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20 ANIVERSARIO

Novedades en el tratamiento del hepatocarcinoma

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SPEAKING HONORARIA	Roche, Lilly, Servier, MSD, Amgen, Eisai, BMS, Pierre-Fabré, Astellas
ADVISORY ROLE	Roche, Servier, BMS, Astellas, Lilly, Pierre-Fabré, Astra-Zeneca, Boehringer
RESEARCH FUNDING	
TRAVELLING & ACCOMODATION SUPPORT	Merck, Roche, Servier, Astellas

Novedades en el tratamiento del HCC

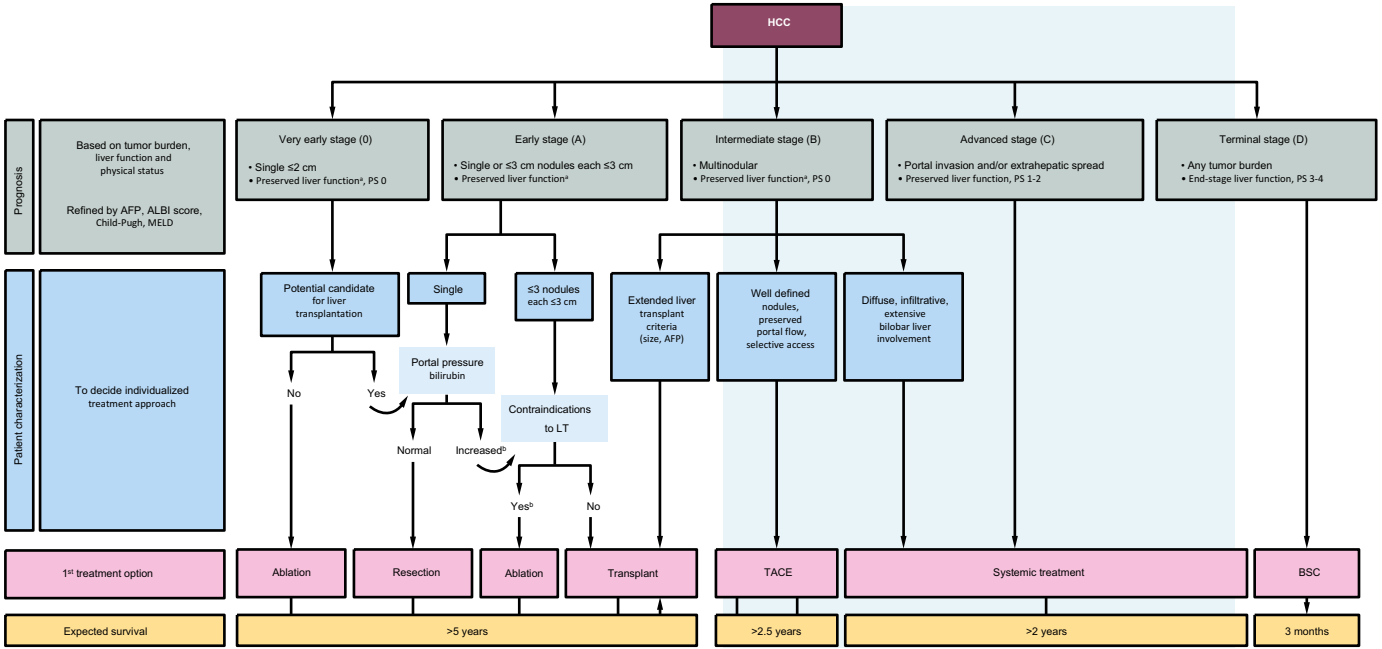
Tratamiento del estadio avanzado

- CheckMate 9DW
- Triple terapia
  - ✓ IMBrave 152
  - ✓ Triplet-HCC
- Atezolizumab+ Bevacizumab (vida real)

Tratamiento del estadio intermedio

- ¿TACE + Terapia sistémica?
- ¿Terapia sistémica inicial de elección? (IKF 035-ABC/HCC).

BCLC is the Most Widely Used and Validated Staging System[1,2]



The BCLC staging system identifies patients according to patient prognostic and disease characteristics, and recommends initial treatments accordingly

[a]Except for those with tumor burden acceptable for transplant; [b]Resection may be considered for single peripheral HCC with adequate remnant liver volume.

AFP = alpha-fetoprotein; ALBI = albumin-bilirubin; BCLC = Barcelona Clinic Liver Cancer; BSC = best supportive care; HCC = hepatocellular carcinoma; LT = liver transplantation; MELD = model for end-stage liver disease; PS = performance status; TACE = transarterial chemoembolization.

1. Parikh ND et al. *PLoS Med.* 2016;13:e1002005. 2. Reig M et al. *J Hepatol.* 2022;76:681-693.

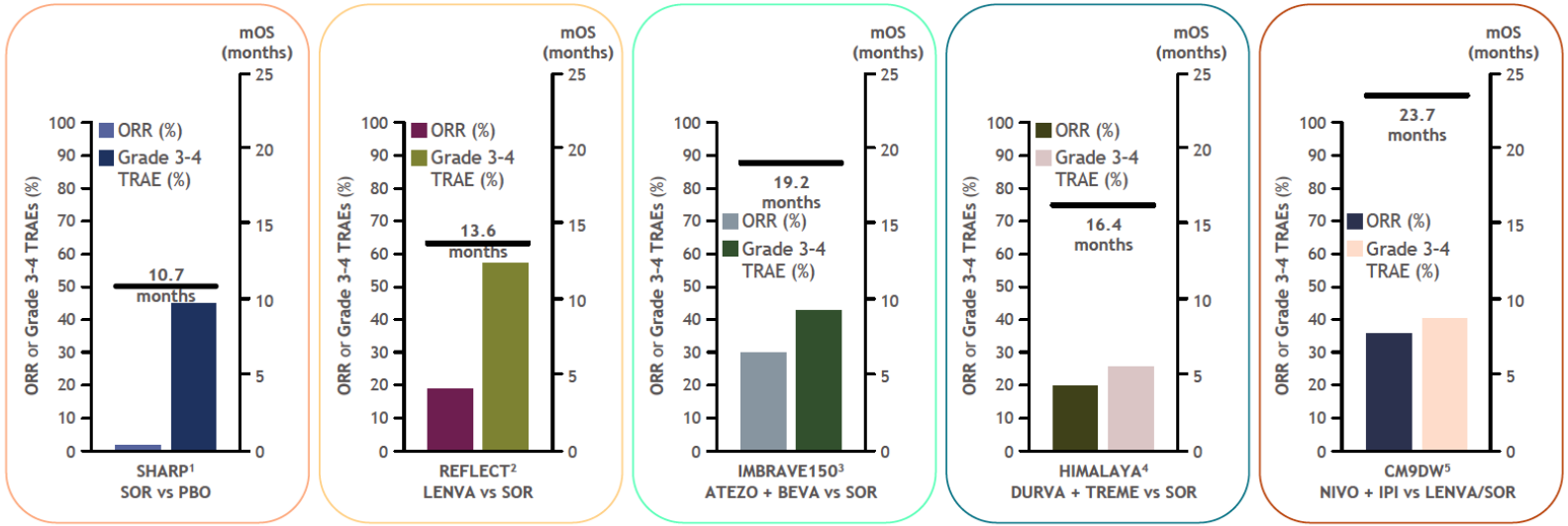
HCC avanzado
Tratamientos de 1ª línea con inmunoterapia + antiangiogénicos

	Estudio	N	Rama Control	Rama en investigación
Antiangiogenico + anti- PD-1/PDL-1	**IMBrave 150**	501	Sorafenib	Atezolizumab + Bevacizumab
	ORIENT-32	571	Sorafenib	Sintilimab + Bevacizumab
	SHR 1210	510	Sorafenib	Camrelizumab + apatinib
	COSMIC-312	640	Sorafenib	Atezolizumab + Cabozantinib
	LEAP-002	750	Lenvatinib	Pembrolizumab + Lenvatinib

HCC avanzado
Tratamientos de 1ª línea con doble inmunoterapia (anti-PDL-1+anti CTLA-4)

	Estudio	N	Rama control	Rama en investigación
Anti PD-1/PDL-1CTLA-41	**CheckMate 9DW**	1084	Sorafenib or Lenvatinib	Nivolumab + Ipilimumab
	HIMALAYA	1200	Sorafenib	Durvalumab or Durvalumab + Tremelimumab

