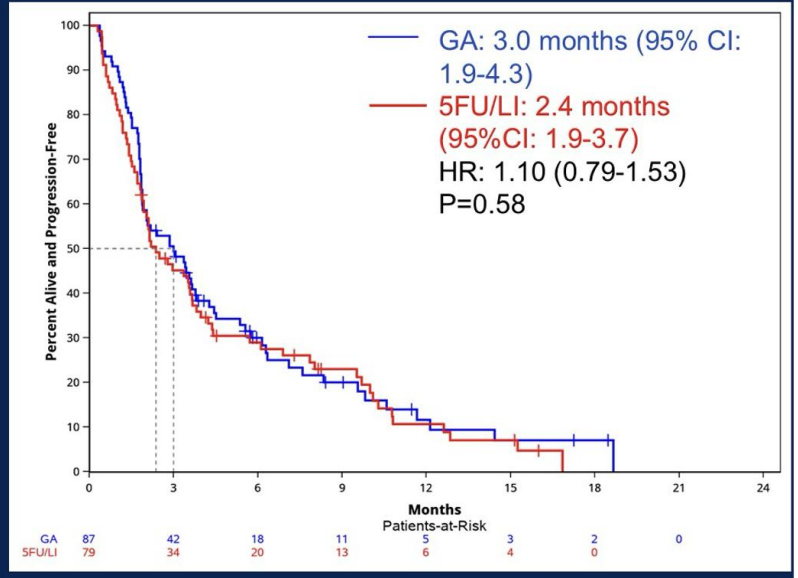


Overall Survival



Progression Free Survival

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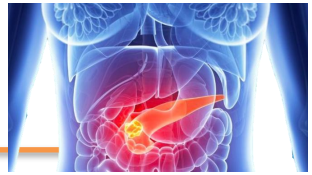

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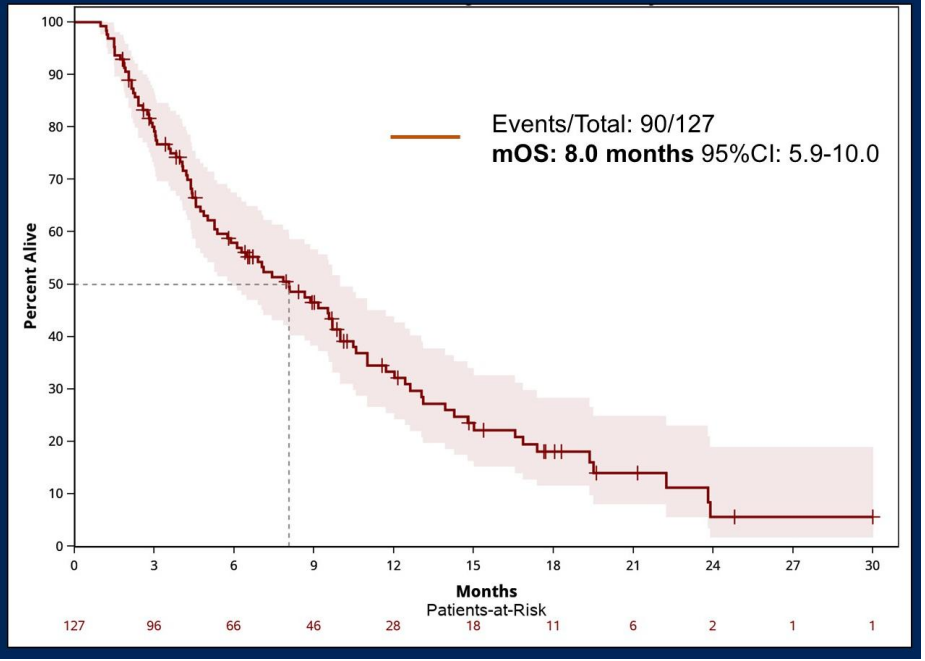
OS analysis of patients who received ≥ 4 weeks of treatment

Number of treatments	N (%)
0	22 (12.5%)
1	22 (14.3%)
≥2	127 (72%)



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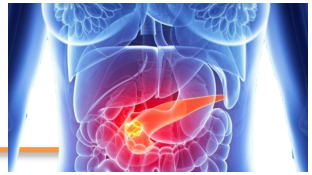

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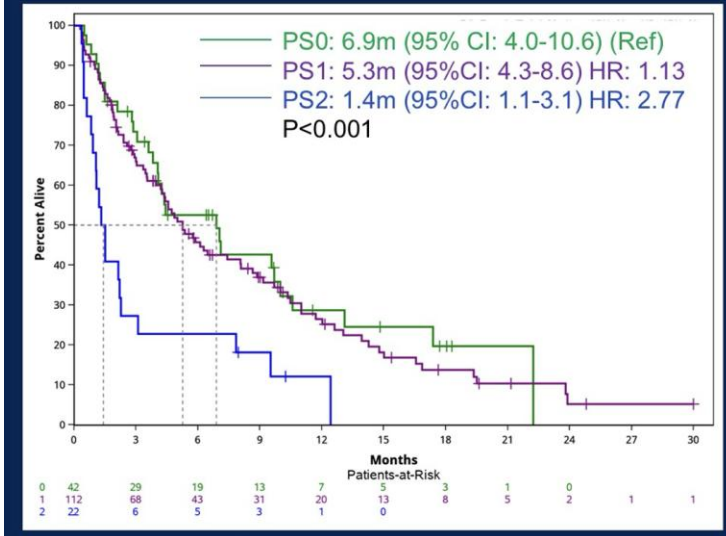
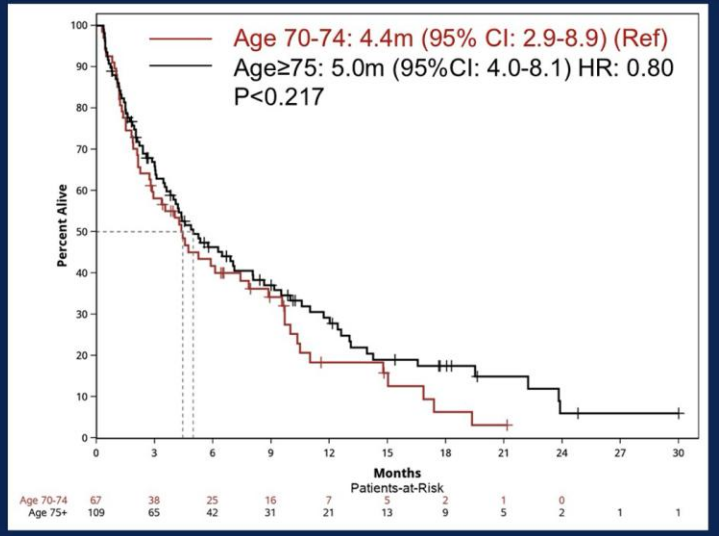
Primary end point OS – by stratification factors:



Performance Status



Age

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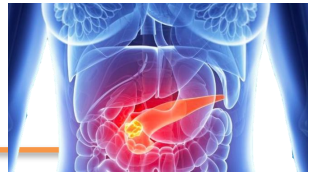

ECOG-ACRIN cancer research group

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Correlation of baseline GA/QOL and OS

