Colangitis biliar primaria (CBP) no respondedora a AUDC y síndrome de “overlap” CBP-HAI: Alternativas actuales.

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Málaga, 16 de Mayo de 2024.

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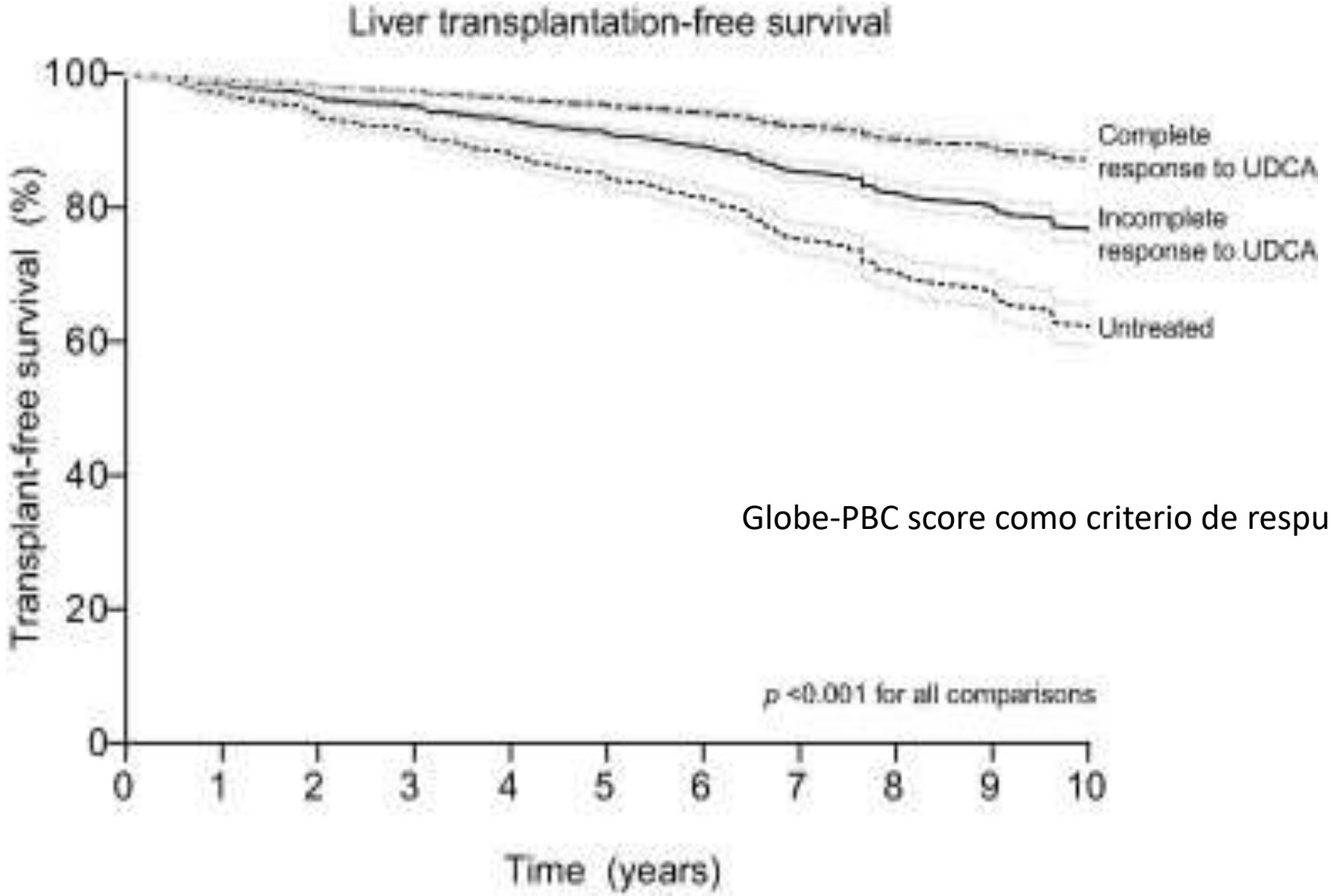
Sinopsis.

1. Criterios de no respuesta al AUDC.
2. Tratamientos de segunda línea.
3. Triple terapia.
4. Manejo del síndrome de solapamiento CBP-HAI.

Acido Ursodeoxicólico (AUDC)

- Las guías de la EASL recomiendan la administración de ácido ursodesoxicólico (AUDC) a dosis de 13-15 mg/kg/día en pacientes con CBP [1].
- En un estudio de cohorte (n=3902) el tratamiento con AUDC redujo el riesgo de trasplante de hígado o fallecimiento independientemente del estadio ([HR] 0,46 (IC95% 0,40–0,52; p<0,001)[2].
- Estos hallazgos se confirmaron en un meta-análisis de siete ensayos controlados aleatorios y seis de seguimiento[3]. Los efectos secundarios comunes del AUDC incluyen debilitamiento del pelo, aumento de peso y flatulencia [4].
- Hasta un 30-40% de los pacientes no responden al AUDC[5].

