

XVII SIMPOSIUM BASES BIOLÓGICAS DEL CÁNCER E INNOVACIÓN TERAPÉUTICA

MÁS DE 20 AÑOS A LA VANGUARDIA DE LA FORMACIÓN
EN LA BIOLOGÍA Y TRATAMIENTO DEL CÁNCER

SALAMANCA, 22 Y 23 DE MAYO DE 2025

“Novedades en el tratamiento del hepatocarcinoma”

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“Mis conflictos...”

- 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.



Agenda para hoy...

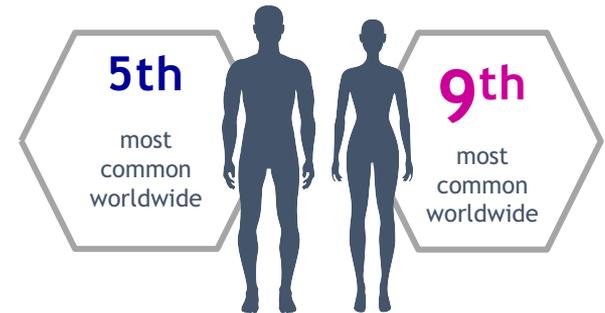
- “Puesta en escena...”
- "No hace tanto tiempo..."(antes de 2019)
"Otros se unieron rápidamente..."
"Y no se quedaron ahí..."
"Próximos pasos..."
- Conclusiones



Conceptos Generales

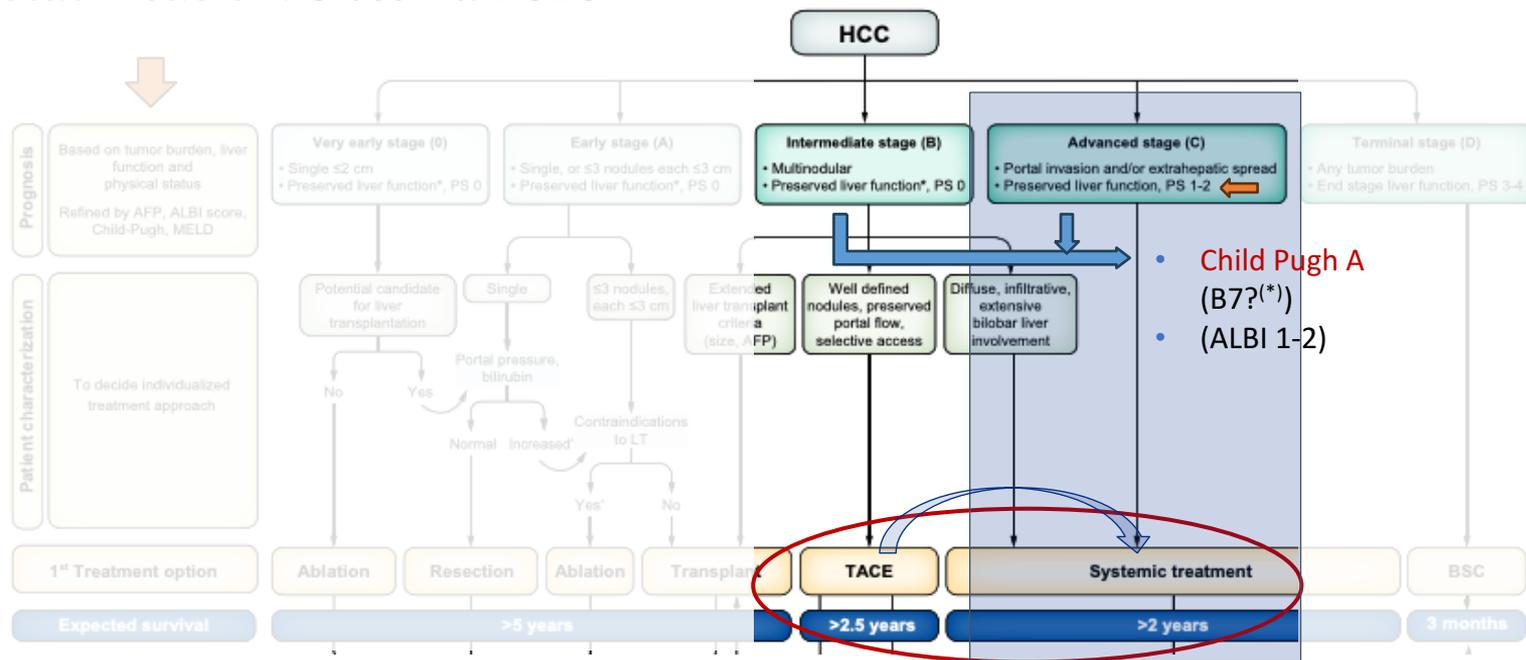
“Hepatocarcinoma: Problema de Salud”

- El HCC es la **3ª causa principal de muerte por cáncer** en todo el mundo, habiendo sido responsable de **868.391 muertes (7,3%)** en 2022.
El cáncer de hígado es **más frecuente en los hombres**
En **España**, en 2024 se diagnosticaron:
 - 6.856 nuevos casos de cáncer de hígado (**90% son HCC**)
 - 5.184 fallecimientos (**7ª causa**) por este tumor (Aprox. **75%**)



“De que estamos hablando...”

- Estadificación: **Sistema BCLC**



(*) Fuera de ficha técnica





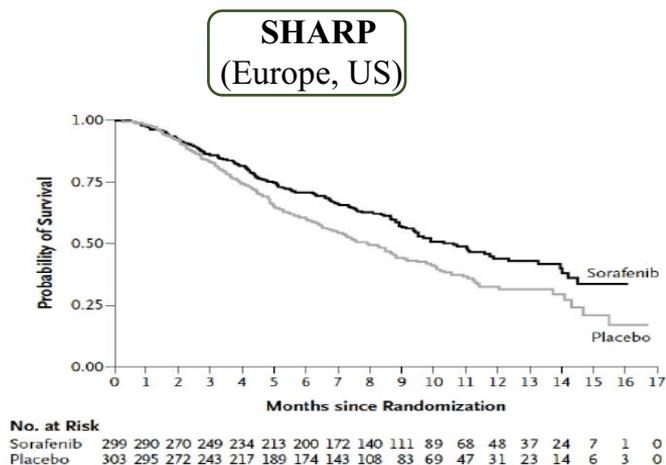
“In just 20 years...”



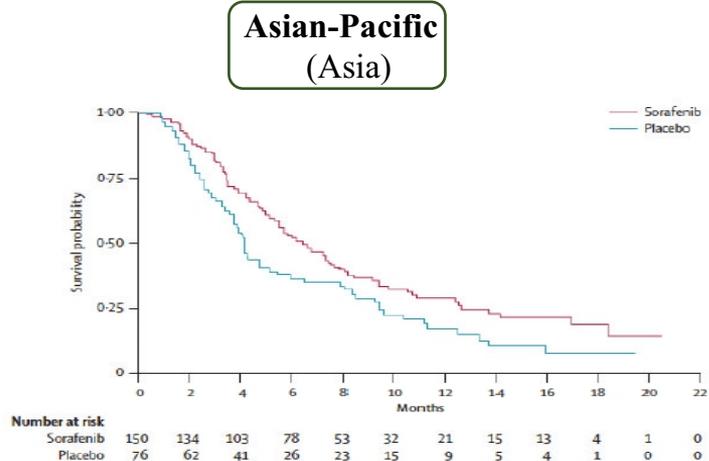
“No hace tanto tiempo...”

- “Opciones antes de 2019...” (1ª línea: Sorafenib)

Llovet JM, et al. N Engl J Med 2008 & Cheng AL, et al. Lancet Oncol 2009



OS: 7.9 vs 10.7 mo (HR:0.69) $p = 0.0001$



OS: 4.2 vs 6.5 mo (HR:0.68) $p = 0.01$



“No hace tanto tiempo...”

- "Opciones antes de 2019..." (1ª línea: **Lenvatinib**)

Global, randomised, open-label, phase 3 **non-inferiority** study

Patients with unresectable HCC (N=954)

- No prior systemic therapy for unresectable HCC
- ≥ 1 measurable target lesion per mRECIST
- BCLC-B (not applicable for TACE) or BCLC-C
- Child-Pugh A
- ECOG-PS ≤ 1
- Adequate organ function
- Patients with $\geq 50\%$ liver occupation, clear bile duct invasion, or portal vein invasion at the main portal vein were excluded

Stratification

- Region: (Asia-Pacific or Western)
- MVI and/or EHS: (yes or no)
- ECOG-PS: (0 or 1)
- Body weight: (<60 kg or ≥ 60 kg)

Randomisation 1:1

Lenvatinib (N=478)

8 mg (BW <60 kg)
or
12 mg (BW ≥ 60 kg)
once daily

Sorafenib (N = 476)

400 mg
twice daily

Primary objective:

- OS

Secondary objectives:

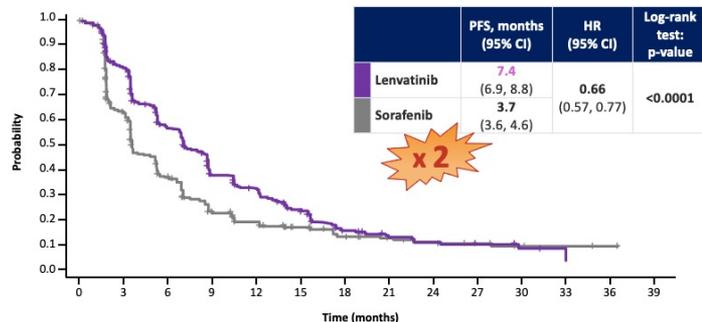
- PFS
- TTP
- ORR
- Quality of life
- PK lenvatinib exposure parameters

* Tumour assessments were performed according to mRECIST by the investigator



"No hace tanto tiempo..."