Measure	OS HR (per unit)	P (two-sided)
Function (ADL)	0.78	0.39
Function (IADL)	**0.84**	**0.023**
Comorbidities (CIRS-G)	0.99	0.75
Cognition (BOMC)	0.99	0.58
Falls last 6m	1.25	0.14
BMI	0.98	0.32
Wt loss last 6m	0.99	0.38
Nutrition: (MNA)	**0.83**	**<0.0001**
Depression: (GDS)	**1.07**	**0.029**
QOL: FACT-HEP	**0.98**	**<0.0001**
Multi variate analysis		
IADL	**0.85**	**0.073**
MNA	**0.86**	**0.0039**
GDS	**1.07**	**0.029**
FACT-HEP	**0.99**	**0.026**

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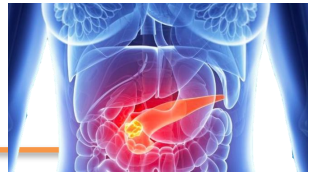

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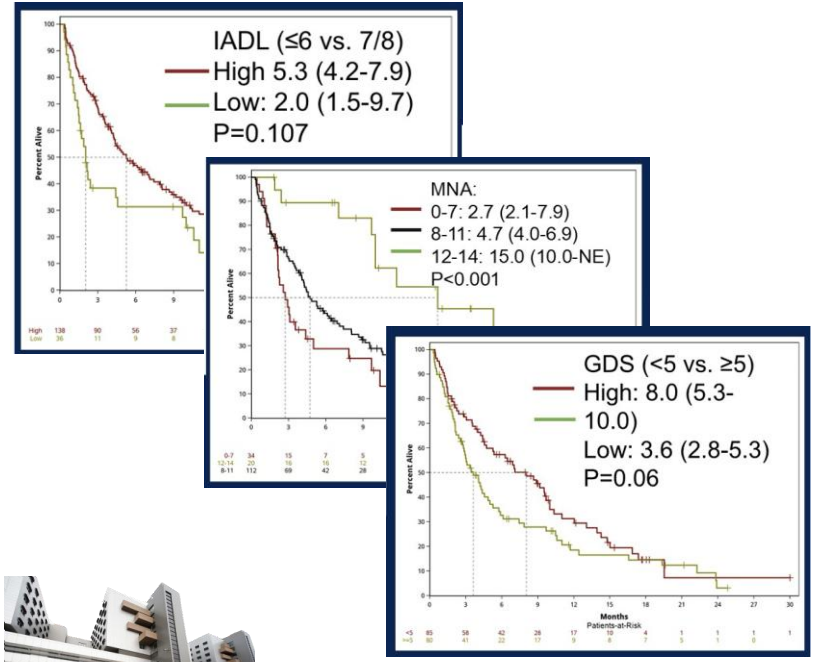

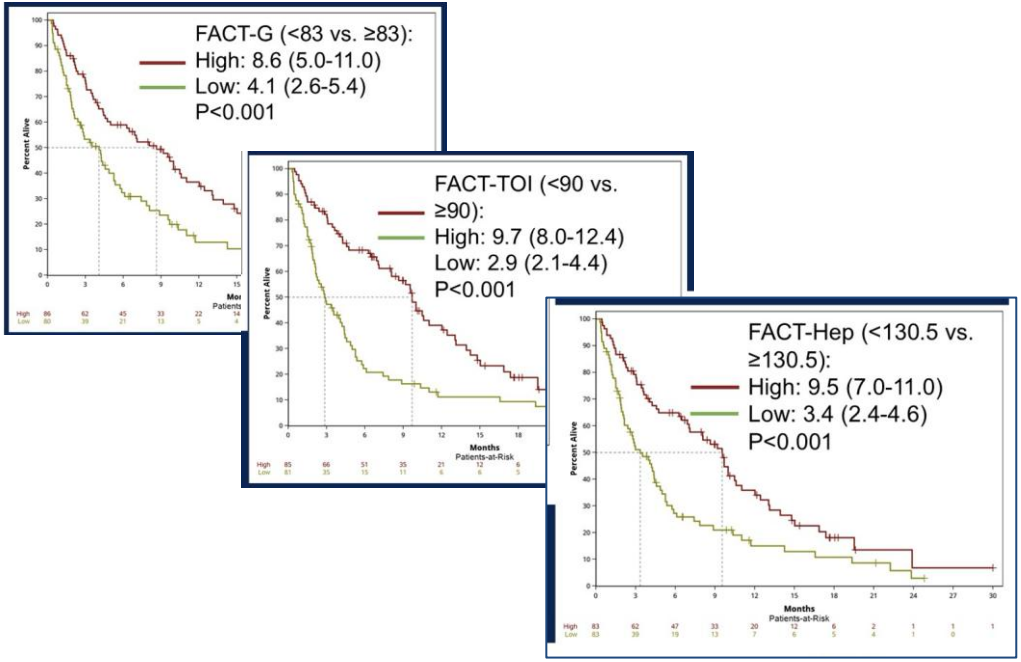

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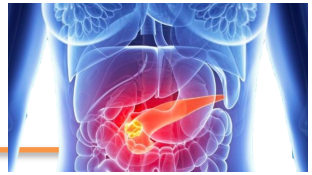
Cáncer de Páncreas Avanzado (Ancianos)



Effect of baseline geriatric and quality of life assessments on treatment outcomes in ECOG-ACRIN EA2186 (GIANT) - A randomized phase II study of Gemcitabine and Nab-Paclitaxel compared with 5-Fluorouracil, Leucovorin, and Liposomal Irinotecan in older patients with treatment-naïve metastatic pancreatic cancer (NCT04233866)

Correlation of baseline GA/QOL and grade 3 toxicity:

Predictor	OR	p
Univariate analysis		
WBC, Median	**0.35**	**0.0054**
GDS, score	**1.20**	**0.021**
MNA, score	0.91	0.25
ADL, score	0.82	0.76
IADL, score	0.76	0.16
FACTG, Score	0.98	0.061
FACTH, Score	0.99	0.15
TOI, Score	0.99	0.30
BMI, value	**1.09**	**0.023**
Multivariable analysis		
WBC, median	**0.29**	**0.0023**
GDS, score	**1.27**	**0.0077**
BMI, value	**1.10**	**0.012**

Dotan E. MD, et al. Abstract #676

XIX JORNADA DE ACTUALIZACIÓN ASCO GI 2025

5 de marzo de 2025

Cáncer de Vía Biliar

Adjuvant chemotherapy or chemo-radiation in gallbladder cancer: a phase III randomized controlled study (ACCELERATE)

Resected gallbladder cancer

≥pT2 or N+

ECOG ≤2

Age ≥18

R0/R1

Randomization

n = 200)

Chemotherapy alone
6 cycles of mGemOx or GemCis

Follow up

3 cycles of chemotherapy mGemOx or CisGem f/b CRT (radiation 45Gyin 25 fractions in 5 weeks with concurrent oral capecitabine)* and further 2-3 cycles of mGemOx or GemCis