Evolution of systemic therapies in 1L HCC: from anti-angiogenics to immune-based therapies[1–5]



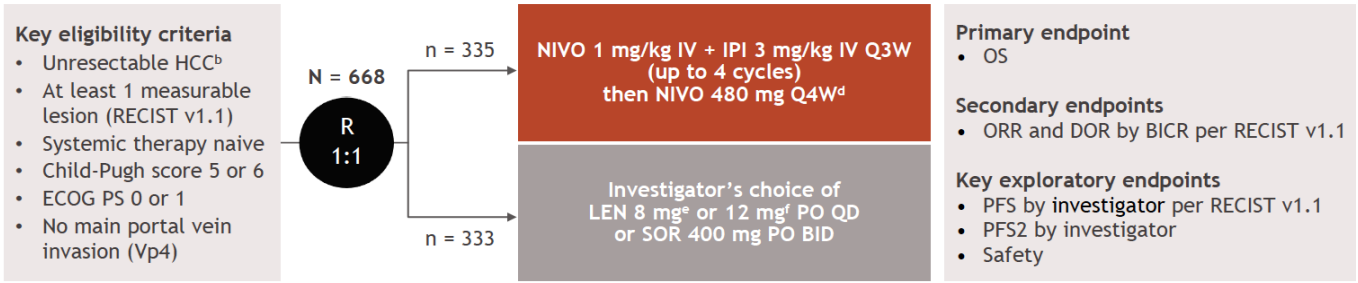
1. Llovet JM et al. N Engl J Med. 2008;359:378–390; 2. Kudo M et al. Lancet. 2018;391:1163–1173; 3. Cheng AL et al. J Hepatol. 2022;76:862–873; 4. Abou-Alfa GK et al. N Eng J Med Evid. 2022;1:EVIDoa210007; 5. Yau T et al. Lancet. 2025;405:1851–1864.

Nivolumab plus ipilimumab versus lenvatinib or sorafenib as first-line treatment for unresectable hepatocellular carcinoma (CheckMate 9DW): an open-label, randomised, phase 3 trial

Lancet 2025; 405: 1851–64

Thomas Yau*, Peter R Galle*, Thomas Decaens, Bruno Sangro, Shukui Qin, Leonardo G da Fonseca, Hatim Karachiwala, Jean-Frederic Blanc, Joong-Won Park, Edward Gane, Matthias Pinter, Ana Matilla Peña, Masafumi Ikeda, David Tai, Armando Santoro, Gonzalo Pizarro, Chang-Fang Chiu, Michael Schenker, Aiwu He, Hong Jae Chon, Joanna Wojcik-Tomaszewska, Gontran Verset, Qi Qi Wang, Caitlyn Stromko, Jaclyn Neely, Prianka Singh, Maria Jesus Jimenez Exposito, Masatoshi Kudo, on behalf of the CheckMate 9DW investigators

- 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]



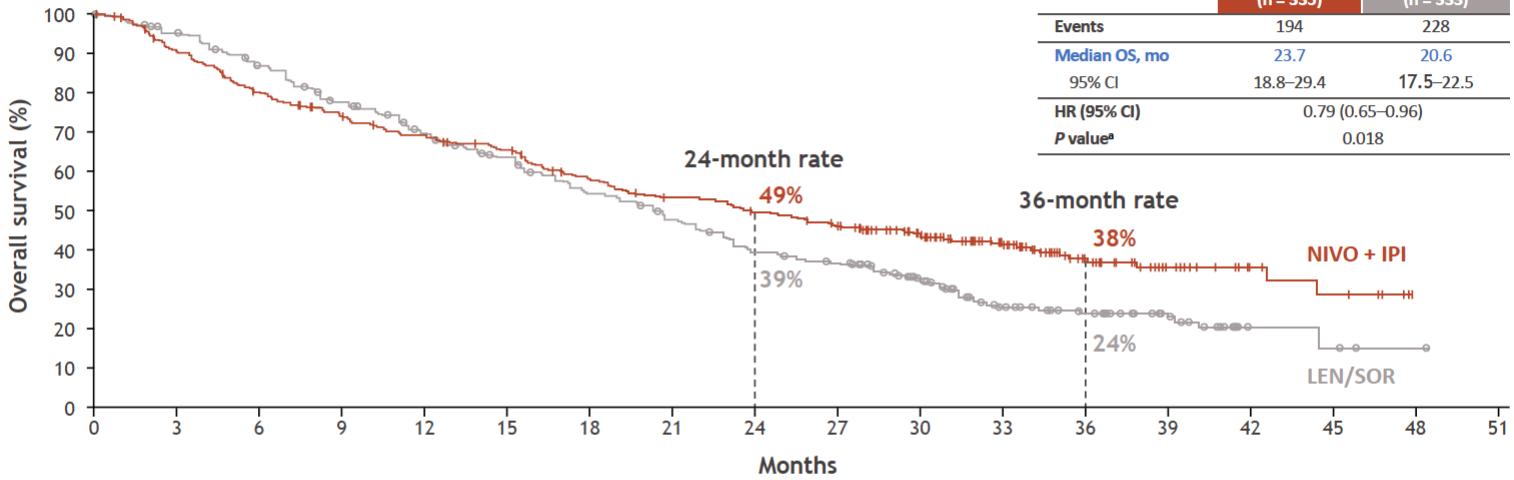
- At data cutoff (January 31, 2024), the median follow-up[g] was 35.2 months (range, 26.8-48.9)

[a]ClinicalTrials.gov: NCT04039607. [b]Disease not eligible for, or progressive disease after, curative surgical and/or locoregional therapies. [c]Based on central lab serology results for stratification purpose. [d]Minimum of 1 dose of NIVO + IPI is required before proceeding to NIVO monotherapy. [e]If body weight < 60 kg. [f]If body weight ≥ 60 kg. [g]Time between randomization date and cutoff date.

CheckMate 9DW

Overall survival

	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	194	228
Median OS, mo	23.7	20.6
95% CI	18.8–29.4	17.5–22.5
HR (95% CI)	0.79 (0.65–0.96)	
P value[a]	0.018	



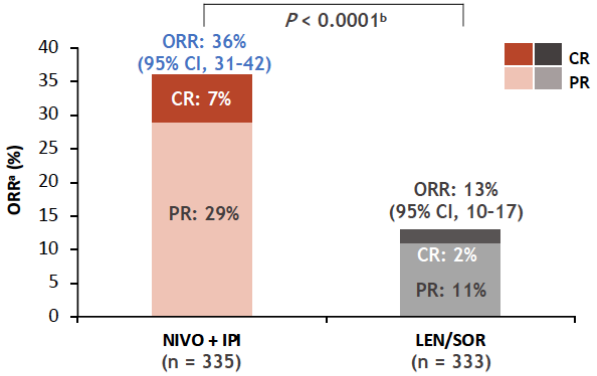
No. at risk																		
NIVO + IPI	335	300	264	239	220	206	179	162	150	137	104	71	42	24	11	8	0	0
LEN/SOR	333	310	280	245	216	194	164	144	116	106	76	44	34	20	4	3	1	0

- Statistically significant and clinically meaningful OS benefit with NIVO + IPI vs LEN/SOR
  - Longer median OS and long-term survival benefit with higher OS rates at 24 and 36 months

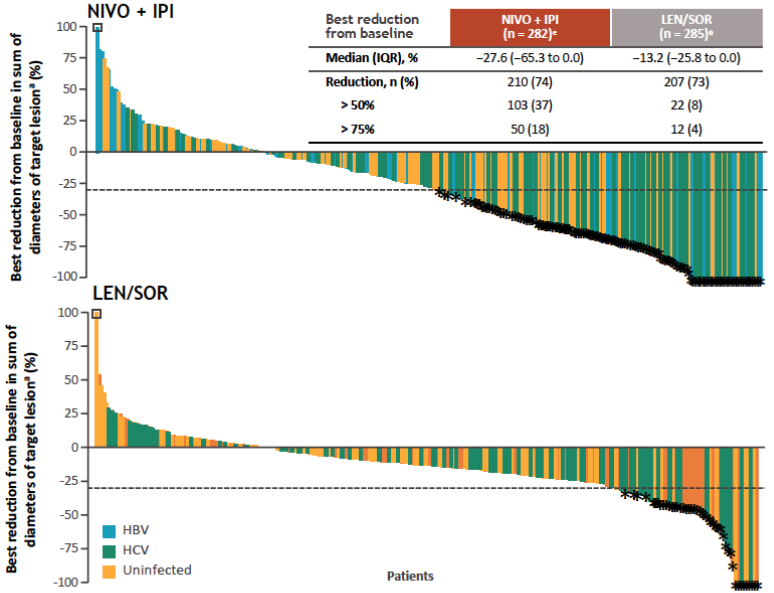
Median OS is estimated using Kaplan-Meier methodology. HR and 95% CI from stratified Cox proportional hazard model. HR is NIVO + IPI over LEN/SOR. Symbols represent censored observations. [a]Two-sided *P* value from stratified log-rank test. Boundary for statistical significance: *P* value ≤ 0.0257.