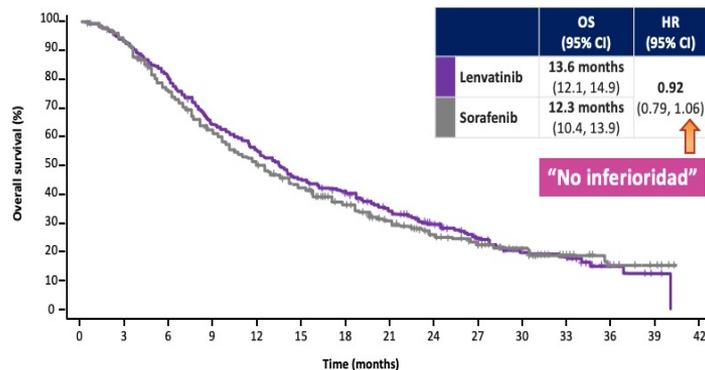
- "Opciones antes de 2019..." (1ª línea: Lenvatinib)



Number of patients at risk:

Lenvatinib	478	345	223	172	106	69	44	28	14	9	4	2	0	0
Sorafenib	476	262	140	94	56	41	33	22	14	9	4	2	2	0

	Investigator assessment (mRECIST)		Independent review			
	Lenvatinib	Sorafenib	mRECIST		RECIST v1.1	
	Lenvatinib	Sorafenib	Lenvatinib	Sorafenib	Lenvatinib	Sorafenib
Response rate						
ORR (95% CI)	24.1 % (20.2, 27.9)	9.2 % (6.6, 11.8)	40.6 % (36.2, 45.0)	12.4 % (9.4, 15.4)	18.8 % (15.3, 22.3)	6.5 % (4.3, 8.7)
Odds ratio (95% CI)	3.13 (2.15, 4.56)		5.01 (3.59, 7.01)		3.34 (2.17, 5.14)	
P-value	p<0.00001		p<0.00001		p<0.00001	
Mean time to ORR (mo)	3.6	4.8	2.7	3.4		



Number of patients at risk:

Lenvatinib	478	436	374	297	253	207	178	140	102	67	40	21	8	2	0
Sorafenib	476	440	348	282	230	192	156	116	83	57	33	16	8	4	0



“No hace tanto tiempo...”

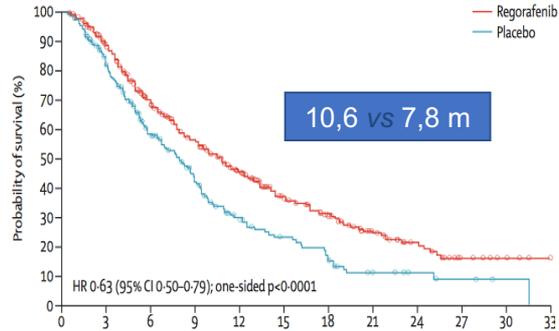
- “Opciones antes de 2019...” (Perfiles de Toxicidad)

AE, n, %	Lenvatinib (N=476)				Sorafenib (N=475)			
	Any grade		Grade 3/4		Any grade		Grade 3/4	
PPE	128	27%	14	3%	249	52%	54	11%
Diarrhoea	184	39%	20	4%	220	46%	20	4%
Hypertension	201	42%	111	23%	144	30%	68	14%
Decreased appetite	162	34%	22	5%	127	27%	6	1%
Decreased weight	147	31%	36	8%	106	22%	14	3%
Fatigue	141	30%	18	4%	119	25%	17	4%
Alopecia	14	3%	0	0%	119	25%	0	0%
Proteinuria	117	25%	27	6%	54	11%	8	2%
Dysphonia	113	24%	1	<1%	57	12%	0	0%
Nausea	93	20%	4	1%	68	14%	4	1%
Abdominal pain	81	17%	8	2%	87	18%	13	3%
Decreased platelet count	87	18%	26	5%	58	12%	16	3%
Elevated AST	65	14%	24	5%	80	17%	38	8%
Hypothyroidism	78	16%	0	0%	8	2%	0	0%
Vomiting	77	16%	6	1%	36	8%	5	1%
Constipation	76	16%	3	1%	52	11%	0	0%
Rash	46	10%	0	0%	76	16%	2	<1%
Increased blood bilirubin	71	15%	31	7%	63	13%	23	5%



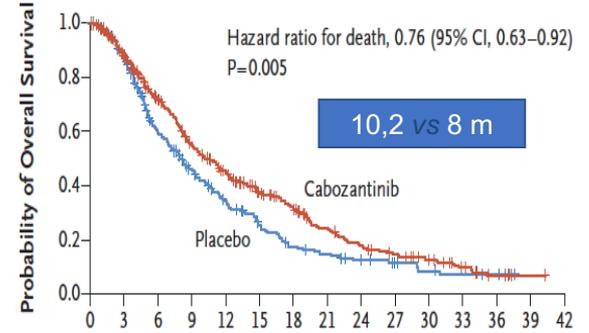
“Opciones hasta 2019...” (2ª línea...“post-SOR”)

Bruix J, et al. Lancet 2017



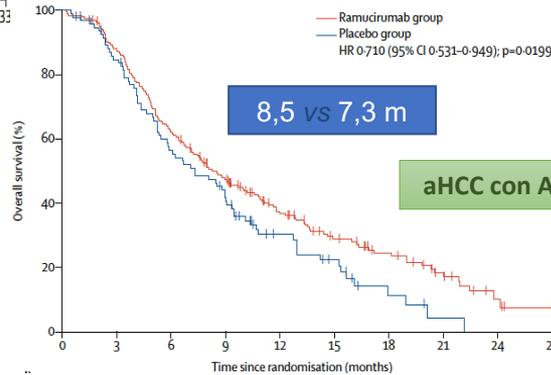
“Tolerantes” a Sorafenib

Abou-Alfa GK, et al. NEJM 2018



“Progresores” a Sorafenib

Zhu AX, et al. Lancet Oncol 2019



aHCC con AFP>400 ng/mL



“Así en el año 2019...”

Terapias Sistémicas para aHCC		
1ª Línea	2ª Línea	3ª Línea?
Sorafenib Lenvatinib	Regorafenib¹ Nivo/Pembro? Cabozantinib Ramucirumab²	Cabozantinib?
PFS 4 - 7,5 m OS 12 - 14 m	PFS 3 - 5 m OS 8,5 - 12 m	

Llovet JM, et al. NEMJ 2008
Kudo M, et al. Lancet 2018
Yau T, et al. ESMO 2019

Bruix J, et al Lancet 2017
El-Koueiry et al. Lancet 2017
Finn RS, et al. ASCO 2019
Abou-Alfa KG, et al NEJM 2018
Zhu AX, et al Lancet Oncol 2019

¹ SOR tolerant pts
² AFP > 400 ng/mL

FDA, EMA, AEMPS
FDA, EMA
FDA





Sorafenib
Lenvatinib

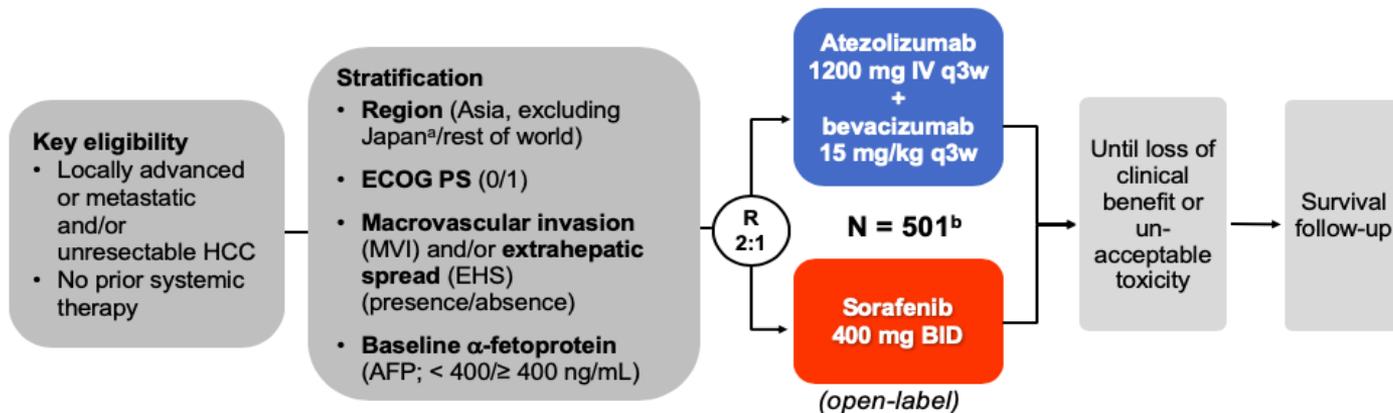
TKis

"Otros se unieron rápidamente..."



“Otros se unieron rápidamente...”

IMbrave150 study design



Co-primary endpoints

- OS
- IRF-assessed PFS per RECIST 1.1

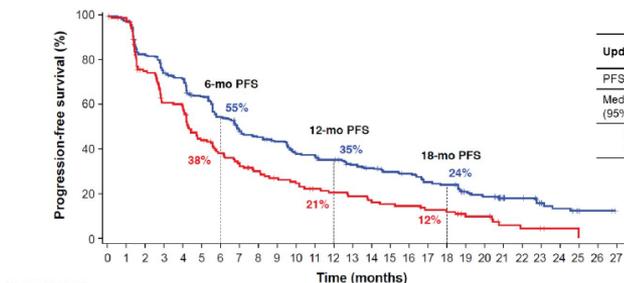
Key secondary endpoints (in testing strategy)

- IRF-assessed ORR per RECIST 1.1
- IRF-assessed ORR per HCC mRECIST



“Otros se unieron rápidamente...”

Updated PFS by IRF RECIST 1.1



No. of patients at risk

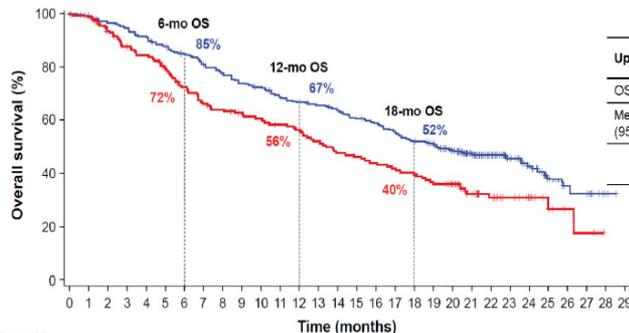
Time (months)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Atezo + Bev	336	323	271	245	234	204	174	149	141	132	113	111	102	93	88	80	77	67	64	47	41	27	25	17	12	4	3	NE
Sorafenib	165	150	110	88	84	63	52	44	39	34	31	26	24	22	19	18	17	14	13	9	9	4	3	2	1	1	NE	NE

Clinical cutoff: August 31, 2020; median follow-up: 15.6 mo.