Follow up

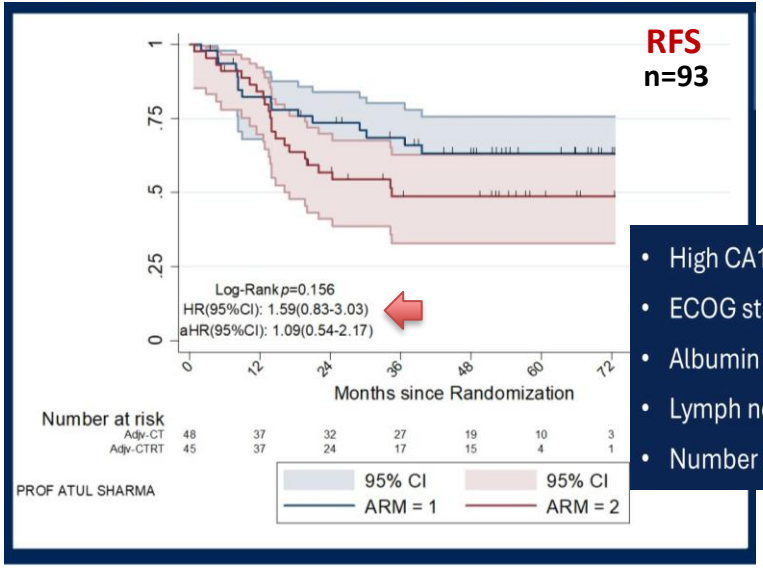
Obj 1º: RFS
Obj 2º: OS & Safety

*further boost of 9 Gy in case of positive margin

Sharma A, MD Abstract #519 ASCO GI 2025

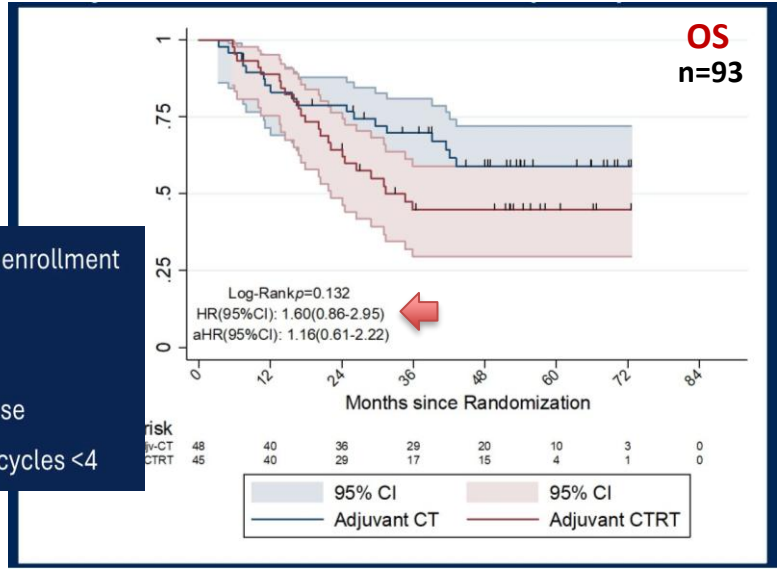
Cáncer de Vía Biliar

Adjuvant chemotherapy or chemo-radiation in gallbladder cancer: a phase III randomized controlled study (ACCELERATE)



"Mal Px"

- High CA19-9 at the time of enrollment
- ECOG status >0
- Albumin level <UNL
- Lymph node positive disease
- Number of chemotherapy cycles <4



"Ligero incremento de AEs g 3/4 (Diarrea y NP) en Brazo 1 (QT)"

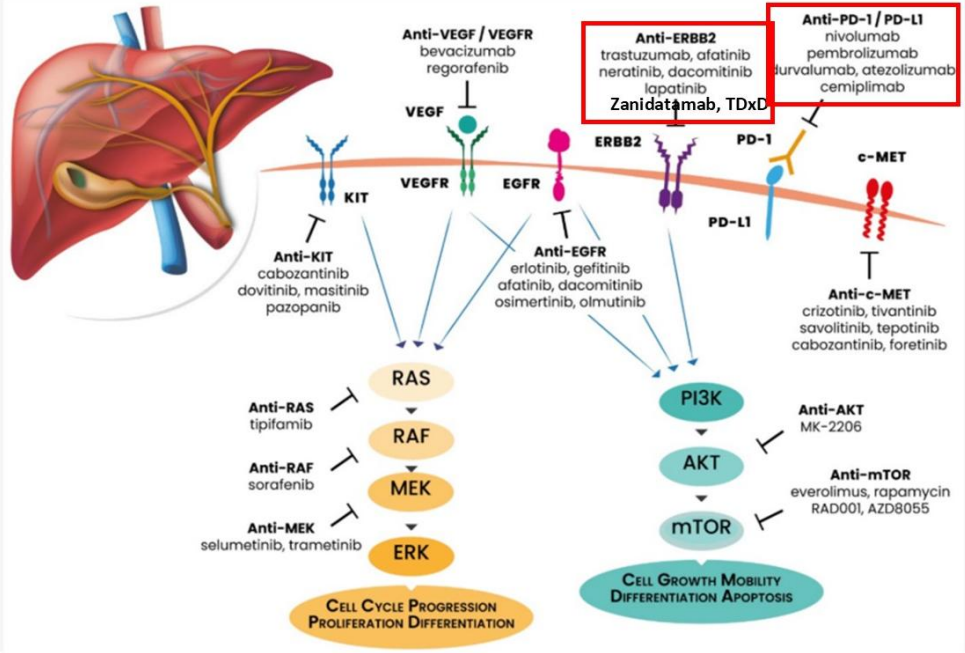
Sharma A, MD Abstract #519

Cáncer de Vía Biliar

Future direction

- ACTICCA-1: adjuvant capecitabine versus cisplatin and gemcitabine).
- ARTEMIDE- Biliary 01 – Rilvegostomib + chemo vs chemo

Figure 1. Main actionable gene mutations of gallbladder cancer with relative targeted therapies.



www.Clinicaltrials.gov

Canale, et.al., *Cancers* **2021**, *13*(22), 5671;

XIX JORNADA DE ACTUALIZACIÓN ASCO GI 2025

5 de marzo de 2025

TNEs-GEP avanzados

A phase III study of combination therapy with everolimus plus lanreotide versus everolimus monotherapy for unresectable or recurrent gastroenteropancreatic neuroendocrine tumor (JCOG1901, STARTER-NET).

JCOG
Japan Clinical Oncology Group

JCOG1901 (STARTER-NET): Trial design

N = 250

Key inclusion criteria

- Histologically proven GEP-NETs with G1/2 (2019 WHO classification)
- Unresectable or recurrent disease
- Non-functional
- Ki-67 5%-20% or Ki-67 <5% with diffuse liver metastases
- No prior treatment for metastatic or recurrent disease
- ECOG PS of 0-2
- Aged ≥ 20

R 1:1

EVE arm
Everolimus (10 mg/day) Monotherapy

EVE/LAN arm
Everolimus (10 mg/day) + Lanreotide (120 mg every 28 days)

- Treatment until disease progression or unacceptable toxicity
- Tumor assessment every 12 weeks up to 48 weeks, then every 16 weeks per RECIST v1.1
- Toxicities graded per CTCAE v5.0

Adjustment factors

- Institution
- Primary organ (pancreas vs. duodenum, jejunum, ileum, cecum, appendix vs. stomach, colon, rectum)
- Ki-67 LI (Ki-67 LI ≥ 10% vs. 5% ≤ Ki-67 LI < 10% vs. Ki-67 LI < 5%)