CheckMate 9DW

Objective response



Best overall response,[a] %		
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)**



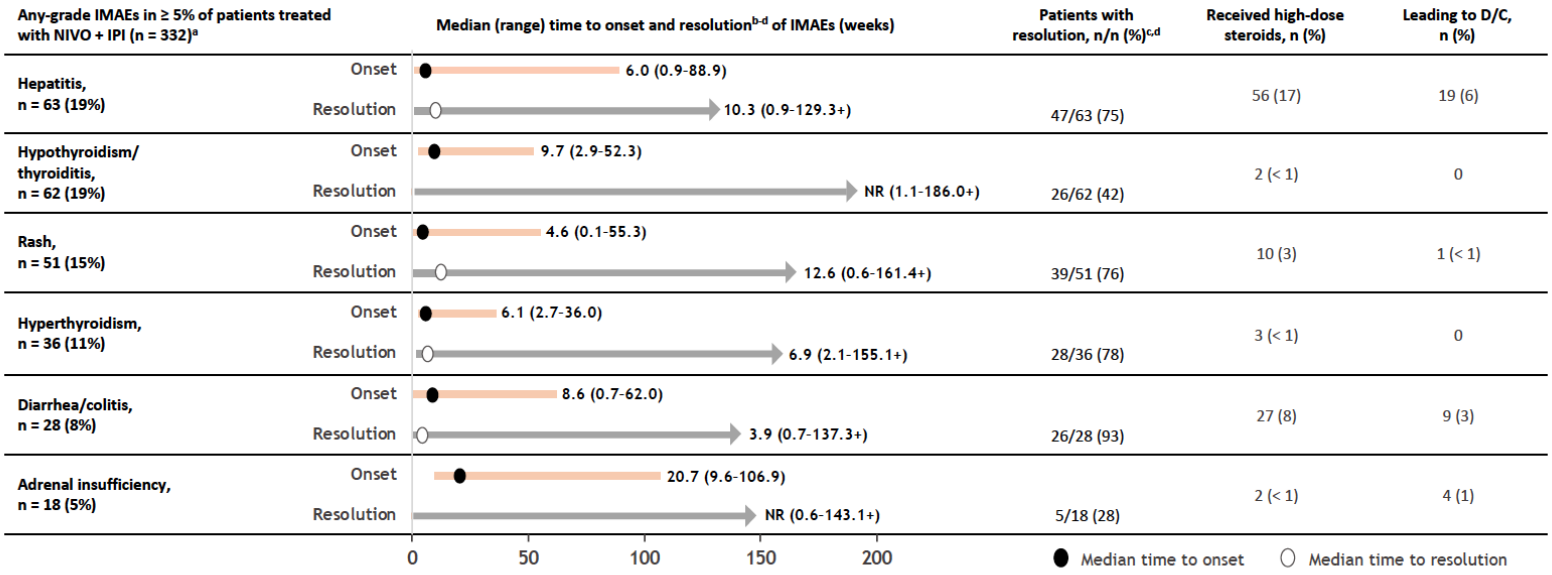
Best reduction from baseline	NIVO + IPI (n = 282)[e]	LEN/SOR (n = 285)[e]
Median (IQR), %	−27.6 (−65.3 to 0.0)	−13.2 (−25.8 to 0.0)
Reduction, n (%)	210 (74)	207 (73)
> 50%	103 (37)	22 (8)
> 75%	50 (18)	12 (4)

- Statistically significant and clinically meaningful improvement in ORR with NIVO + IPI vs LEN/SOR, with a higher complete response rate (7% vs 2%, respectively) and durable responses
- Responses with NIVO + IPI were observed regardless of etiology

[a]Assessed by BICR based on RECIST v1.1. [b]Two-sided *P* value from stratified Cochran-Mantel-Haenszel test. Boundary for statistical significance: *P* value ≤ 0.025. [c]Includes non-CR/non-PD: NIVO + IPI, n = 6 (2%); LEN/SOR, n = 7 (2%). Non-CR/non-PD refers to patients with persistence of 1 or more non-target lesion(s). [d]In confirmed responders (NIVO + IPI: n = 121; LEN/SOR: n = 44). [e]Response evaluable patients defined as those with a best overall response of CR, PR, SD, non-CR/non-PD, or PD; target lesion(s) assessed at baseline; and ≥ 1 on-study assessment of all baseline target lesion(s). Horizontal reference line indicates the 30% reduction consistent with a response per RECIST v1.1. Asterisk symbol, responders; square symbol, percent change truncated to 100%. Ten patients with HBV-HCV coinfections were categorized to HCV.

CheckMate 9DW

IMAEs summary

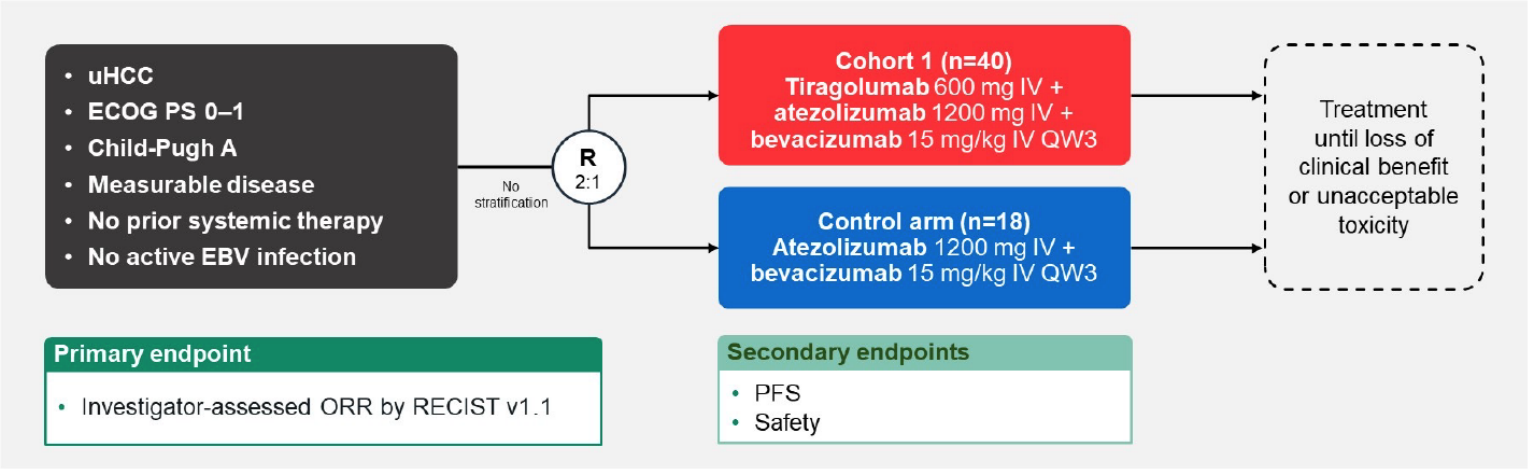


- Any-grade IMAEs occurred in 58% of patients treated with NIVO + IPI; grade 3/4 IMAEs occurred in 28% of patients
- Most IMAEs were manageable and did not result in treatment discontinuation

→ indicates ongoing events. + indicates a censored value. [a]IMAEs are specific events considered as potential immune-mediated events by investigator, occurring within 100 days after the last dose of study treatment, regardless of causality, and, with the exception of endocrine events, are treated with IMM. [b]From Kaplan-Meier estimates. [c]Time to resolution measured from the date of IMAE onset; patients who experienced IMAE without worsening from baseline grade were excluded from time to resolution analysis. Events without a stop date or with a stop date equal to the death and grade 5 events were considered unresolved. [d]Some endocrine IMAEs were considered unresolved due to continuing need for hormone replacement therapy.