Updated PFS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
PFS events, n (%)	257 (76)	130 (79)
Median PFS, mo (95% CI)	6.9 (5.7, 8.6)	4.3 (4.0, 5.6)
Stratified HR (95% CI) ^a	0.65 (0.53, 0.81) P = 0.0001 ^b	

■ Perfil de Seguridad "favorable"...
Impacto en **Calidad de Vida**

Updated OS



No. of patients at risk

Time (months)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Atezo + Bev	336	329	320	312	302	288	278	263	252	240	233	221	214	209	202	192	188	175	164	156	134	105	80	57	42	24	12	11	2	NE
Sorafenib	165	158	144	133	128	119	108	96	92	86	85	81	78	72	66	64	61	56	55	49	44	32	24	18	12	7	3	2	NE	NE

Clinical cutoff: August 31, 2020; median follow-up: 15.6 mo.

Updated OS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
OS events, n (%)	180 (54)	100 (61)
Median OS, mo (95% CI)	19.2 (17.0, 23.7)	13.4 (11.4, 16.9)
Stratified HR (95% CI) ^a	0.66 (0.52, 0.85) P = 0.0009 ^b	

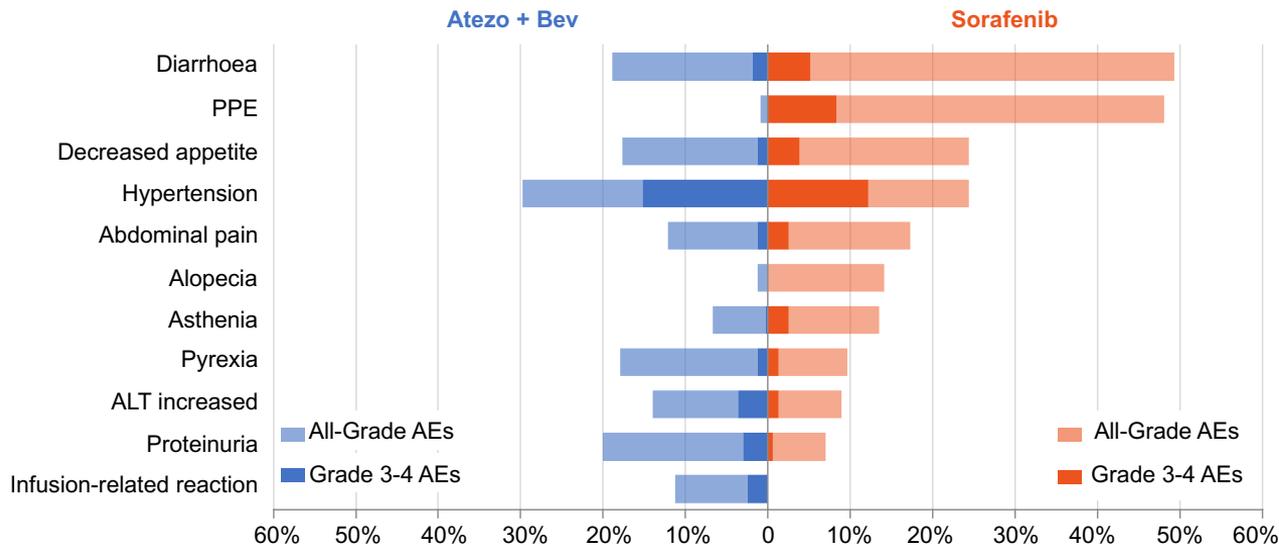
	Updated analysis ^a			
	RECIST 1.1		HCC mRECIST	
	Atezo + Bev (n = 326)	Sorafenib (n = 159)	Atezo + Bev (n = 325)	Sorafenib (n = 158)
Confirmed ORR (95% CI), %	30 (25, 35)	11 (7, 17)	35 (30, 41)	14 (9, 20)
CR, n (%)	25 (8)	1 (< 1)	39 (12)	4 (3)
PR, n (%)	72 (22)	17 (11)	76 (23)	18 (11)
SD, n (%)	144 (44)	69 (43)	121 (37)	65 (41)
DCR, n (%)	241 (74)	87 (55)	236 (73)	87 (55)
PD, n (%)	63 (19)	40 (25)	65 (20)	40 (25)
Ongoing response, n (%)	54 (56)	5 (28)	58 (50)	6 (27)
Median DOR (95% CI), mo ^b	18.1 (14.6, NE)	14.9 (4.9, 17.0)	16.3 (13.1, 21.4)	12.6 (6.1, 17.7)



“Otros se unieron rápidamente...”

Safety^a

≥ 10% frequency of AEs in either arm and > 5% difference between arms



PPE, palmar-plantar erythrodysesthesia.

^a Safety-evaluable population.

“Únicamente 3 casos (0,6%) de HDA (G5) en Atezo-Bev...”

Finn RS, et al. NEJM 2020 & Cheng AL, et al. J. Hepatology 2022





Sorafenib
Lenvatinib

TKis

ICIs + AntiVEGF



Atezo-Beva

"Otros se unieron rápidamente..."

“Otros se unieron rápidamente...”

ICI
+
TKis

COSMIC-312

LEAP-002

Himalaya

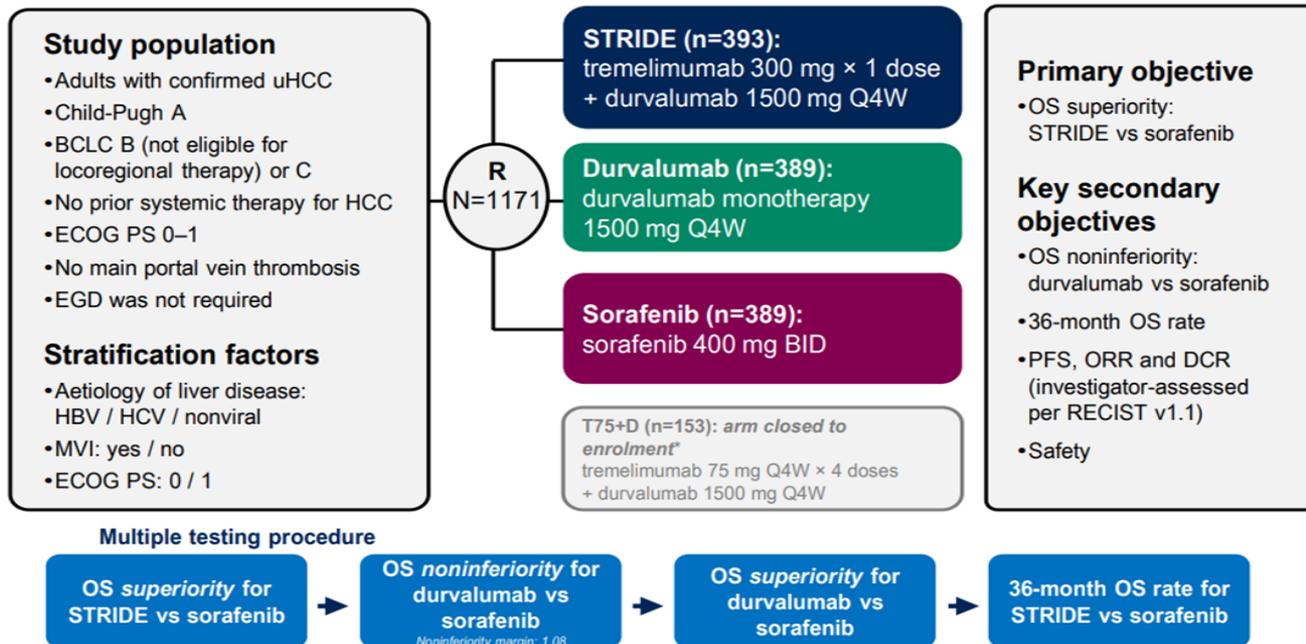
CheckMate-9WD

ICI x 2



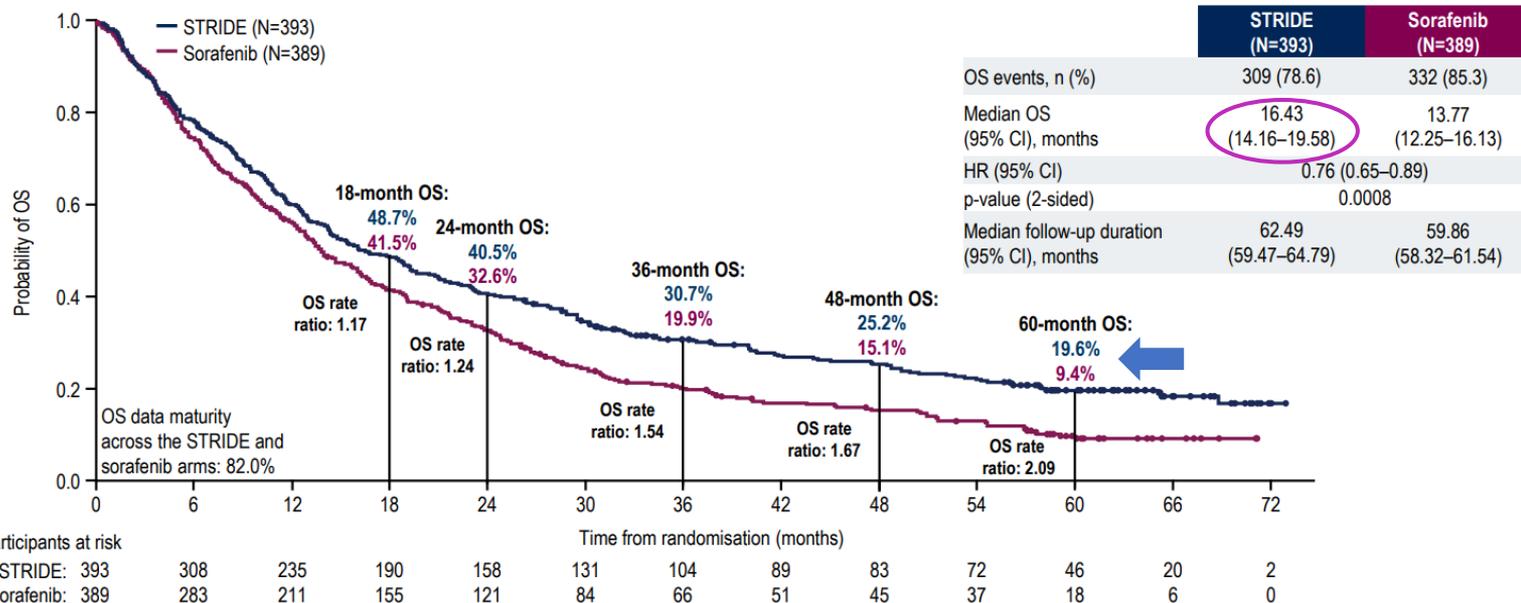
“Otros se unieron rápidamente...”

HIMALAYA: Diseño



“Otros se unieron rápidamente...”