Study endpoints
Primary: PFS
Key secondary: OS
Other secondary: ORR, DCR, safety

Hijioka S, Abstract #652 ASCO GI 2025

TNEs-GEP avanzados

Baseline characteristics

8

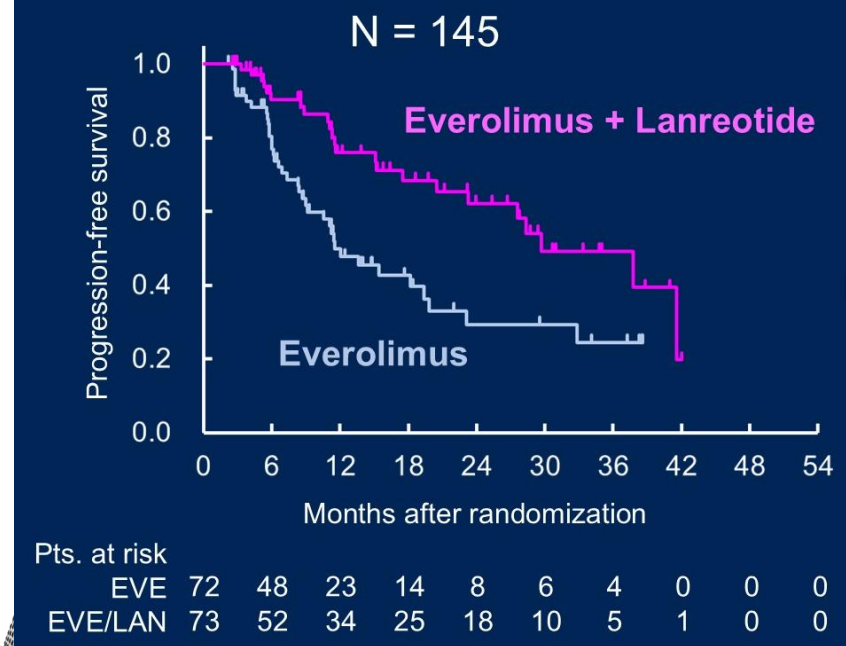
	All patients	
	EVE (n = 88)	EVE/LAN (n = 90)
Median age (range) years	60 (30-82)	64 (31-82)
Male, n (%)	47 (53.4)	42 (46.7)
ECOG PS 0, n (%)	79 (89.8)	71 (78.9)
Primary organ, n (%)		
Pancreas	63 (71.6)	62 (68.9)
Duodenum, jejunum, ileum, cecum, appendix	7 (8.0)	9 (10.0)
Stomach, colon, rectum	18 (20.5)	19 (21.1)
Ki-67 LI, n (%)		
Ki-67 LI < 5%	23 (26.1)	23 (25.6)
5% ≤ Ki-67 LI < 10%	37 (42.0)	39 (43.3)
Ki-67 LI ≥ 10%	28 (31.8)	28 (31.1)

ECOG: Eastern Cooperative Oncology Group

Hijioka S, Abstract #652 ASCO GI 2025

TNEs-GEP avanzados

"Pre-specified" **Interim analysis for PFS (Jun. 2024)**



	mPFS	95% CI
EVE	11.5 m	9.0-19.8
EVE/LAN	29.7 m	20.5-NE

- Stratified HR 0.38 [99.91% CI: 0.15–0.96]
- One-sided P = 0.00017
  < significance level of 0.00046

P-value by stratified log-rank test
Stratification factor was Ki-67 LI (≥10% vs. 5%-10% vs. <5%)

- Predictive probability of showing superiority in the final analysis: 98.1%

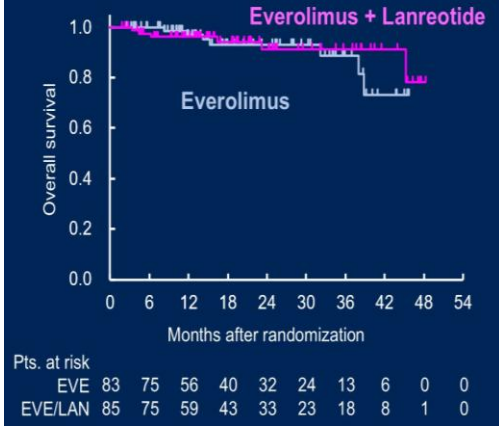
- The trial was terminated on the recommendation of the JCOG Data and Safety Monitoring Committee.

Hijioka S, Abstract #652 ASCO GI 2025

TNEs-GEP avanzados

Overall survival (Nov. 2024)

N = 168



	mOS	1-year survival
EVE	NE	97.0% [88.4-99.2%]
EVE/LAN	NE	96.2% [88.8-98.8%]

- HR 0.74 [95% CI: 0.25-2.24]
- Number of observed events: 13
  - 11 deaths from the primary disease
  - 1 death from other disease
  - 1 unknown

Objective response rate (ORR) and disease control rate (DCR)

	All patients	
	EVE (n = 84)	EVE/LAN (n = 87)
Best overall response, n (%)		
CR	0 (0.0)	0 (0.0)
PR	7 (8.3)	20 (23.0)
SD	64 (76.2)	60 (69.0)
PD	9 (10.7)	2 (2.3)
NE	4 (4.8)	5 (5.7)
ORR, n (%) [95% CI]	8.3% [3.4-16.4]	23.0% [14.6-33.3]
p-value*	0.011	
DCR, n (%) [95% CI]	84.5% [75.0-91.5]	92.0% [84.1-96.7]
p-value*	0.16	

*Fisher's two-sided p-value for the direct probability test

Hijioka S, Abstract #652 ASCO GI 2025

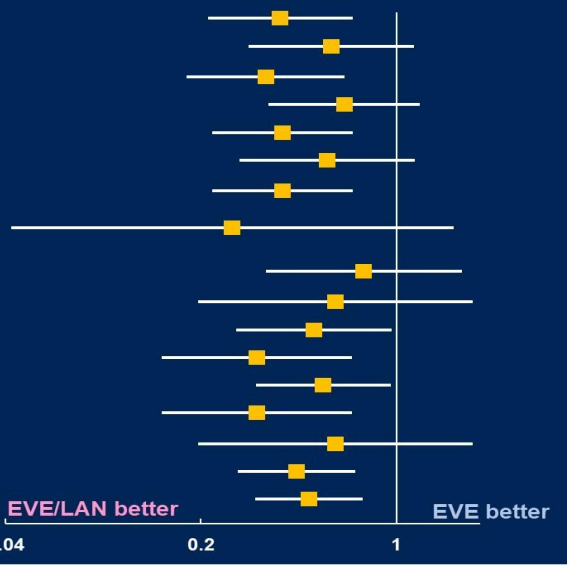
TNEs-GEP avanzados

Subgroup analyses for PFS

13

Factors	Levels	n	MST (month) EVE	MST (month) EVE/LAN	HR
Age	< 65 years	99	14.3	29.7	**0.39**
	≥ 65 years	69	10.5	28.4	**0.59**
Sex	Male	85	11.8	23.2	**0.34**
	Female	83	18.2	34.2	**0.65**
Primary site 1	Pancreas	118	15.4	38.2	**0.39**
	Gastrointestinal tract	50	11.1	23.2	**0.57**
Primary site 2	Pancreas	118	15.4	38.2	**0.39**
	Duodenum, jejunum, ileum, cecum, and appendix	15	11.8	NE	**0.26**
	Stomach, colon, rectum	35	9.1	16.9	**0.77**
Ki-67 1	< 5%	43	32.8	42.7	**0.61**
	5%-10%	72	11.3	23.2	**0.51**
	≥ 10%	53	11.5	29.7	**0.32**
Ki-67 2	< 10%	115	13.6	28.4	**0.55**
	≥ 10%	53	11.5	29.7	**0.32**
Ki-67 3	< 5%	43	32.8	42.7	**0.61**
	≥ 5%	125	11.3	27.6	**0.44**
Overall		168	13.6	29.7	**0.49**