MORPHEUS-Liver: a phase Ib/II, open-label, multicenter, randomized study

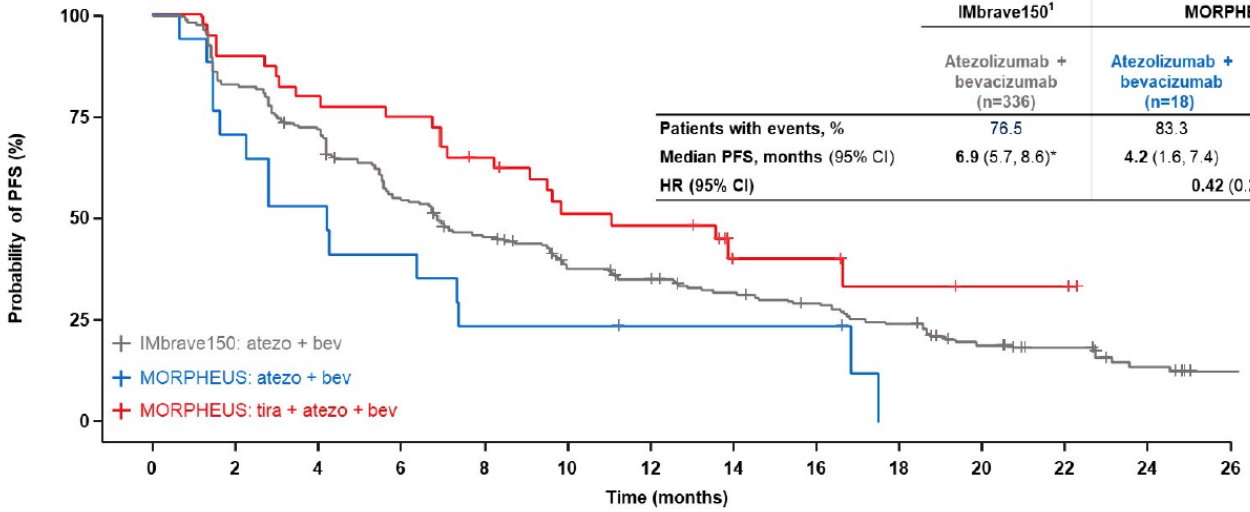
- MORPHEUS-Liver is an umbrella study evaluating multiple immunotherapy-based treatment combinations in participants with uHCC who have not yet received prior systemic therapy
- Cohort 1 investigated the addition of tiragolumab to atezolizumab + bevacizumab



Q3W, every 3 weeks; EBV, Epstein-Barr virus; ECOG PS, Eastern Cooperative Oncology Group performance status
IV, intravenous; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors

NCT04524871

Investigator-assessed PFS per RECIST v1.1



	IMbrave150[1]	MORPHEUS-liver	
	Atezolizumab + bevacizumab (n=336)	Atezolizumab + bevacizumab (n=18)	Tiragolumab + atezolizumab + bevacizumab (n=40)
Patients with events, %	76.5	83.3	57.5
Median PFS, months (95% CI)	**6.9** (5.7, 8.6)*	**4.2** (1.6, 7.4)	**11.1** (8.2, NE)
HR (95% CI)		**0.42** (0.22, 0.82)	

IMbrave150: atezo + bev	336	271	234	174	141	113	102	88	77	64	41	25	12	3
MORPHEUS: atezo + bev	18	12	9	7	4	4	3	3	3	0	0	0	0	0
MORPHEUS: tira + atezo + bev	40	36	32	30	25	17	16	7	7	5	2	2	0	0

Efficacy evaluable population. Data cut-off: 28 November 2022
*Independent-review facility assessed PFS

1. Cheng et al. J Hepatol 2022; NCT03434379

IMbrave152/SKYSCRAPER-14: a phase 3, double-blind, placebo-controlled, randomised, global study

- 669 patients randomised to treatment between 14 September 2023 and 23 September 2024

Key eligibility criteria
- Aged ≥18 years
- Unresectable locally advanced or metastatic HCC
- ECOG PS 0 or 1
- Child-Pugh A
- No prior systemic therapy for advanced disease
- Systemic adjuvant treatment permitted (recurrence ≥6 months from treatment completion)*

R 1:1

Tira 600 mg + atezo 1200 mg + bev 15 mg/kg, IV Q3W n=331

Pbo + atezo 1200 mg + bev 15 mg/kg, IV Q3W n=338

Imaging every 6 ± 1 weeks†

Treat until loss of clinical benefit or unacceptable toxicity

No crossover permitted

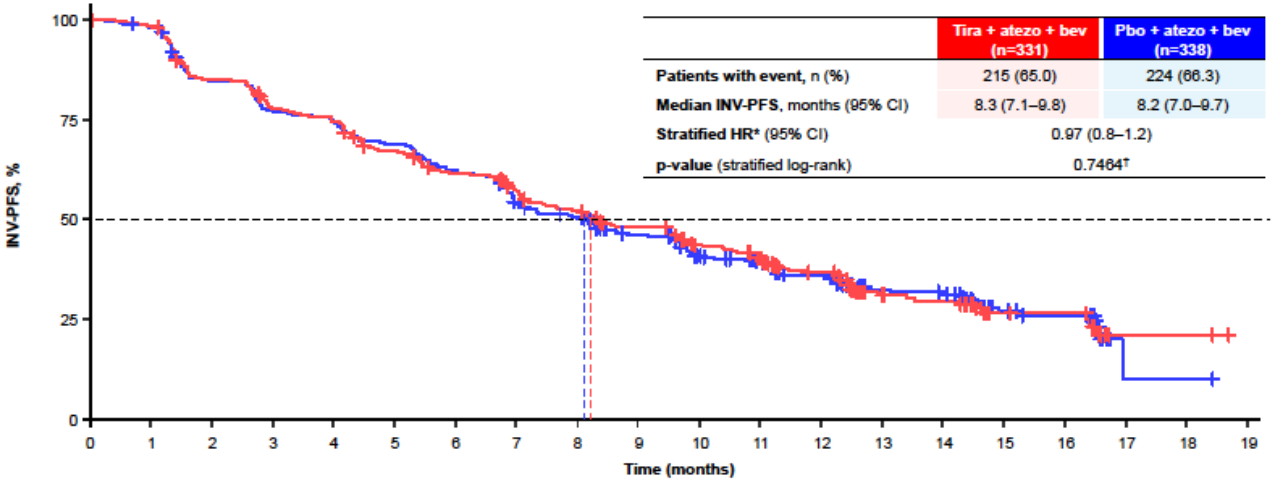
Stratification factors
- **Geographic region** (Asia and Africa, excluding Japan, vs rest of world, including Japan)
- **MVI and/or EHS** (presence vs absence)
- **Baseline AFP** (<400 vs ≥400 ng/mL)
- **HCC aetiology** (viral vs non-viral)

Primary endpoints
- **INV-PFS** per RECIST v1.1
- **OS**

Other key secondary endpoints
- ORR
- DOR
- **PFS/OS rate** at selected time points
- **Safety**
- PROs

NCT05904886.
*Allowed for adjuvant atezolizumab/bevacizumab, which may be approved during the conduct of the study; † Interval changed to every 9 ± 1 weeks after Week 54
AFP, alpha-fetoprotein; atezo, atezolizumab; bev, bevacizumab; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EHS, extrahepatic spread; INV-PFS, investigator-assessed progression-free survival
IV, intravenous; MVI, macrovascular invasion; ORR, overall response rate; OS, overall survival; pbo, placebo; PRO, patient-reported outcomes; Q3W, every 3 weeks; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours; tira, tiragolumab

Primary endpoint: INV-PFS per RECIST v1.1



	Tira + atezo + bev (n=331)	Pbo + atezo + bev (n=338)
Patients with event, n (%)	215 (65.0)	224 (66.3)
Median INV-PFS, months (95% CI)	8.3 (7.1–9.8)	8.2 (7.0–9.7)
Stratified HR* (95% CI)	0.97 (0.8–1.2)	
p-value (stratified log-rank)	0.7464†	

Patients at risk:

Tira + atezo + bev	331	321	276	250	239	213	192	175	159	142	122	110	85	42	38	18	17	3	3	0
Pbo + atezo + bev	338	326	279	254	246	227	205	174	162	136	112	98	87	54	51	26	22	1	1	0