HIMALAYA: Eficacia



OS data maturity across the STRIDE and sorafenib arms: 82.0%



“Otros se unieron rápidamente...”

HIMALAYA: Eficacia



	Full analysis set ¹		eLTS [†] (≥48 months)	
	STRIDE (n=393)	Sorafenib (n=389)	STRIDE (n=83)	Sorafenib (n=45)
BOR, n (%)				
CR	12 (3.1)	0	10 (12.0)	0
PR	67 (17.0)	20 (5.1)	41 (49.4)	7 (15.6)
SD	157 (39.9)	216 (55.5)	23 (27.7)	30 (66.7)
PD	141 (35.9)	118 (30.3)	8 (9.6)	6 (13.3)
NE	16 (4.1)	35 (9.0)	1 (1.2)	2 (4.4)
Median TTR (IQR), months	2.17 (1.84–3.98)	3.78 (1.89–8.44)	2.10 (1.84–3.94)	5.49 (1.64–11.01)
Median DoR (IQR), months	22.34 (8.54–NR)	18.43 (6.51–25.99)	NR (20.50–NR)	NR (8.31–NR)
DCR*, n (%)	236 (60.1)	236 (60.7)	74 (89.2)	37 (82.2)

60%

20%

eLTS included participants regardless of response

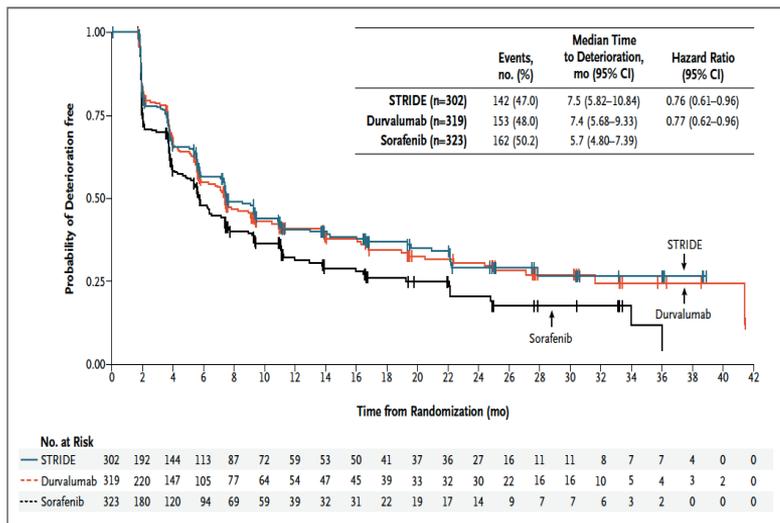
* Extended “long term survivors”

Rimassa L, et al. ESMO 2024



“Otros se unieron rápidamente...”

HIMALAYA: Seguridad



“Patients’ QOL...”

Table 4. Treatment-Emergent Adverse Events That Occurred in 10% or More of Patients or Grade 3 or 4 Treatment-Emergent Adverse Events That Occurred in 2% or More of Patients in Any Treatment Arm in the Safety Analysis Population.*

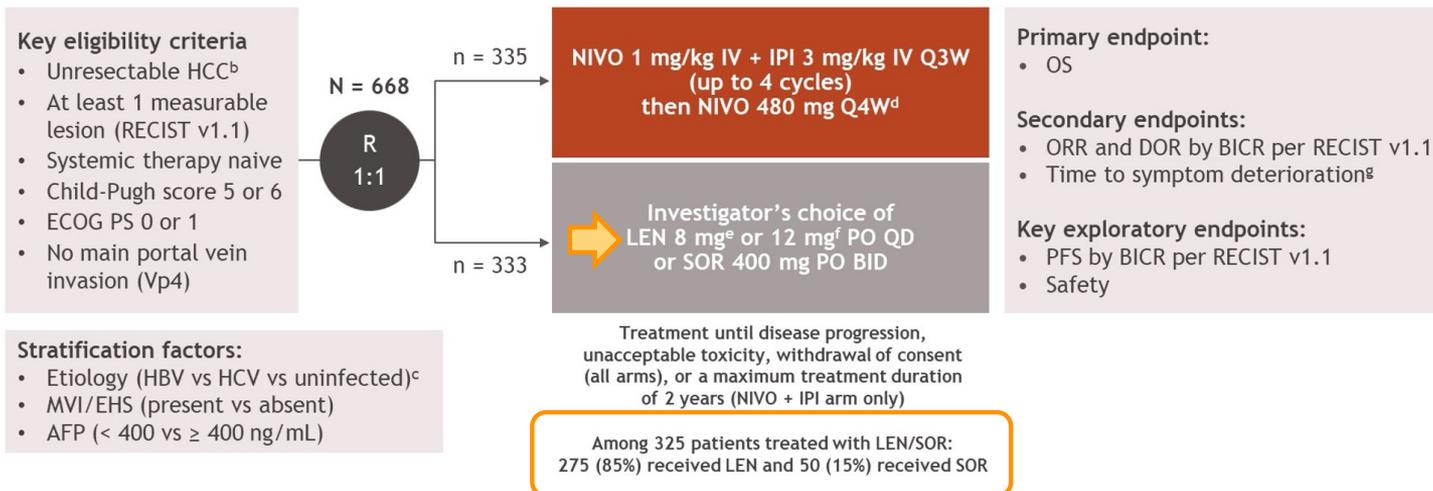
Event	STRIDE (n=388)		Durvalumab (n=388)		Sorafenib (n=374)		T75+D (N=152)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Diarrhea	103 (26.5)	17 (4.4)	58 (14.9)	6 (1.5)	167 (44.7)	16 (4.3)	32 (21.1)	4 (2.6)
Constipation	36 (9.3)	0	42 (10.8)	0	35 (9.4)	0	12 (7.9)	1 (0.7)
Abdominal pain	46 (11.9)	5 (1.3)	37 (9.5)	4 (1.0)	63 (16.8)	12 (3.2)	26 (17.1)	3 (2.0)
Nausea	47 (12.1)	0	37 (9.5)	0	53 (14.2)	0	14 (9.2)	0
Pruritus	89 (22.9)	0	56 (14.4)	0	24 (6.4)	1 (0.3)	27 (17.8)	0
Rash	87 (22.4)	6 (1.5)	40 (10.3)	1 (0.3)	51 (13.6)	4 (1.1)	27 (17.8)	0
Alopecia	2 (0.5)	0	5 (1.3)	0	53 (14.2)	0	1 (0.7)	0
Palmar-plantar erythrodysesthesia syndrome	3 (0.8)	0	1 (0.3)	0	174 (46.5)	34 (9.1)	3 (2.0)	1 (0.7)
Aspartate aminotransferase increased	48 (12.4)	20 (5.2)	56 (14.4)	26 (6.7)	24 (6.4)	12 (3.2)	16 (10.5)	10 (6.6)
Alanine aminotransferase increased	36 (9.3)	10 (2.6)	44 (11.3)	12 (3.1)	20 (5.3)	7 (1.9)	10 (6.6)	5 (3.3)
Amylase increased	29 (7.5)	14 (3.6)	9 (2.3)	3 (0.8)	10 (2.7)	4 (1.1)	6 (3.9)	4 (2.6)
Blood bilirubin increased	20 (5.2)	3 (0.8)	23 (5.9)	7 (1.8)	29 (7.8)	8 (2.1)	5 (3.3)	1 (0.7)
Gamma-glutamyltransferase increased	18 (4.6)	8 (2.1)	12 (3.1)	7 (1.8)	19 (5.1)	7 (1.9)	7 (4.6)	4 (2.6)
Lipase increased	34 (8.8)	24 (6.2)	23 (5.9)	16 (4.1)	15 (4.0)	11 (2.9)	8 (5.3)	5 (3.3)
Decreased appetite	66 (17.0)	5 (1.3)	53 (13.7)	2 (0.5)	67 (17.9)	3 (0.8)	25 (16.4)	1 (0.7)
Asthenia	39 (10.1)	7 (1.8)	49 (12.6)	8 (2.1)	44 (11.8)	10 (2.7)	20 (13.2)	2 (1.3)
Fatigue	66 (17.0)	8 (2.1)	38 (9.8)	0	71 (19.0)	11 (2.9)	25 (16.4)	2 (1.3)
Pyrexia	50 (12.9)	1 (0.3)	36 (9.3)	7 (1.8)	33 (8.8)	0	16 (10.5)	0
Edema peripheral	33 (8.5)	2 (0.5)	24 (6.2)	1 (0.3)	19 (5.1)	0	16 (10.5)	0
Cough	30 (7.7)	0	31 (8.0)	0	22 (5.9)	1 (0.3)	17 (11.2)	0
Insomnia	40 (10.3)	1 (0.3)	21 (5.4)	0	16 (4.3)	0	10 (6.6)	0
Hypothyroidism	47 (12.1)	0	19 (4.9)	0	16 (4.3)	0	20 (13.2)	1 (0.7)
Hypertension	23 (5.9)	7 (1.8)	17 (4.4)	4 (1.0)	68 (18.2)	23 (6.1)	6 (3.9)	3 (2.0)
Anemia	36 (9.3)	11 (2.8)	29 (7.5)	9 (2.3)	33 (8.8)	12 (3.2)	15 (9.9)	3 (2.0)
Hyperkalemia	20 (5.2)	6 (1.5)	20 (5.2)	8 (2.1)	13 (3.5)	9 (2.4)	4 (2.6)	2 (1.3)
Hypokalemia	13 (3.4)	4 (1.0)	9 (2.3)	3 (0.8)	12 (3.2)	2 (0.5)	4 (2.6)	4 (2.6)
Hyponatremia	21 (5.4)	16 (4.1)	12 (3.1)	5 (1.3)	15 (4.0)	11 (2.9)	2 (1.3)	1 (0.7)



“Otros se unieron rápidamente...”