Unstratified HR (95% CI)

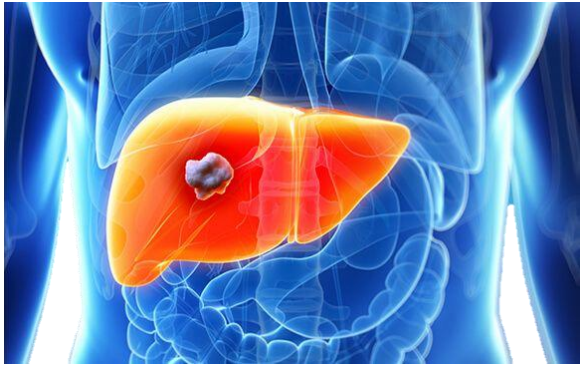


"Incremento en AEs g 3/4… posiblemente por > exp. a **EVE**…"

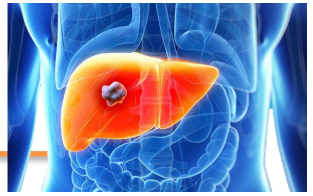
Hijioka S, Abstract #652 ASCO GI 2025

XIX JORNADA DE ACTUALIZACIÓN ASCO GI 2025

5 de marzo de 2025



Hepatocarcinoma Avanzado



Nivolumab plus ipilimumab vs lenvatinib or sorafenib as first-line therapy for unresectable hepatocellular carcinoma: CheckMate 9DW expanded analyses

CheckMate 9DW study design

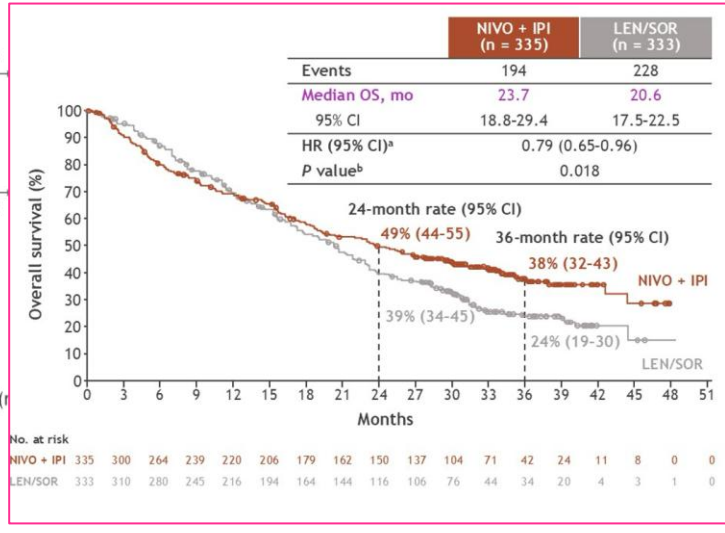
- CheckMate 9DW is a global, phase 3, randomized, open-label study of NIVO in combination with IPI compared with LEN or SOR as 1L treatment in patients with unresectable HCC[a]

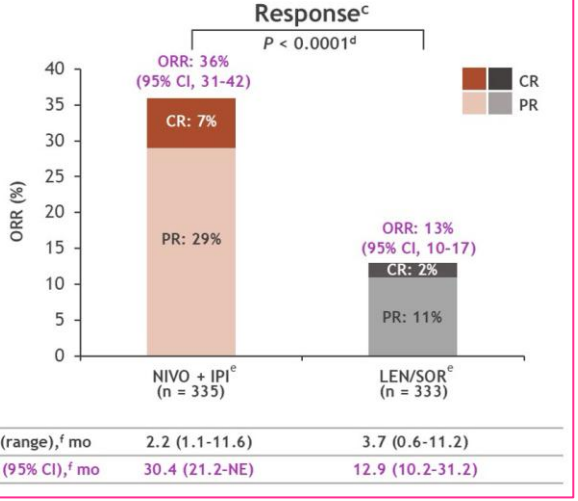
Key eligibility criteria:
- Unresectable HCC[b]
- At least 1 measurable lesion (RECIST v1.1)
- Systemic therapy naive
- Child-Pugh score 5 or 6
- ECOG PS 0 or 1
- No main portal vein invasion (Vp4)

N = 668 → R 1:1 → n = 335 / n = 333

Stratification factors:
- Etiology (HBV vs HCV vs uninfected)[c]
- MVI/EHS (present vs absent)
- AFP (< 400 vs ≥ 400 ng/mL)

- At data cutoff (January 31, 2024), median (r

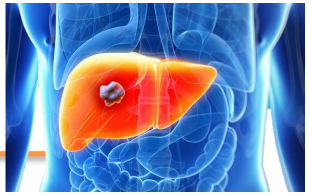




	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Median TTR (range),[f] mo	2.2 (1.1-11.6)	3.7 (0.6-11.2)
Median DOR (95% CI),[f] mo	30.4 (21.2-NE)	12.9 (10.2-31.2)

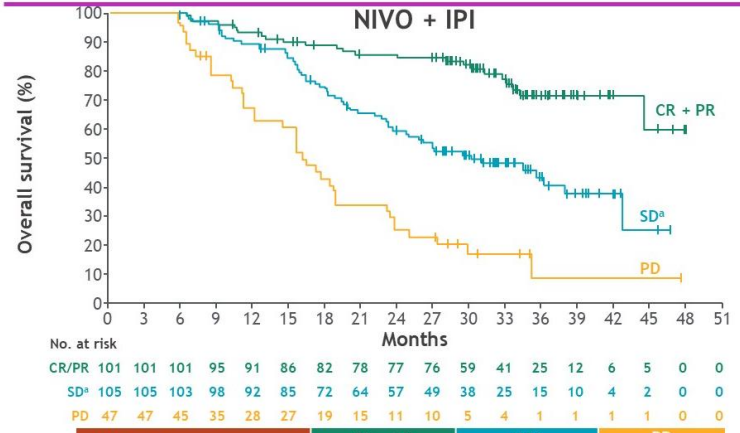
Kudo M, et al. Abstract #520 ASCO GI 2025

Hepatocarcinoma Avanzado

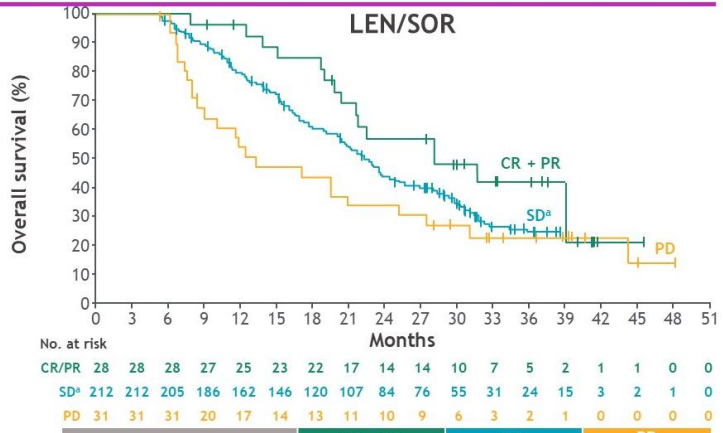


Nivolumab plus ipilimumab vs lenvatinib or sorafenib as first-line therapy for unresectable hepatocellular carcinoma: CheckMate 9DW expanded analyses