NCT05904886. Data cutoff date: 8 May 2025. Minimum FU=7.5 months. Median FU=12.5 months. *Stratification factors: geographic region (Africa and Asia, excluding Japan, vs rest of world, including Japan); HCC aetiology (viral vs non-viral); MVI and/or EHS (presence vs absence); and baseline AFP (<400 vs ≥400 ng/mL); †Statistical boundary: 0.005. CI, confidence interval; FU, follow-up; HR, hazard ratio

BERLIN 2025 ESMO congress

Adding Ipilimumab to Atezolizumab plus Bevacizumab in patients with unresectable hepatocellular carcinoma in first-line systemic therapy

PRODIGE 81/FFCD 2101 - TRIPLET HCC

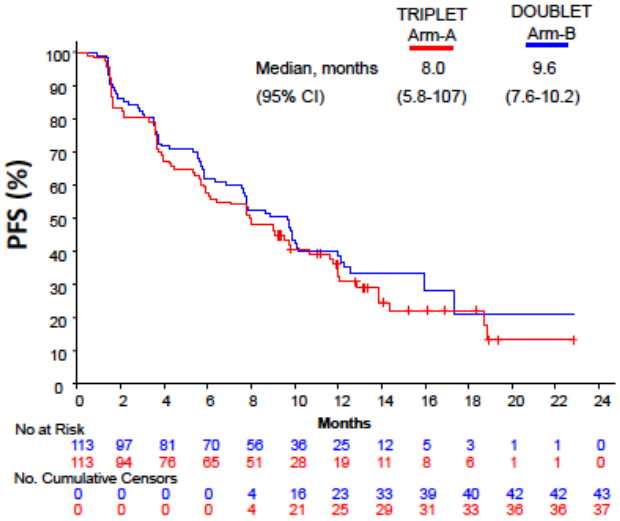
MERLE Philippe, BLANC Jean-Frédéric, EDELINE Julien, Karine LE MALICOT, PERON Jean-Marie, BOURGEOIS Vincent, BOUATTOUR Mohamed, TOUCHEFEU Yann, VITELLIUS Carole, KHEMISSA AKOUZ Faiza, HEURGUE Alexandra, GIROT Paul, ASSENAT Eric, NGUYEN KHAC Eric, BRONOWICKI Jean-Pierre, VIAUD Juliette, BEN ABDELGHANI Meher, NAULT Jean-Charles, MANFREDI Sylvain, PHELIP Jean-Marc

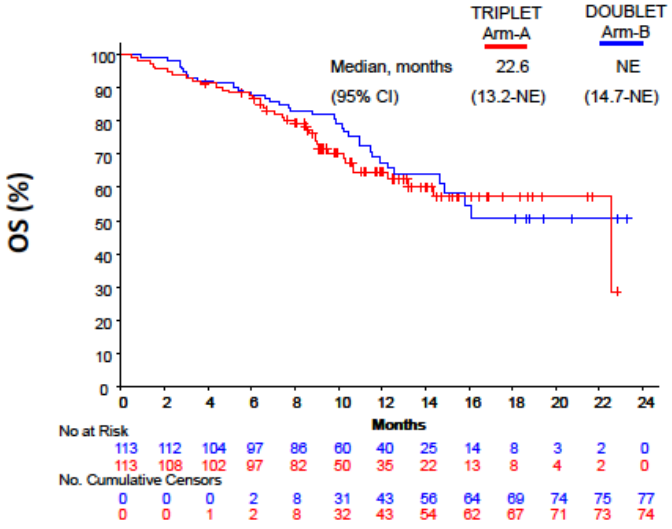
18 October 2025

Objective response Recist 1.1	Objective response	Disease control	Progressive disease	Non evaluable
Arm-A TRIPLET n=113	34 (30.1%)	84 (74.3%)	12 (10.6%)	17 (15.0%)
Arm-B DOUBLET n=113	31 (27.4%)	96 (85.0%)	11 (9.7%)	6 (5.3%)

RESULTS (2) – Secondary endpoints of efficacy

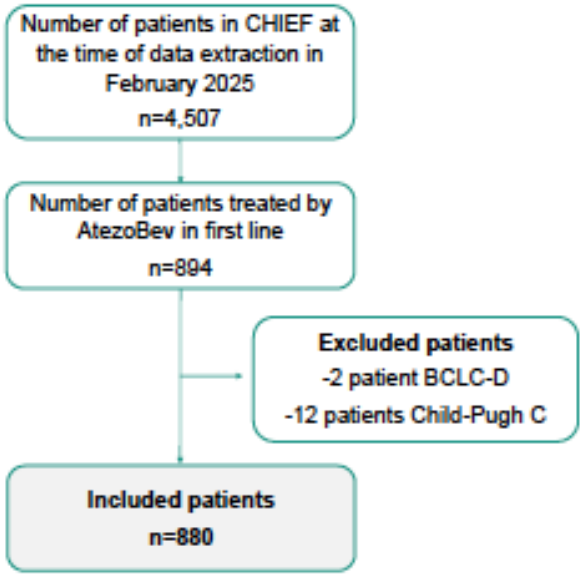
median (95% CI) follow-up of 12.0 mo (10.6-13.1) for arm-A vs 12.5 (11.2-13.4) for arm-B





1487P- EXTENDED FOLLOW-UP AT 42 MONTHS OF ATEZOLIZUMAB-BEVACIZUMAB INSIGHTS FROM THE CHIEF PROSPECTIVE STUDY

FLOW CHART OF THE STUDY

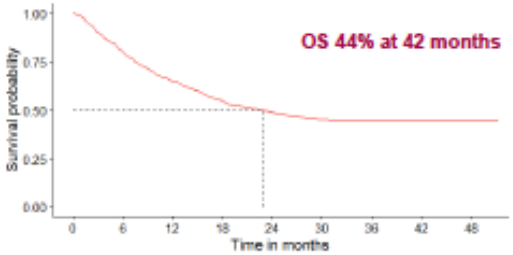


Data updated in April 2025

CARACTERISTICS OF THE POPULATION		Whole cohort N=880
Gender (male)		88 %
Age		69 [63, 75]
Underlying liver disease	Alcohol only	28 %
	Viral only	14 %
	MASLD only	16 %
	At least alcohol	58 %
Liver function	Child-Pugh A	78 %
	MELD	8 [7 – 11]
	Albi Grade 1/2/3	33 %/ 61 % / 6 %
	Esophageal varices	57 %
	Large size varices	26 %
	Ascite	6 %
HCC features	BCLC-A/-B/-C	5 %/ 28 % / 67 %
	Multinodular form	35 %
	Vascular invasion	47 %
	Metastasis	32 %
	AFP (ng/mL)	47 [7 –606]
	AFP > 400 ng/mL	30 %

1487P- EXTENDED FOLLOW-UP AT 42 MONTHS OF ATEZOLIZUMAB-BEVACIZUMAB INSIGHTS FROM THE CHIEF PROSPECTIVE STUDY

Overall survival

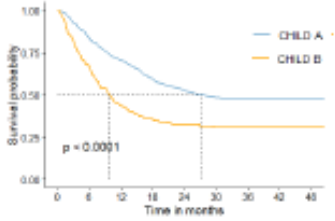


Median OS 22.8 months

Predictive factors of mortality

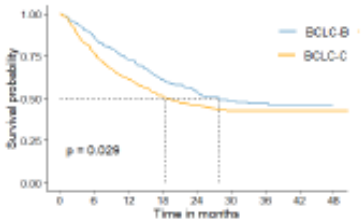
	Multivariate analysis	
	HR	p
Esophageal varices	1.26	0.04
Ascites	1.51	0.02
ALBI grade 2	1.35	0.005

OS according to Child-Pugh score



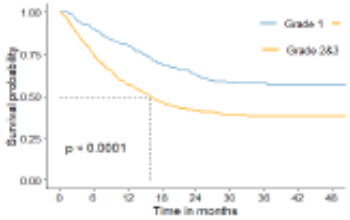
Median OS 27.4 months for Child-Pugh A and 9.8 months for Child-Pugh B.

OS according to BCLC



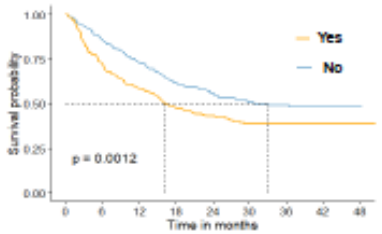
Median OS 27.8 months for BCLC-B and 18.5 months for BCLC-C.

OS according to ALBI grade



Median OS not reached for ALBI grade 1 and 15.9 months for ALBI grade 2/3.

OS according to vascular invasion



Median OS 16.2 months in case of vascular invasion and 33.0 months without.