CheckMate-9DW : Diseño

- 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



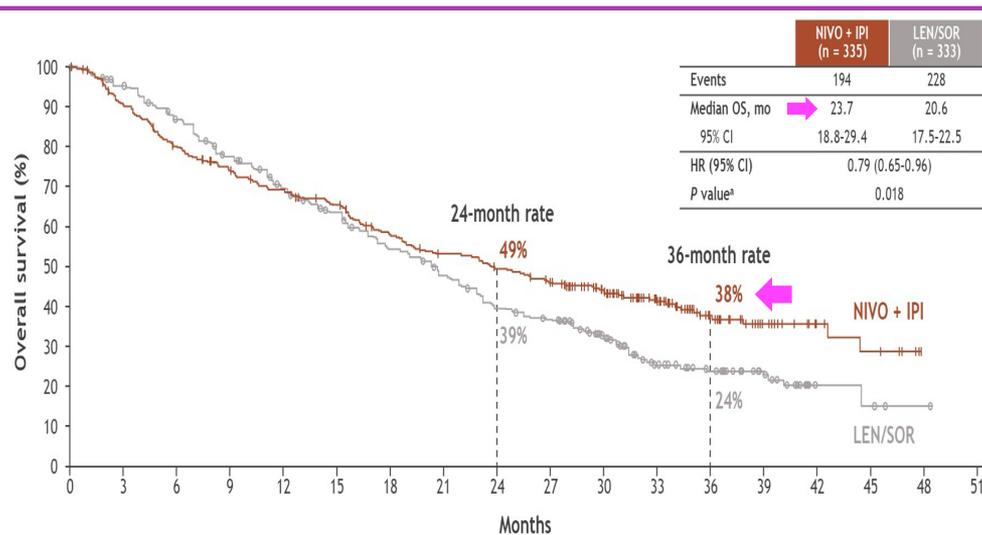
- At data cutoff (January 31, 2024), median (range) follow-up^h was 35.2 (26.8-48.9) months



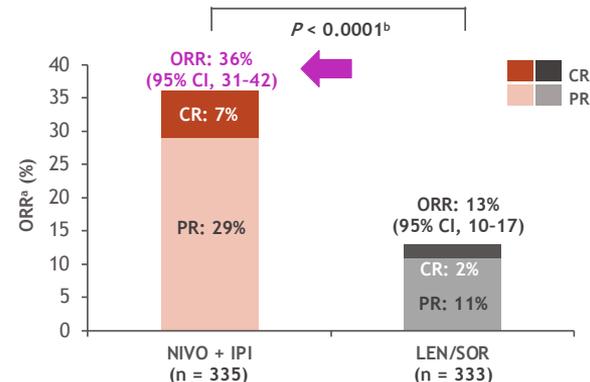
“Otros se unieron rápidamente...”

CheckMate-9DW : Eficacia

Overall survival



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51
NIVO + IPI	335	300	264	239	220	206	179	162	150	137	104	71	42	24	11	8	0	0
LEN/SOR	333	310	280	245	216	194	164	144	116	106	76	44	34	20	4	3	1	0



Best overall response, ^a %	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
SD ^c	32	62
PD	20	14
Not evaluable	12	11
Median TTR (range), ^{a,d} mo	2.2 (1.1-11.6)	3.7 (0.6-11.2)
Median DOR (95% CI), ^{a,d} mo	30.4 (21.2-NE)	12.9 (10.2-31.2)

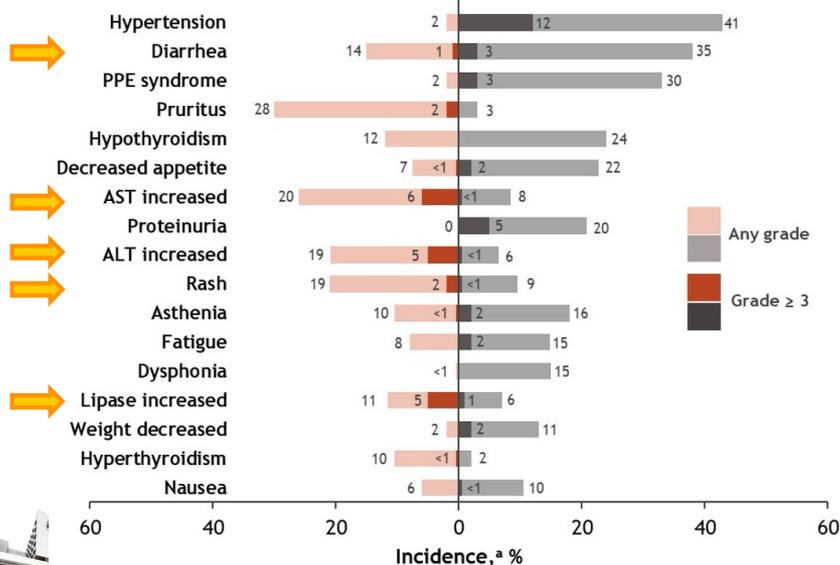
“Otros se unieron rápidamente...”

CheckMate-9DW : Seguridad

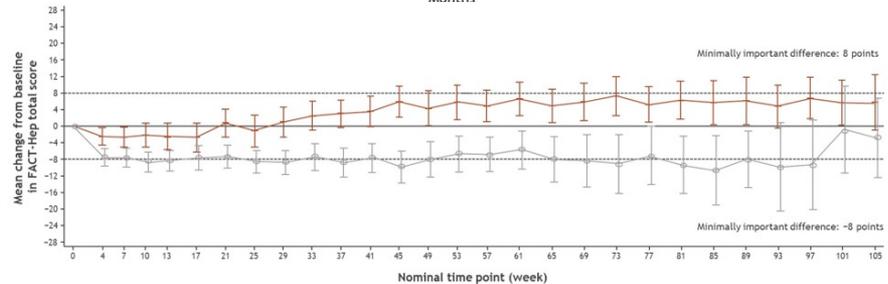
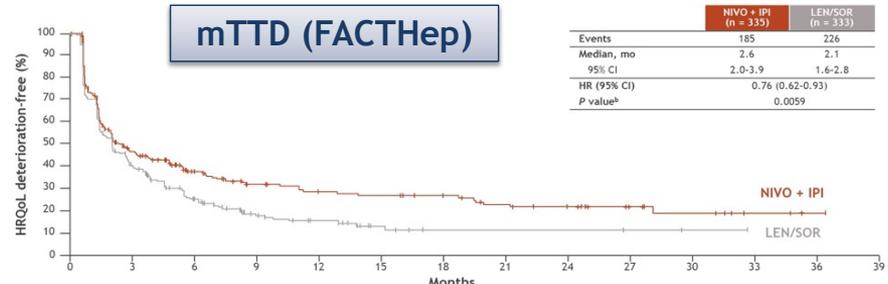
TRAEs occurring in $\geq 10\%$ of patients

NIVO + IPI (n = 332)

LEN/SOR (n = 325)



mTTD (FACTHep)



No. at risk	329	274	231	194	179	170	159	143	140	131	122	117	111	104	93	92	86	85	75	74	73	73	68	63	64	62	59	38
NIVO + IPI	329	274	231	194	179	170	159	143	140	131	122	117	111	104	93	92	86	85	75	74	73	73	68	63	64	62	59	38
LEN/SOR	326	287	271	239	233	203	176	164	156	137	129	112	104	95	90	88	77	62	57	52	38	35	33	27	26	23	19	21





Sorafenib
Lenvatinib

TKis

ICIs + AntiVEGF



Atezo-Beva



STRIDE

"Double" ICIs



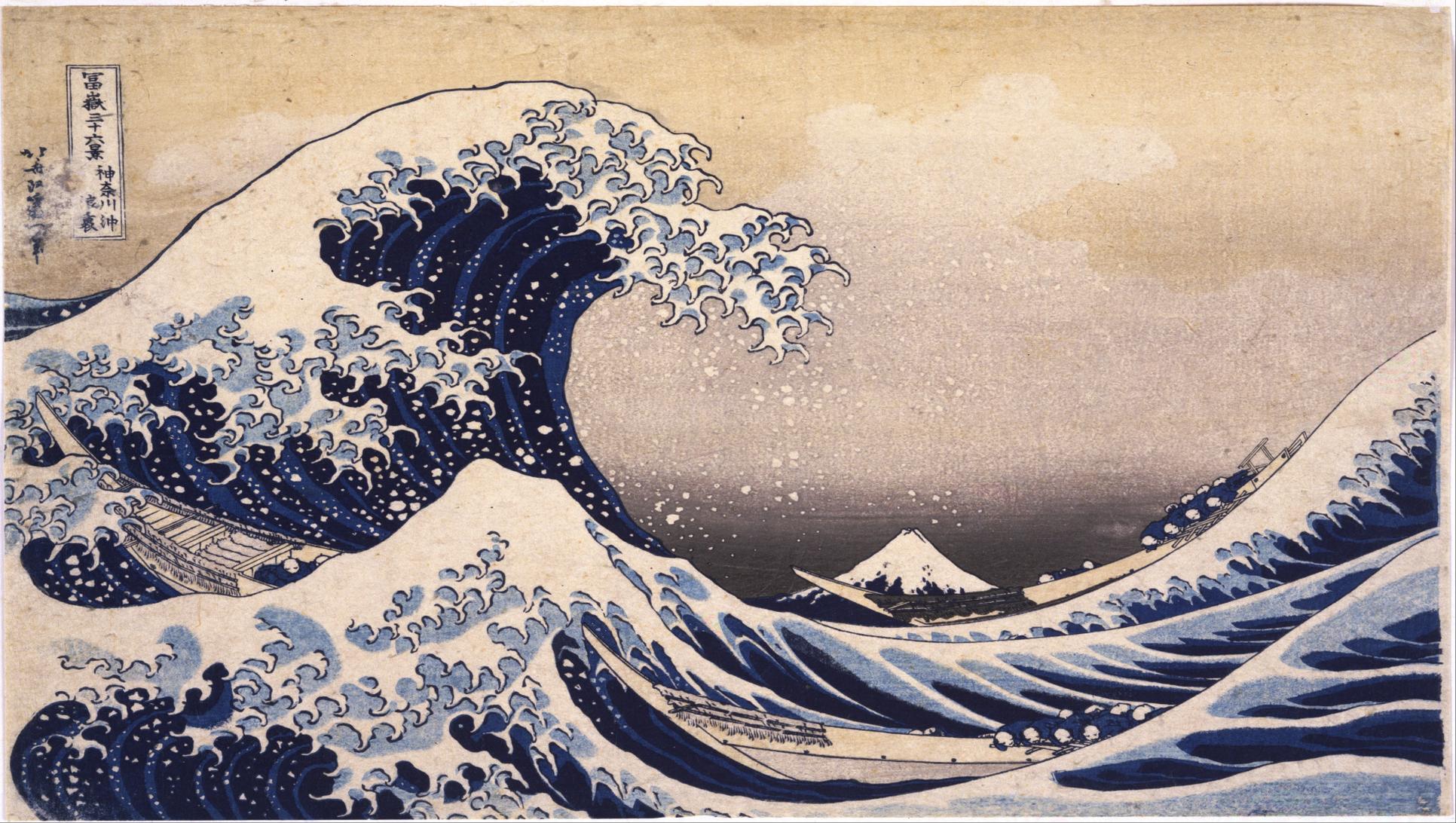
Nivo-IPI

"Otros se unieron rápidamente..."