Overall survival by best overall response at 24-week landmark



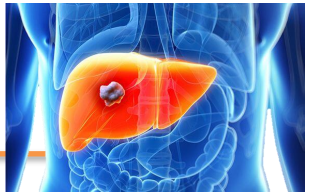
NIVO + IPI	CR + PR (n = 101)	SDa (n = 105)	PD (n = 47)
Events	24	56	38
Median OS, mo	NR	30.0	16.0
95% CI	44.4-NE	23.5-37.8	12.0-18.7
HR (95% CI), CR+PR vs PD	0.14 (0.08-0.24)		
HR (95% CI), SDa vs PD	0.40 (0.26-0.60)		



LEN/SOR	CR + PR (n = 28)	SDa (n = 212)	PD (n = 31)
Events	15	145	23
Median OS, mo	28.3	22.5	13.5
95% CI	20.6-NE	20.5-24.8	8.7-25.3
HR (95% CI), CR+PR vs PD	0.45 (0.23-0.86)		
HR (95% CI), SDa vs PD	0.69 (0.45-1.08)		

Kudo M, et al. Abstract #520 ASCO GI 2025

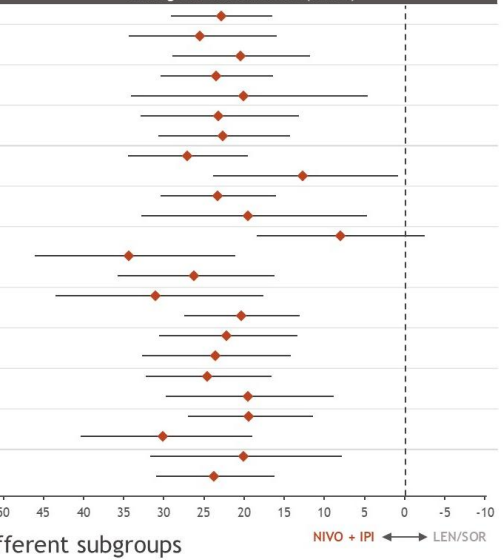
Hepatocarcinoma Avanzado



Nivolumab plus ipilimumab vs lenvatinib or sorafenib as first-line therapy for unresectable hepatocellular carcinoma: CheckMate 9DW expanded analyses

Best overall response subgroup analysis

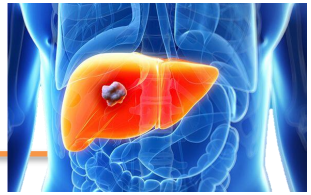
Category	Subgroup	ORR, % NIVO + IPI	ORR, % LEN/SOR	Unweighted ORR difference, %
Overall (N = 668)		36.1	13.2	22.9
Age, years	< 65 (n = 311)	38.9	13.4	25.5
	≥ 65 (n = 357)	33.5	13.0	20.5
Sex	Male (n = 548)	36.5	13.0	23.5
	Female (n = 120)	34.4	14.3	20.1
Region	Asia (n = 280)	36.8	13.6	23.2
	Non-Asia (n = 388)	35.6	12.9	22.7
ECOG PS	0 (n = 476)	39.5	12.3	27.1
	≥ 1 (n = 191)	28.4	15.7	12.7
Child-Pugh score	5 (n = 517)	36.6	13.3	23.3
	6 (n = 130)	33.3	13.8	19.5
Etiology[a,b]	HBV (n = 229)	24.6	16.5	8.0
	HCV (n = 186)	50.0	15.6	34.4
	Uninfected (n = 243)	34.7	8.4	26.3
MVI[a]	Yes (n = 169)	44.2	13.0	31.1
	No (n = 499)	33.7	13.3	20.4
EHS[a]	Yes (n = 360)	36.2	14.0	22.2
	No (n = 308)	36.1	12.4	23.6
MVI/EHS[a]	Yes (n = 438)	38.0	13.4	24.6
	No (n = 230)	32.5	12.9	19.5
Baseline AFP, ng/ml	< 400 (n = 447)	34.4	15.0	19.4
	≥ 400 (n = 221)	39.8	9.7	30.1
BCLC at baseline	≤ B (n = 177)	32.6	12.5	20.1
	C (n = 488)	37.4	13.6	23.8



ORR per BICR was consistently higher with NIVO + IPI vs LEN/SOR across different subgroups

Kudo M, et al. Abstract #520 ASCO GI 2025

Hepatocarcinoma Avanzado



A multicenter prospective study to evaluate the efficacy of resection for initially unresectable hepatocellular carcinoma after atezolizumab combined with bevacizumab (the RACB study): short-term outcomes

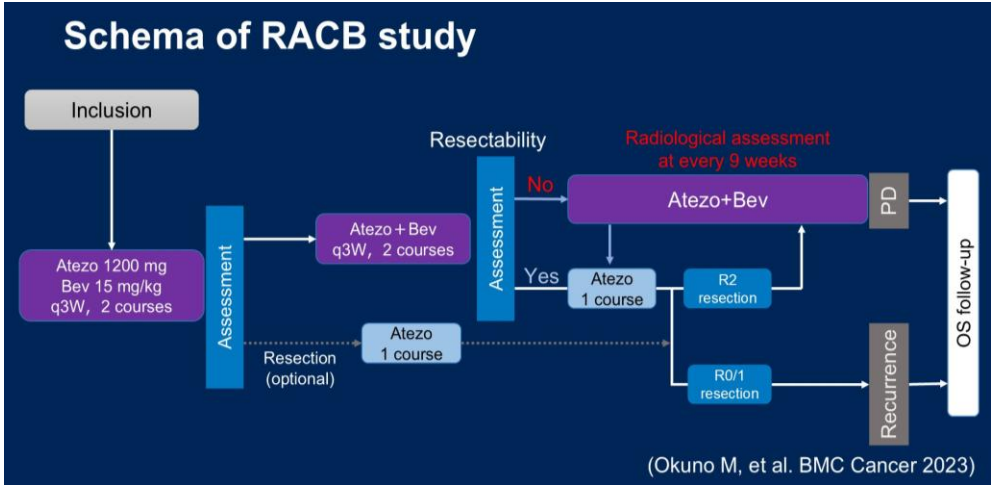
Definition of unresectable

A	Intrahepatic vascular invasion	
B	Synchronous extrahepatic metastases	
C	Intrahepatic vascular invasion and synchronous extrahepatic metastasis	
D	Macroscopic residual tumor	
E	Metachronous extrahepatic metastases	

(Okuno M, et al. BMC Cancer 2023)