ATHECA: Final safety and efficacy analysis of a phase IIIb study of atezolizumab + bevacizumab in Spanish patients with unresectable HCC

FPN 159P

M.E. Reig[1], N. Luque[2], J.L. Lledó[3], A.M. Matilla[4], J.L. Montero[5], R. Pazo-Cid[6], M. Varela[7], M. Vergara[8], J.M. Ordóñez[9], P. Vieitez[3], J. Argemi[10], J. Bruix[1], C. Gómez[11], R. Pérez-López[12], J. Rimola[13], B. Sangro[14], J. Sastre[15]

[1]BCLC Group, Liver Unit, Hospital Clínic y Provincial de Barcelona, Barcelona, IDIBAPS, CIBEREHD Spain; [2]Hospital Universitario de Jaén, Jaén, Spain; [3]Gastroenterology and Hepatology Service. Hospital Universitario Ramón y Cajal, IRYCIS, Universidad de Alcalá, CIBERehd, Madrid, Spain; [4]Digestive Service, Hospital General Universitario Gregorio Marañón, Madrid, CIBEREHD Spain; [5]Liver Unit, Hospital Universitario Reina Sofía, Córdoba, Spain; [6]Medical Oncology Department, Hospital Universitario Miguel Servet, Zaragoza, Spain; [7]Department of Gastroenterology. Liver Unit. Hospital Universitario Central de Asturias. IUOPA. ISPA. FINBA. Universidad de Oviedo. Oviedo, Spain; [8] Liver Unit. Digestive Disease Service. Parc Taulí Sabadell University Hospital, Investigation and Innovation Institute Parc Taulí I3PT, Universitat Autónoma of Barcelona, Sabadell, CIBEREHD Spain.[9]Medical Department, Roche Farma S.A., Madrid, Spain; [10]Liver Unit, Clínica Universidad de Navarra, Pamplona, CIBEREHD Spain; [11]Medical Oncology, University Hospital 12 de Octubre, Madrid, Spain; [12]Radiomics Group, Vall d'Hebron Institute of Oncology – Cellex Center, Barcelona, Spain; [13]BCLC Group, Radiology Dept, Hospital Clínic y Provincial de Barcelona, Barcelona, CIBEREHD Spain; [14]Liver Unit, Clínica Universidad de Navarra, Pamplona-Madrid, CIBEREHD Spain; [15]Medical Oncology, Hospital Clínico Universitario San Carlos, Madrid, Spain.

Table 1. Baseline characteristics

	All (N=100)
Male, %	87
Median age, years	66
ECOG PS 0	80
BCLC stage A / stage B / stage C, %	1 / 28 / 71
Non-viral HCC/Hepatitis B / C, %	63 / 6 / 33 *
Macrovascular Invasion (MVI), %	24.2
Alpha-fetoprotein (AFP) ≥ 400 ng/ml, %	24.5
Varices, %	32
large, %	31.3
treated, %	34.4
Comorbidities	
Hypertension /Diabetes Mellitus / Cardiovascular disease, %	57 / 34 / 12
Dyslipidaemia, %	20
BMI (<25 / 25≤BMI<30 / ≥30), %	39 / 38 / 23
Alcohol consumption, (never/current/previous), %	28 / 15 / 57
Prior locoregional treatments	11.0
radiofrequency ablation, %	4.0
transarterial chemoembolization, %	7.0
transarterial embolization, %	3.0
transarterial radioembolization, %	2.0

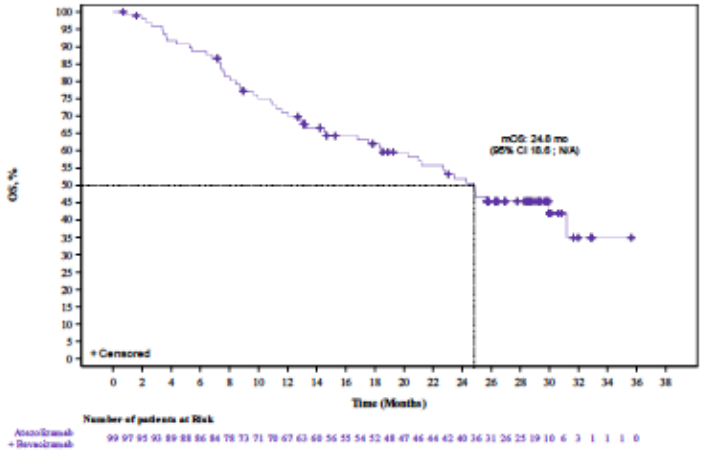
MVI and AFP % are based on available data of 99 and 98 patients respectively.
*2 patients had Hepatitis B and C
% of large and treated varices are based on total N of varices.

Table 2. Safety primary endpoint

	All (N=100)
Duration of ATZ / BEV, median (months)	8.6 / 8.0
Duration of follow-up, median (months)	29.2
Patients with AE, %	99
Patients with AE G3-4, %	58
Patients with TRAEs, %	82
Patients with SAEs, %	46
AEs G3-4 leading to discontinuation*, %	19
Immunomediated AEs, %	4

* Discontinuation of ATZ and/or BEV; AE: adverse event; G: grade, TRAE: treatment related adverse event: SAE: serious adverse event.

Overall survival (OS)



OS by baseline BCLC category

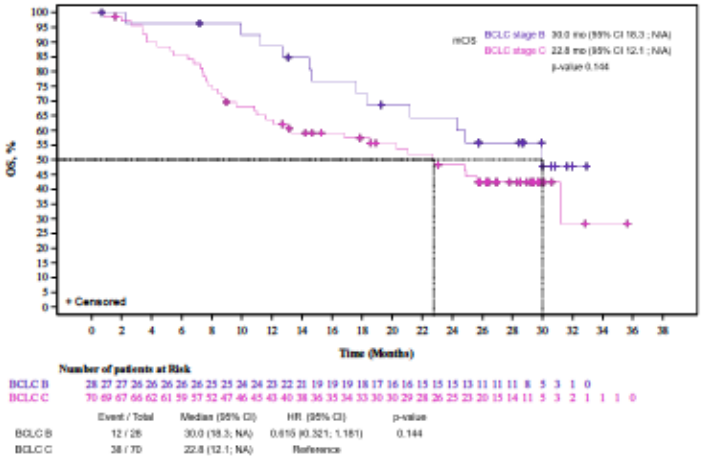
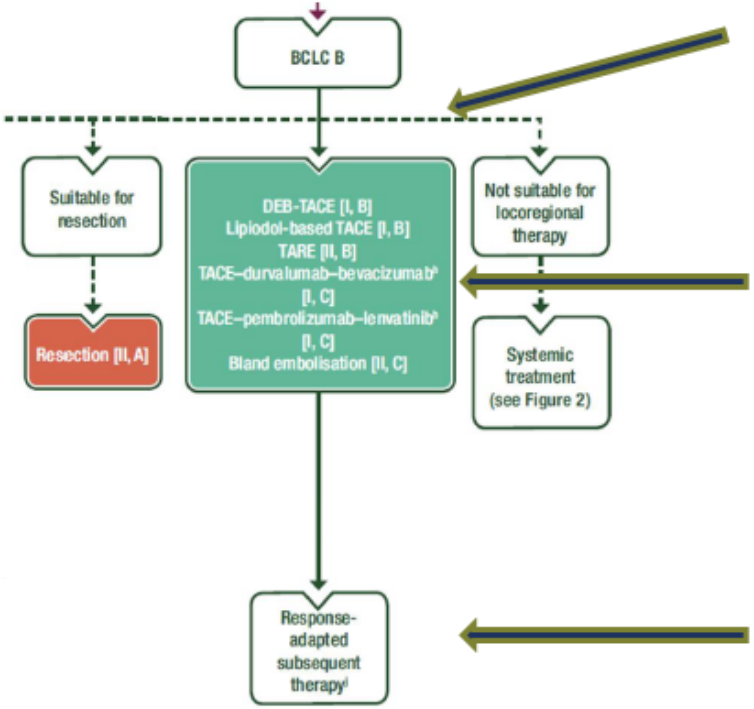


Table 4. Objective response rate (ORR)

	All (N=99)
ORR during the study [n, (%)]	24 (24.2) [95% CI: 16.9 - 33.5]
Best Overall Response (BOR)	
Complete Response (CR)	4 (4.0)
Partial Response (PR)	20 (20.2)
Stable Disease (SD)	59 (59.6)
Progressive Disease (PD)	12 (12.1)
Not evaluable	0 (0.0)
Missing	4 (4.0)
Disease Control Rate (DCR)	
CR + PR + SD	83 (83.8)