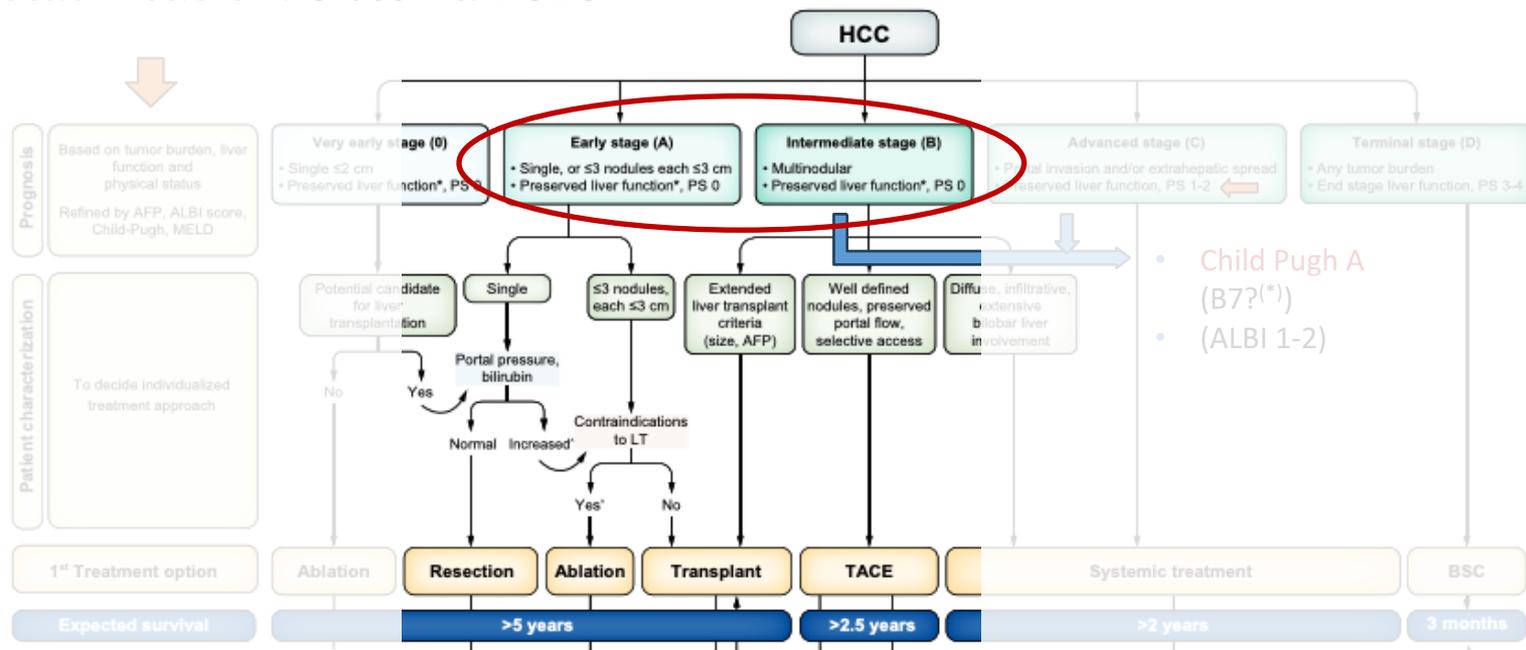
富嶽三十六景 神奈川 波

江戶 葛飾 一筆



“De que estamos hablando...”

- Estadificación: **Sistema BCLC**

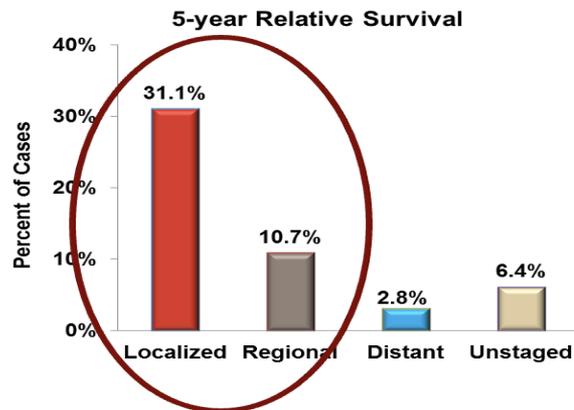
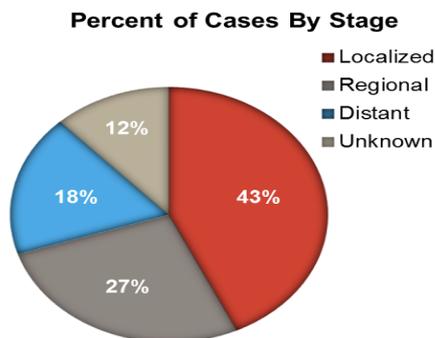


(*) Fuera de ficha técnica



“Y NO se quedarán ahí...”

Liver Cancer: 5-year Survival Rates^a

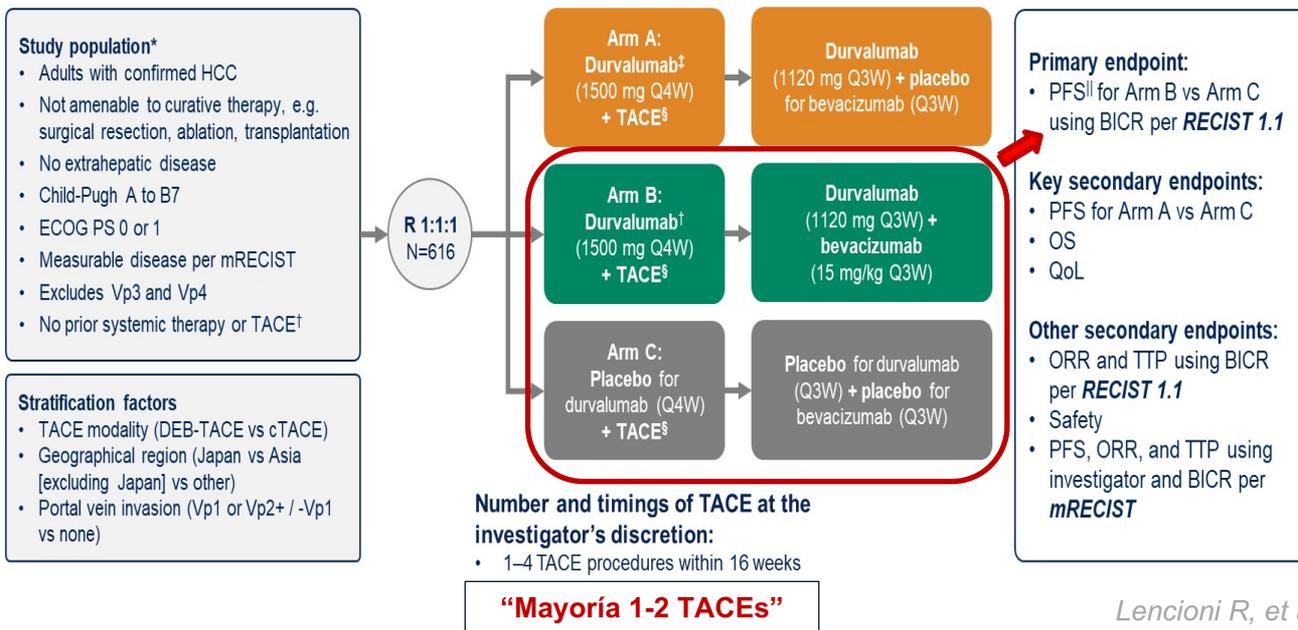


5-year survival rate for well-selected patients (receiving potentially curative treatments) can be as high as 60%-70%

“Y NO se quedarán ahí...”

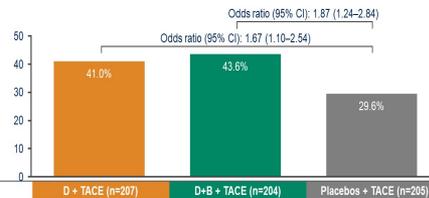
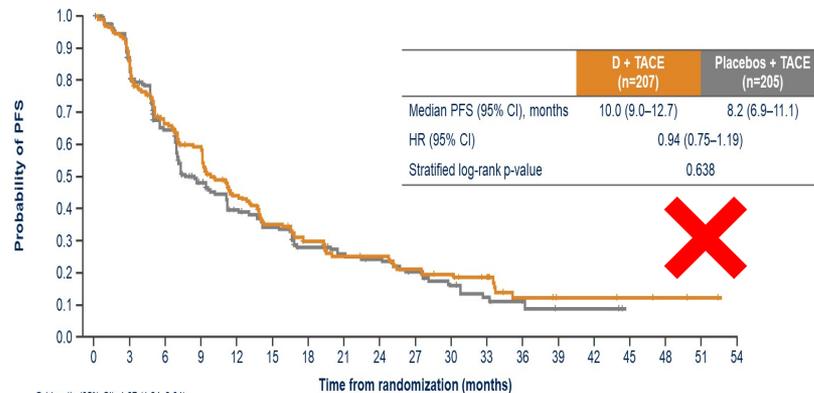
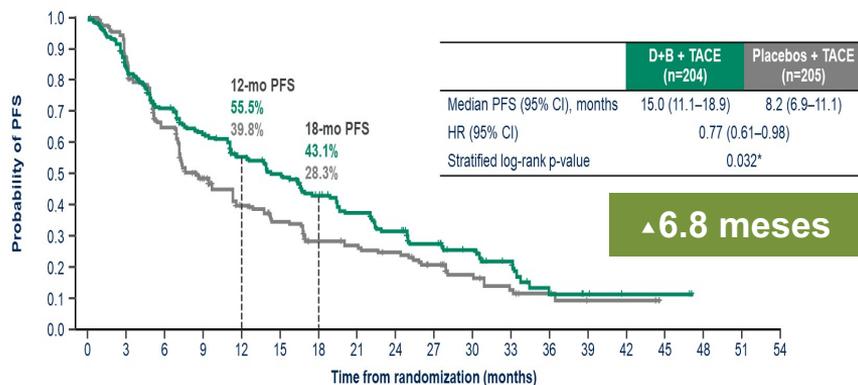
Estadio Intermedio BCLC-B & Terapia Sistémica

EMERALD-1 was a global, double-blind, placebo-controlled Phase 3 study



“Y NO se quedarán ahí...”