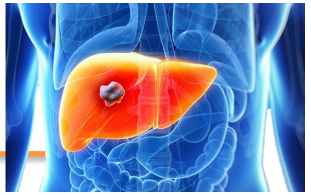
Fase II multicéntrico

- Obj 1º: PFS (RECIST 1.1)
- Obj 2º: ORR, PFS (mRECIST), OS, R0/R1, Safety…



Takayama M, et al. Abstract #521 ASCO GI 2025

Hepatocarcinoma Avanzado



Baseline characteristics

		N=50
Sex	male / female	36 (72%)/ 14 (28%)
Age, median (range)		75 (41-90)
PS	0	41 (82.0%)
	1	9 (18.0%)
ICG-R15 (%), median (range)		12.3 (2.1-39)
Child-Pugh	5	42 (84.0%)
	6	8 (16.0%)
HBV infection		9 (18.0%)
HCV infection		19 (38.0%)
Prior therapy for HCC		7 (14.0%)
Type of inclusion criteria	A	34 (68.0%)
	B	2 (4.0%)
	C	4 (8.0%)
	D	8 (16.0%)
	E	2 (4.0%)
AFP(ng/mL), median (range)		54.2 (1.9-214148)
DCP (AU), median (range)		1527 (16-699105)
Macrovascular invasion	Absent	12 (24.0%)
	Present	38 (76.0%)
Number of liver tumor		1 (0-5)
Diameter of largest liver tumor (mm), median (range)		76 (4-161)
Resectability criteria	BR1	12 (24.0%)
(JLCA a JHBPS expert consensus)	BR2	38 (76.0%)

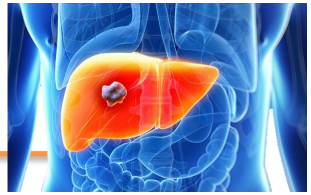
> 80% M0

		N=50
BCLC stage	B	8 (16.0%)
	C	42 (84.0%)
UICC TNM stage	IB	1 (2.0%)
	II	11 (22.0%)
	IIIA	7 (14.0%)
	IIIB	23 (46.0%)
	IVA	2 (4.0%)
	IVB	6 (12.0%)
UICC (T)	No residual primary tumor	2 (4.0%)
	IB	1 (2.0%)
	II	12 (24.0%)
	III	10 (20.0%)
	IIIB	25 (50.0%)
UICC (N)	0	48 (96.0%)
	1	2 (4.0%)
UICC (M)	0	44 (88.0%)
	1	6 (12.0%)
Site of metastases	Lung	3
	LN	1
	Peritoneum	1
	Bone	1

JLCA: the Japan Liver Cancer Association;
JHBPS: the Japanese Society of Hepato-Biliary-Pancreatic Surgery

Takayama M, et al. Abstract #521 ASCO GI 2025

Hepatocarcinoma Avanzado



Efficacy evaluation set (N=46)		
RECIST		
PR	6 (13.0%)	vs 27%*
SD	32 (69.6%)	
PD	8 (17.4%)	
mRECIST		
CR	1 (2.2%)	vs 33%*
PR	12 (26.1%)	
SD	25 (54.3%)	
PD	8 (17.4%)	

* IMBrave 150. Chang AL, et al ESMO Asia 2019

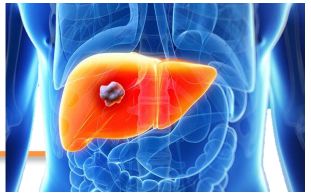
Surgical outcomes

Per Protocol Set (N=50)		
No resection	26 (52.0%)	
Resection	24 (48.0%)	On-protocol resection rate (18/50) 36.0%
R0	21 (87.5%)	
R1	1 (4.2%)	BR1 (7/12) Resection rate: 58.3%
R2	2 (8.3%)	BR2 (17/38) Resection rate: 44.7% — P=0.514

"Baja tasa de complicaciones postIQ…"

Takayama M, et al. Abstract #521 ASCO GI 2025

Hepatocarcinoma Avanzado



Transarterial chemoembolization (TACE) combined with camrelizumab and rivoceranib versus TACE alone in the treatment of unresectable hepatocellular carcinoma: a multicenter, open-label, randomized, phase 2 study (CARES-005)

CARES-005 Study Design

Key eligibility criteria

- Confirmed HCC not amenable to curative treatment
- No extrahepatic metastasis
- At least one measurable lesion per RECICL
- Child-Pugh A
- ECOG PS of 0 or 1

N=200

R 1:1

- **cTACE+** Camrelizumab (200 mg, IV, Q3W) + Rivoceranib (250 mg, PO, QD)
- **cTACE§**

UnTACEable progression, or unacceptable toxicity

Survival follow-up

Stratification factors
- Prior TACE procedures: 0 vs.1-2
- Vascular Invasion: Yes vs. No
- Prior TKI therapy: Yes vs. No

Statistical considerations
- Analysis would be performed when approximately 135 PFS events were observed
- At data cut-off date on Oct 16, 2024, the final PFS analysis was conducted

Cross permitted

Primary endpoint
- PFS*

Secondary endpoints:
- PFS (mRECIST)
- TTUP, ORR, DCR, DoR, OS
- Safety

	TACE+C+R (N = 100)	TACE (N = 100)
BCLC stage		
A	14 (14.0)	14 (14.0)
B	44 (44.0)	42 (42.0)
C	42 (42.0)	44 (44.0)
Tumor burden at baseline		
Within up-to-7 criteria (≤7)	11 (11.0)	10 (10.0)
Beyond up-to-7 criteria (>7)	89 (89.0)	90 (90.0)
PVTT type		
Vp1/Vp2	13 (13.0)	14 (14.0)
Vp3/Vp4	27 (27.0)	27 (27.0)
Number of prior TACE procedure		
1-2	25 (25.0)	24 (24.0)
0	75 (75.0)	76 (76.0)
Previous TKI therapy		
Yes	2 (2.0)	3 (3.0)
No	98 (98.0)	97 (97.0)

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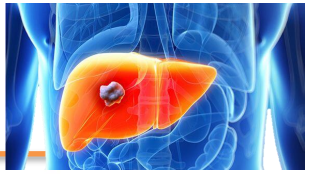
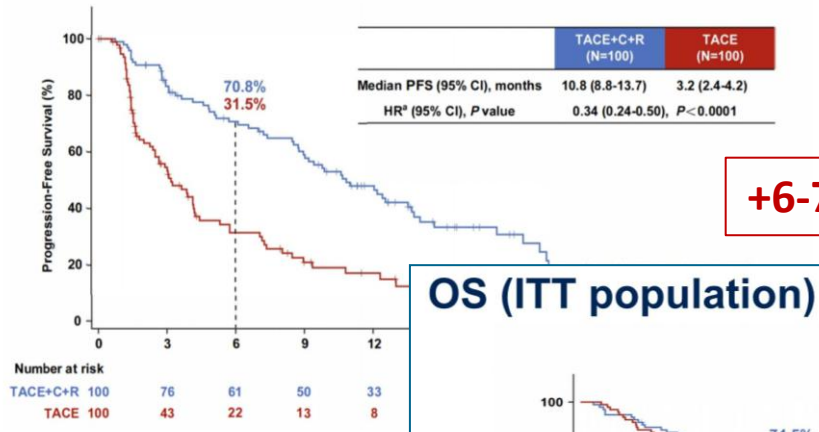
Hepatocarcinoma Avanzado