Clinical trial identification: EUDRACT 2020-005268-71, NCT04732286

NUEVAS INTERROGANTES EN EL MANEJO DEL ESTADIO BCLC-B



Selección de pacientes para terapias de rescate (importancia de la RO)

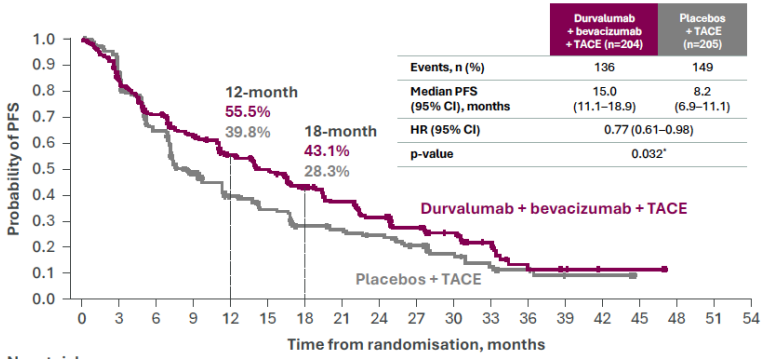
Combinación de TACE + Terapia sistémica (¿Cuando?, ¿Como?)

¿Se puede prescindir de la TACE?
¿En qué pacientes?

Phase-3 studies evaluating the combination of TACE with immunotherapy in HCC:

	Phase	Investigational arm(s)	Patient enrolment, N	Primary endpoint(s)	Outcomes (primary endpoint)
✓ **EMERALD-1**[1] NCT03778957	3	Arm A: TACE + durvalumab Arm B: TACE + durvalumab + bevacizumab	724 (actual)	**PFS** (Arm B vs Arm C; BICR)	Showed a statistically significant improvement in PFS
? **EMERALD-3**[2] NCT05301842	3	Arm A: TACE + STRIDE + lenvatinib Arm B: TACE + STRIDE	725 (estimated)	**PFS** (Arm A vs Arm C; RECIST 1.1 by BICR)	Results not yet reported
✓ **LEAP-012**[3] NCT04246177	3	TACE + pembrolizumab + lenvatinib	450 (estimated)	**PFS** (RECIST 1.1 by BICR) OS	Showed a statistically significant improvement in PFS
? **TACE-3**[4] NCT04268888	2 / 3	TACE / TAE + nivolumab	522 (estimated)	**OS**	Results not yet reported
✓ **TALENTACE**[5,6] NCT04712643	3	TACE + atezolizumab + bevacizumab	342 (actual)	**TACE PFS** (investigator-assessed) OS	Showed a statistically significant improvement in TACE-PFS
✓ **CARES-005**[7] NCT04559607	2	TACE + camrelizumab + apatinib	188 (actual)	**PFS** (investigator-assessed)	Showed a statistically significant improvement in PFS

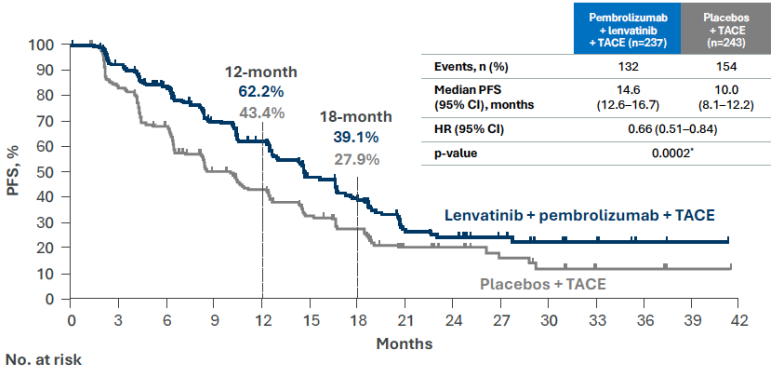
Combination immunotherapy improves PFS in embolization eligible HCC



	Durvalumab + bevacizumab + TACE (n=204)	Placebos + TACE (n=205)
Events, n (%)	136	149
Median PFS (95% CI), months	15.0 (11.1–18.9)	8.2 (6.9–11.1)
HR (95% CI)	0.77 (0.61–0.98)	
p-value	0.032*	

No. at risk

204	162	134	114	94	82	64	53	43	32	23	15	6	4	2	2	0	0	0
205	159	121	81	62	51	39	35	32	24	15	10	5	2	2	0	0	0	0

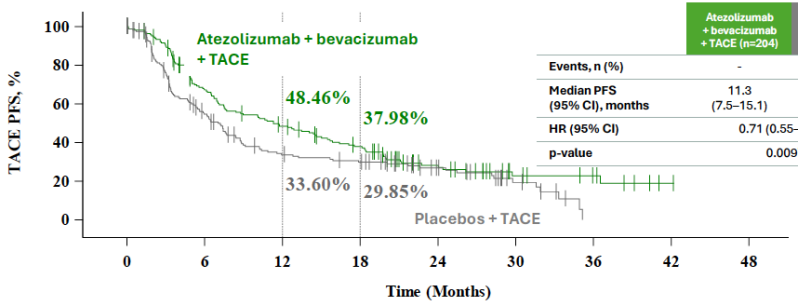


	Pembrolizumab + lenvatinib + TACE (n=237)	Placebos + TACE (n=243)
Events, n (%)	132	154
Median PFS (95% CI), months	14.6 (12.6–16.7)	10.0 (8.1–12.2)
HR (95% CI)	0.66 (0.51–0.84)	
p-value	0.0002*	

No. at risk

237	207	176	136	112	72	57	26	22	15	10	7	2	1	0
243	190	144	89	72	48	37	18	12	8	5	3	3	1	0

Progression by RECICL
>2 TACE without response
CPB8 deterioration



	Atezolizumab + bevacizumab + TACE (n=204)	Placebos + TACE (n=205)
Events, n (%)	-	-
Median PFS (95% CI), months	11.3 (7.5–15.1)	7.0 (5.3–8.4)
HR (95% CI)	0.71 (0.55–0.92)	
p-value	0.009*	

No. of Patients at Risk

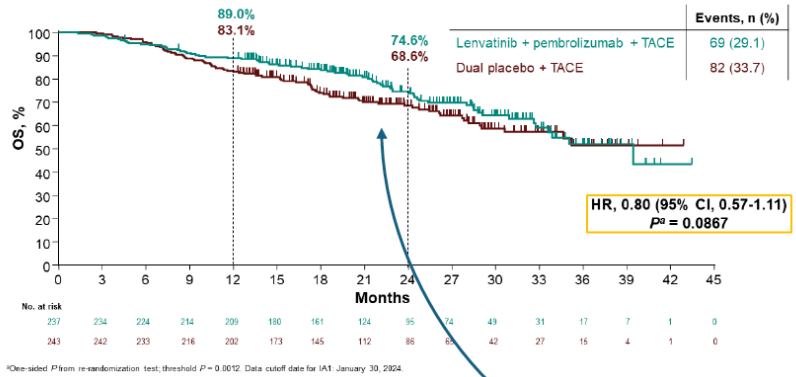
171	104	73	52	26	11	7	1	0
171	81	46	39	22	9	0		

Sangro B, et al. *Lancet* 2025;405:216–232.
Kudo M, et al. *Lancet* 2025:405:203–215.
Dong J, et al. ESMO Gastrointestinal Cancers Congress 2025, LBA2

However...

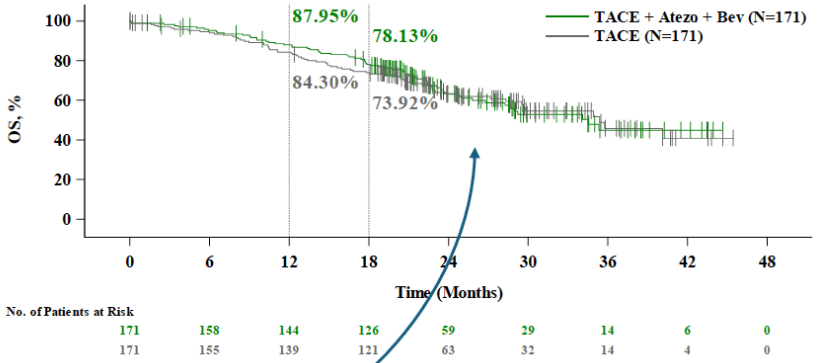
*No evidence for **OS** benefit*

LEAP-012



[a]One-sided *P* from re-randomization test; threshold *P* = 0.0012. Data cutoff date for IA1: January 30, 2024.