Estadio Intermedio BCLC-B & Terapia Sistémica



	D + TACE (n=207)	D+B + TACE (n=204)	Placebos + TACE (n=205)
Participants with measurable disease at baseline	205	202	203
Confirmed response, n (%)	84 (41.0)	88 (43.6)	60 (29.6)
Complete response, n (%)	3 (1.5)	6 (3.0)	5 (2.5)
Partial response, n (%)	81 (39.5)	82 (40.6)	55 (27.1)
Stable disease ≥20 weeks, n (%)	42 (20.5)	45 (22.3)	63 (31.0)
Median duration of response, (LQ-UQ) months	14.0 (6.9–30.7)	22.1 (11.2–30.3)	16.4 (6.3–26.3)

AEs g3/4 < 6%



“Y NO se quedarán ahí...”

Estadio Intermedio BCLC-B & Terapia Sistémica

LEAP-012

Key Eligibility Criteria

- Confirmed HCC not amenable to curative treatment
- ≥ 1 measurable HCC lesion per RECIST v1.1
- All lesions treatable with TACE in 1 or 2 sessions
- No portal vein thrombosis or extrahepatic disease
- Child-Pugh liver class A
- ECOG PS of 0 or 1

Stratification Factors

- Study site
- Alpha fetoprotein (≤ 400 ng/mL vs >400 ng/mL)
- ECOG PS (0 vs 1)
- ALBI grade (1 vs 2 or 3)
- Tumor burden score^{1,a} (≤ 6 vs >6 but ≤ 12 vs >12)

R
1:
1

Lenvatinib 12 mg (BW ≥ 60 kg) or
8 mg (BW < 60 kg) PO QD
+
Pembrolizumab 400 mg IV Q6W
(up to 2 years)
+
TACE^b

Placebo PO QD +
Placebo IV Q6W (up to 2 years)
+
TACE^b

End Points

- **Primary: PFS^c and OS**
 - IA1 is the final analysis for PFS
- Secondary: ORR,^{c,d} DOR,^{c,d} DCR,^{c,d} TTP,^{c,d} PFS,^d and safety

Analyses and Power Estimates:

- ✓ PFS: 276 events for 89% power to detect HR of 0.68.
- ✓ OS: 318 events for 79% power to detect HR of 0.73.
- ✓ **Positive Study: If null hypothesis for PFS is rejected.**

The overall median follow-up was 25.6 months (IQR 19.5–32.4)

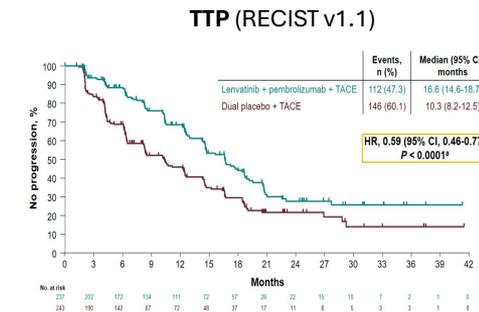
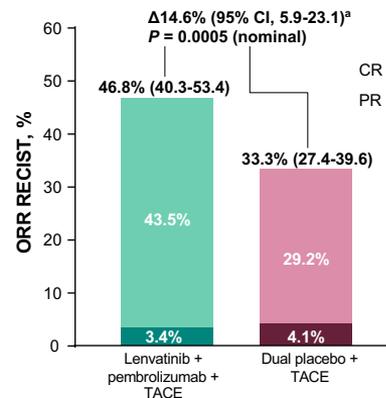
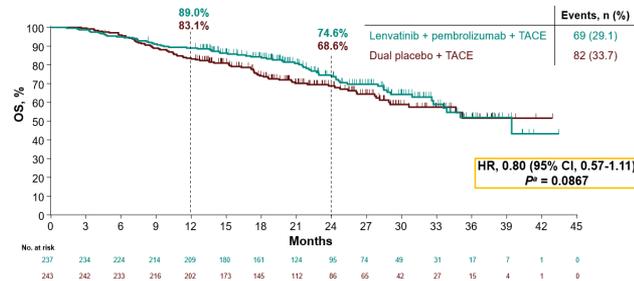
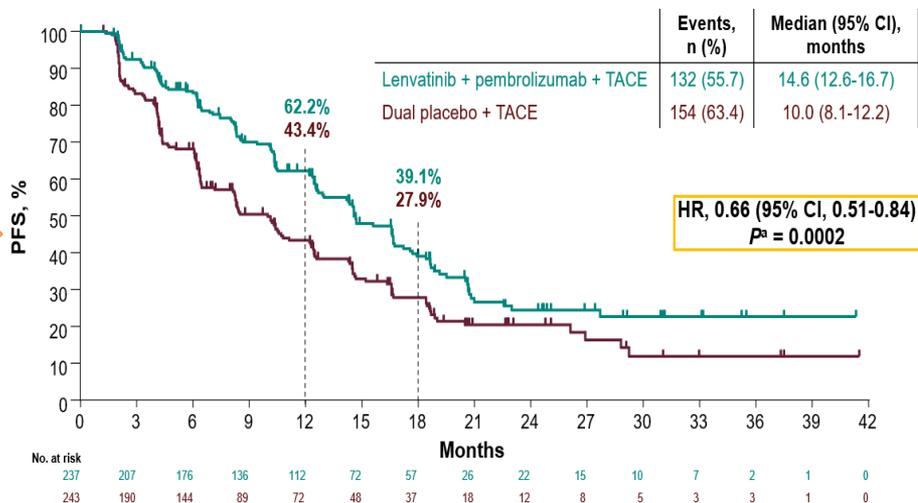
Kudo M. et al Lancet. 2025 Jan 18;405(10474):203-215



“Y NO se quedarán ahí...”

Estadio Intermedio BCLC-B & Terapia Sistémica

LEAP-012



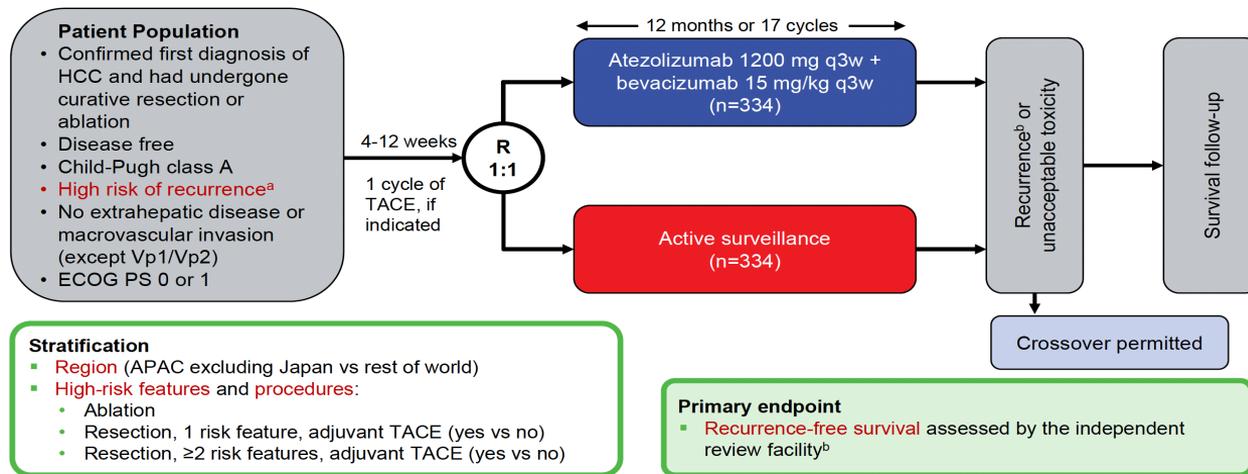
Perfil de Tox. “conocido”



“Y NO se quedarán ahí...”

Estadio precoz BCLC-A & Terapia Sistémica

IMbrave050 study design



ClinicalTrials.gov, NCT04102098. ECOG PS; Eastern Cooperative Oncology Group performance status; Q3W, every three weeks; R, randomization; TACE, transarterial chemoembolization.

^a **High-risk features** include: tumor >5 cm, >3 tumors, microvascular invasion, minor macrovascular invasion Vp1/Vp2, or Grade 3/4 pathology.

^b Intrahepatic recurrence defined by EASL criteria. Extrahepatic recurrence defined by RECIST 1.1.

Chow et al IMbrave050
<https://bit.ly/3ZPKzGM> 5

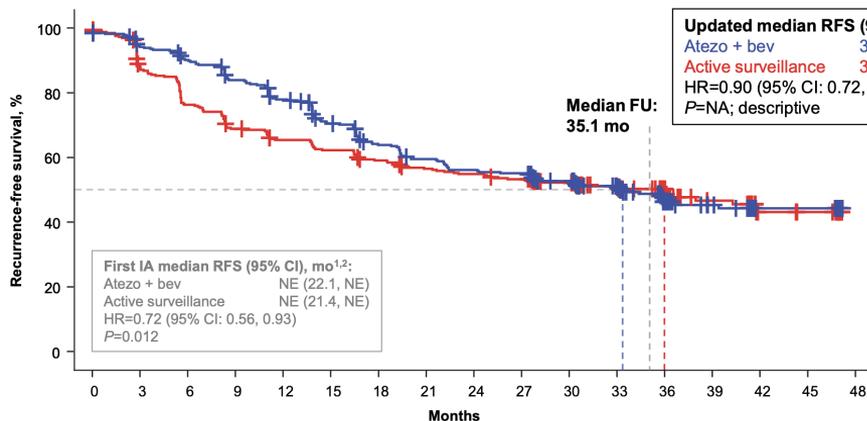


“Y NO se quedarán ahí...”