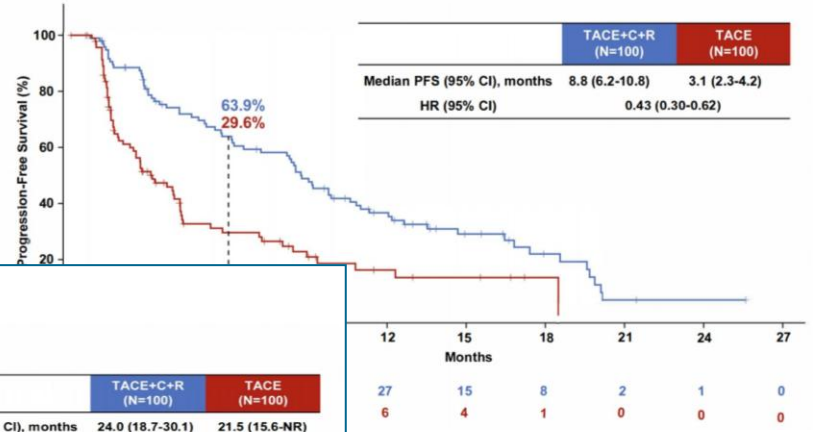
PFS per RECICL (ITT population)



	TACE+C+R (N=100)	TACE (N=100)
Median PFS (95% CI), months	10.8 (8.8-13.7)	3.2 (2.4-4.2)
HR[a] (95% CI), *P* value	0.34 (0.24-0.50), *P*<0.0001	

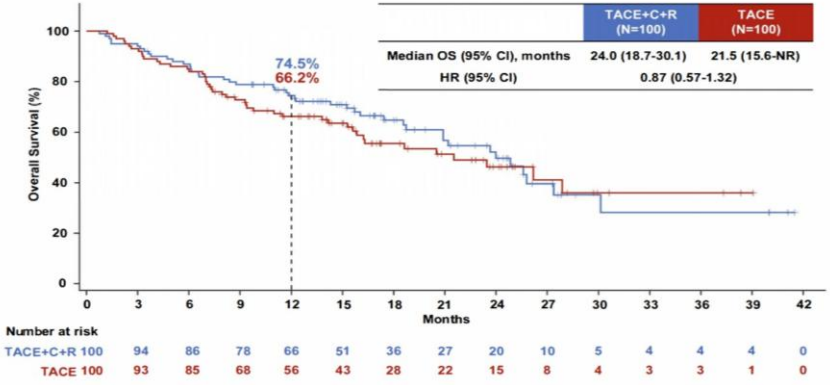
+6-7 m

PFS[※] per mRECIST (ITT population)



	TACE+C+R (N=100)	TACE (N=100)
Median PFS (95% CI), months	8.8 (6.2-10.8)	3.1 (2.3-4.2)
HR (95% CI)	0.43 (0.30-0.62)	

OS (ITT population)



	TACE+C+R (N=100)	TACE (N=100)
Median OS (95% CI), months	24.0 (18.7-30.1)	21.5 (15.6-NR)
HR (95% CI)	0.87 (0.57-1.32)	

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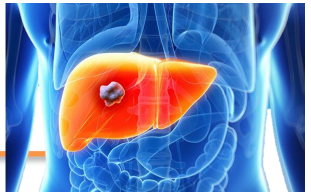
Hepatocarcinoma Avanzado

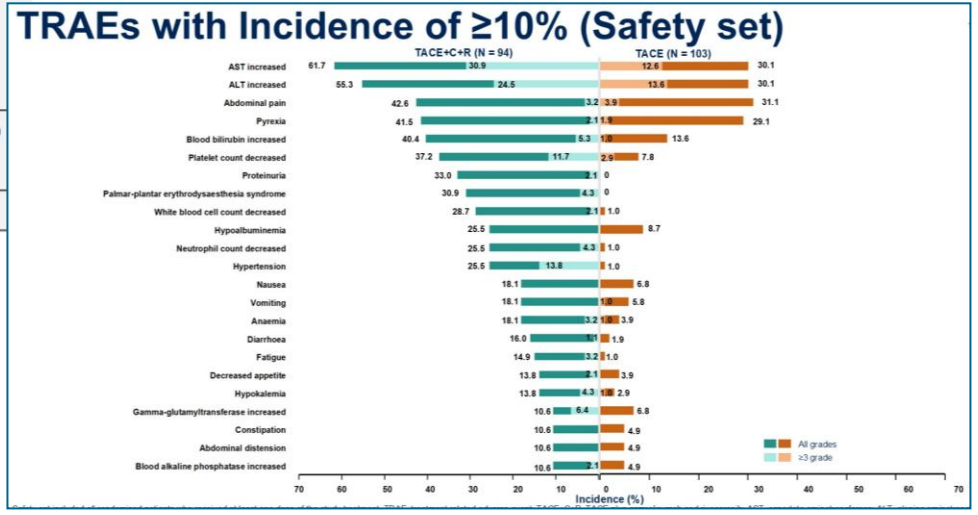


Tumor Response per RECICL/mRECIST

	RECICL		mRECIST	
	TACE+C+R (N = 100)	TACE (N = 100)	TACE+C+R (N = 100)	TACE (N = 100)
ORR, % (95% CI)	65.0 (54.8, 74.3)	29.0 (20.4, 38.9)	61.0 (50.7, 70.6)	29.0 (20.4, 38.9)
CR	16 (16.0)	4 (4.0)	16 (16.0)	4 (4.0)
PR	49 (49.0)	25 (25.0)	45 (45.0)	25 (25.0)
SD	22 (22.0)	34 (34.0)	24 (24.0)	29 (29.0)
PD	5 (5.0)	30 (30.0)	7 (7.0)	35 (35.0)
NE	8 (8.0)	7 (7.0)	8 (8.0)	7 (7.0)
DCR, % (95% CI)	87.0 (78.8, 92.9)	63.0 (52.8, 72.4)	85.0 (76.5, 91.4)	58.0 (47.7, 67.8)
mDoR, months (95% CI)	11.4 (9.0, 17.5)	6.9 (4.3, 9.8)	7.6 (6.9, 11.4)	4.7 (2.4, 7.0)
mTTUP, months (95% CI)	13.7 (10.7, 19.6)	3.9 (2.5, 5.7)	-	-

x2

"Mismo mensaje que **LEAP-012** & **EMERALD-1**…"



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REAL-WORLD TRIAL RESULTS
& PHASE II CLINICAL TRIALS
ASCO GI 2025
ASCO GI 2025

“Take Home Messages…”

- El **Cáncer de Páncreas** continúa siendo una “**necesidad médica no cubierta**”… “Terapia antiestromal” (Pamrevlumab): **“Una nueva decepción…”**
  - “A grandes males…**Soluciones novedosas**” → “**Nuevos diseños** de EC” (Optimización)
  - Valoración Geriátrica Integral **(VGI) fundamental** en este contexto
- La **QT/RT** adyuvante **NO es útil** en carcinomas de de **Vesícula Biliar**
- La combinación **EVE+ASS** es **superior** a EVE en **aNETs**…(↑ PFS & ORR)
  - ”Especialmente en pNETs & Ki67 > 5-10% o con alta carga Hg…”
- En pacientes con **HCC**…
  - “Los **respondedores**” a Nivo/IPI (SD + PR/CR), más que con TKis, “**van mejor**”…(mOS > 30m)
  - Atezo-Bev “neoadyuvante” en aHCC es seguro y podría rescatar entre 1/3 & 1/2 de casos…**¿PFS?**
  - En uHCC AntiPD-1 + TKi *vs* TACE: ↑ **PFS** & **ORR**…**¿OS?**…(3º Fase III con mismo mensaje)

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