TALENTACE



Largely immature datasets

Kudo M, et al. *Lancet* 2025:405:203–215.
Dong J, et al. ESMO Gastrointestinal Cancers Congress 2025, LBA2

Phase-3 studies evaluating the combination of TACE with immunotherapy in HCC:

We have accepted PFS as primary endpoint for these **clinical trials**

And the trails have met the **primary endpoint of PFS**: positive trials

But…

The combination is not widely implemented in clinical practice, because

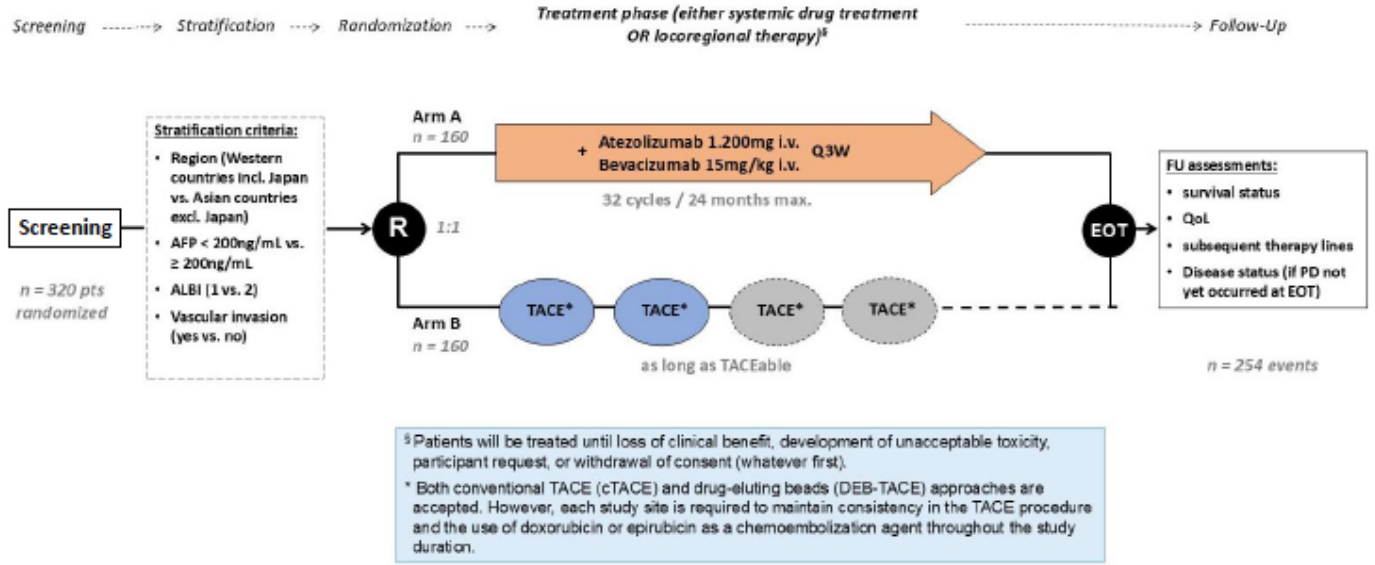
we have not accepted PFS as only primary endpoint to change clinical practice

Unmet need: we need to agree on **clinically meaningful endpoints**

	NCT04559607		apatinib			PFS

IKF-035/ABC-HCC Study Design

an international, randomized, multicenter, open-label, investigator-initiated phase 3b trial



Main Inclusion Criterion: Intermediate stage HCC - not amenable to curative surgery, liver transplantation or curative ablation BUT disease amenable to TACE (minimal vascular invasion Vp1/Vp2 allowed)

Primary endpoint:

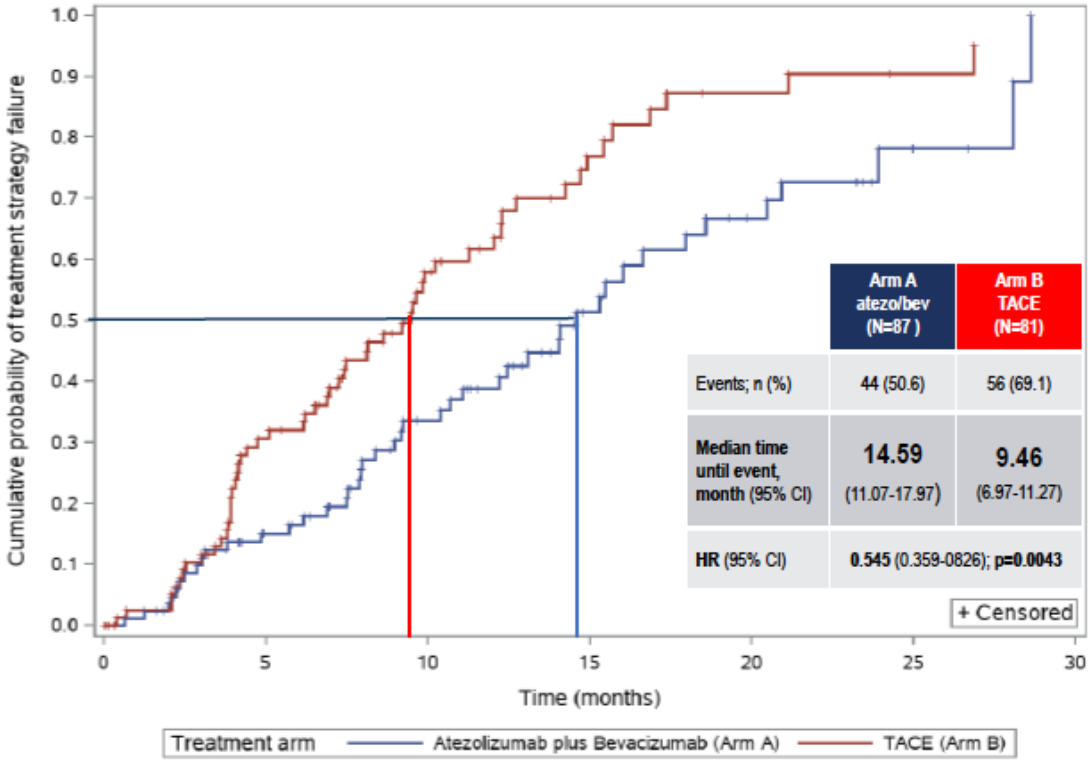
allowing a fair comparison between two modalities ***(Systemic Tx vs. locoregional Tx)***

Time to failure of treatment strategy (TTFS)

Failure of strategy =	Arm A (Atezo/Bev)	Arm B (TACE)
1st condition →	radiologic progession	radiologic progression or stable disease
2nd condition →	**AND** any of the following: ▪ loss of clinical benefit OR – Progression at critical anatomical sites – Development of symptoms and signs (including laboratory values) unequivocal progression of disease – Decline in ECOG performance status attributed to disease progression – No evidence of clinical benefit as assessed by the investigator ▪ unacceptable toxicity OR ▪ liver function deterioration OR ▪ therapy not further applicable for other reasons	

Peter R. Galle

Time to Failure of Treatment Strategy (TTFS)



CONCLUSIONES

La terapia sistémica con anti.PD-1/PDL-1 + antiangiogénico o doble inmunoterapia anti-PD1/anti-CTLA4 es el tratamiento de elección en pacientes con HCC avanzado, pacientes en estadio B de patrón difuso y tras fallo a terapia local.

Los estudios de vida real refrendan los datos obtenidos de los ensayos clínicos pivotales y aportan información sobre la eficacia y toxicidad de poblaciones infrarrepresentadas en dichos ensayos pivotales.

El doble bloqueo inmunológico asociado a antiangiogénico no ha demostrado mejorar los resultados.

En pacientes con HCC estadio B candidatos a TACE, la asociación de inmunoterapia +/- antiangiogénicos incrementa la tasa de respuestas y la SLP pero no mejora la SG.

La selección del tratamiento en pacientes con estadio B es un nuevo reto terapéutico y se necesitan nuevos estudios en poblaciones hiper-seleccionadas.

Resultados preliminares de un estudio fase III abren la posibilidad de un tratamiento sistémico inicial sin TACE en el estadio B.