Estadio precoz BCLC-A & Terapia Sistémica

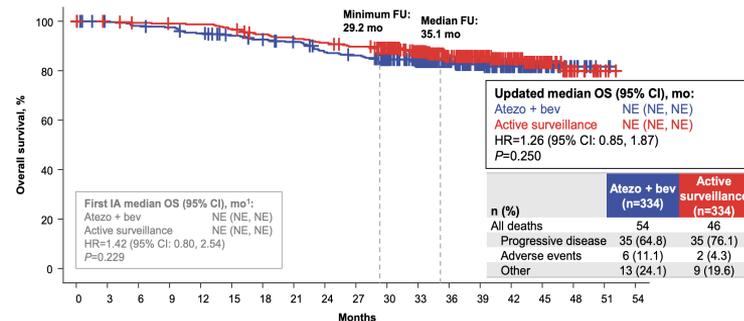
Early RFS benefit was not maintained with longer follow-up

BARCELONA 2024 ESMO congress



Updated OS remained immature but showed numerical improvement from the first IA

BARCELONA 2024 ESMO congress

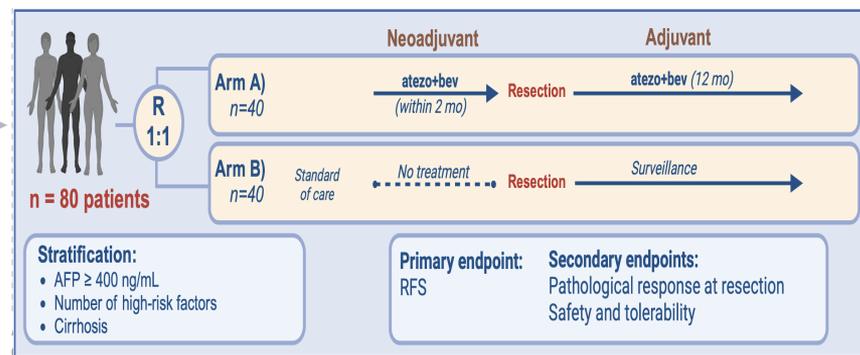
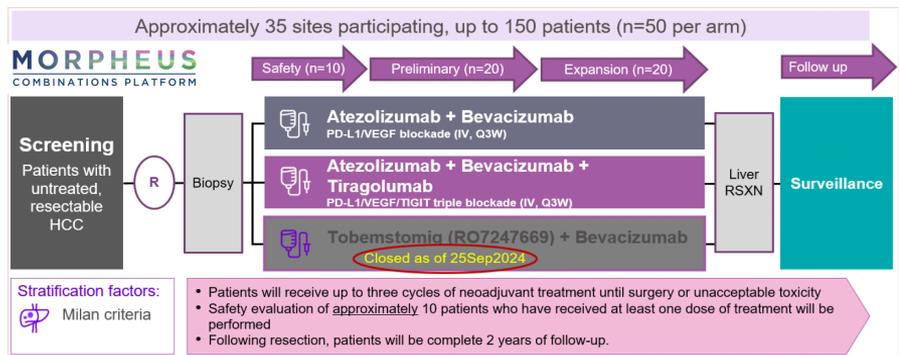


WHAT'S

NEXT

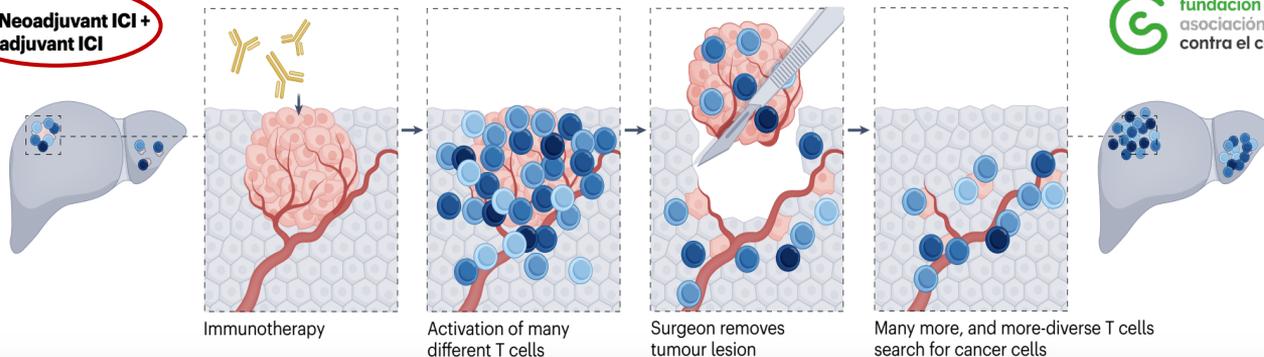


“Próximos pasos...”



NCT05908786

b Neoadjuvant ICI + adjuvant ICI



fundación científica
asociación española
contra el cáncer

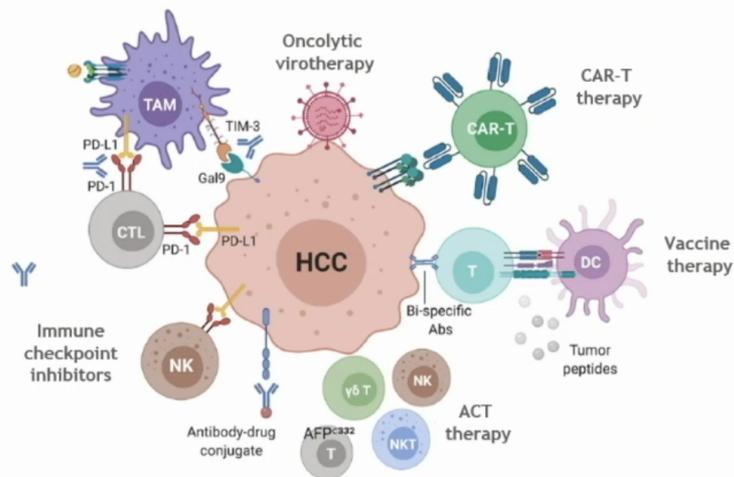
ASPIRE
AECC



“Próximos pasos...”

“Future directions in the treatment landscape...”

- New I-O agents
 - Anti-TIGIT (eg, tiragolumab: MORPHEUS-liver and IMbrave152/SKYSCRAPER-14)
 - Anti-TIM-3 (eg, cobolimab: NCT03680508)
 - Bispecific antibodies (eg, cadonilimab: COMPASSION-03)
 - CAR T cell therapy (eg, GPC3-CAR-T/C-CAR031: NCT05155189)
- Targeting pathways of immune escape
 - Epithelial-mesenchymal transition (eg, NP137: Liver-NET1)
 - Wnt pathway (eg, E7386: NCT04008797)
 - Hypoxia (eg, belzutifan: MK-6482-016)
 - Macrophage differentiation
- Using new agent to increase TAA presentation to immune cells
 - Vaccines (mRNA, dendritic cells)
 - Oncolytic viruses



Adapted from *Front Immunol*.

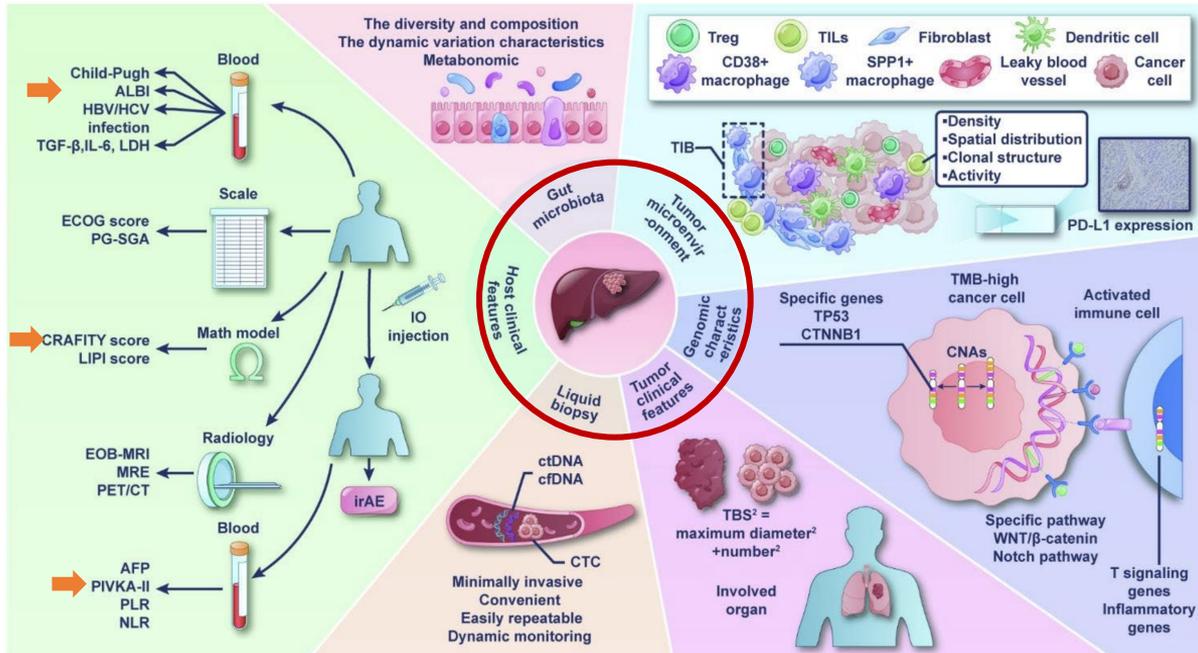
ACT, adoptive cell therapy; CAR, chimeric antigen receptor; CTL, cytotoxic T lymphocyte; HCC, hepatocellular carcinoma; I-O, immuno-oncology; ITIM, immunoreceptor tyrosine-based inhibitory motif; NK, natural killer cell; NKT, natural killer T cell; PD-1, programmed death-1; PD-L1, programmed death ligand 1; T, T cell; TAA, tumor-associated antigens; TAM, tumor-associated macrophage; TIGIT, T-cell immunoreceptor with immunoglobulin and ITIM domain; TIM-3, T cell immunoglobulin and mucin-domain containing-3.

Giraud J et al. *Front Immunol*. 2021;12:655697.



“Próximos pasos...”

“Biomarkers are **urgently needed**...”



Conclusiones...

- "Antes de 2019..." Sólo TKis: **SOR & LEN**
 - ✓ mOS 12-14m & ORR 10-25%
- "Otros se unieron rápidamente..."
 - ✓ ICI + AntiVEGF (**Atezo-Bev**): mOS 19 m & ORR 30% + QOL
 - ✓ Doble ICIs (**STRIDE & Nivo-IPI**): mOS 16-24m + LTS* & ORR 20-35% + QOL
- "La terapia sistémica **sigue avanzando...**"
 - ✓ En "BCLC-A/B": **TACE + Durva/Bev** o **LEN/PEM** → Beneficio **ORR & PFS/TTP** pero **¿OS?**
 - ✓ En "BCLC-A de alto riesgo": **Adyuvancia NO** (por ahora...)
- "Próximos pasos..."
 - ✓ ¿Beneficio de la **Neoadyuvancia?**
 - ✓ Múltiples **combinaciones** en 1ªL y **posteriores...**
 - ✓ Se necesitan **BIOMARCADORES** sólidos "con urgencia"...
- "El **futuro** es **prometedor...**"



X SIMPOSIO ONCOPROMESAS VS ONCOSAURIOS

ASIMILANDO LOS PROGRESOS EN ONCOLOGÍA

SANTANDER 18/20 JUNIO '25

GRAN HOTEL SARDINERO. PLAZA DE ITALIA, 1