1. EASL clinical practice guidelines: the diagnosis and management of patients with primary biliary cholangitis. *J Hepatol*. 2017;67:145–172; 2. Harms MH et al. *J Hepatol*. 2019;71:357–365: 3. Shi J et al. *Am J Gastroenterol*. 2006;101:1529–1538; 4. Onofrio FQ et al. *Gastroenterol Hepatol (N Y)*. 2019;15:145–154.; 5. Goel A, Kim WR. *Clin Liver Dis*. 2018;22:563–578

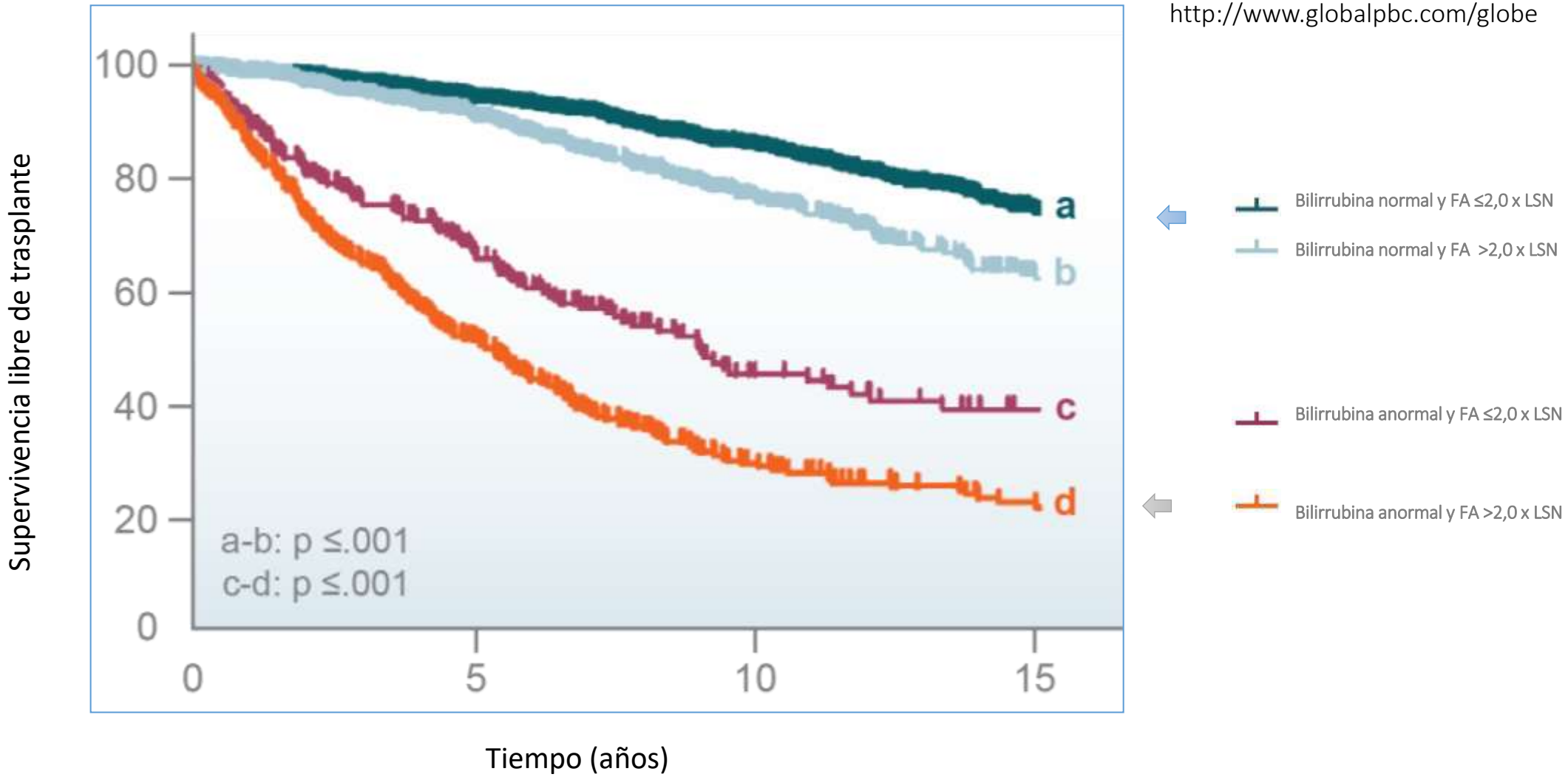


Globe-PBC score como criterio de respuesta

Harms MH et al. J Hepatol. 2019;71:357-365

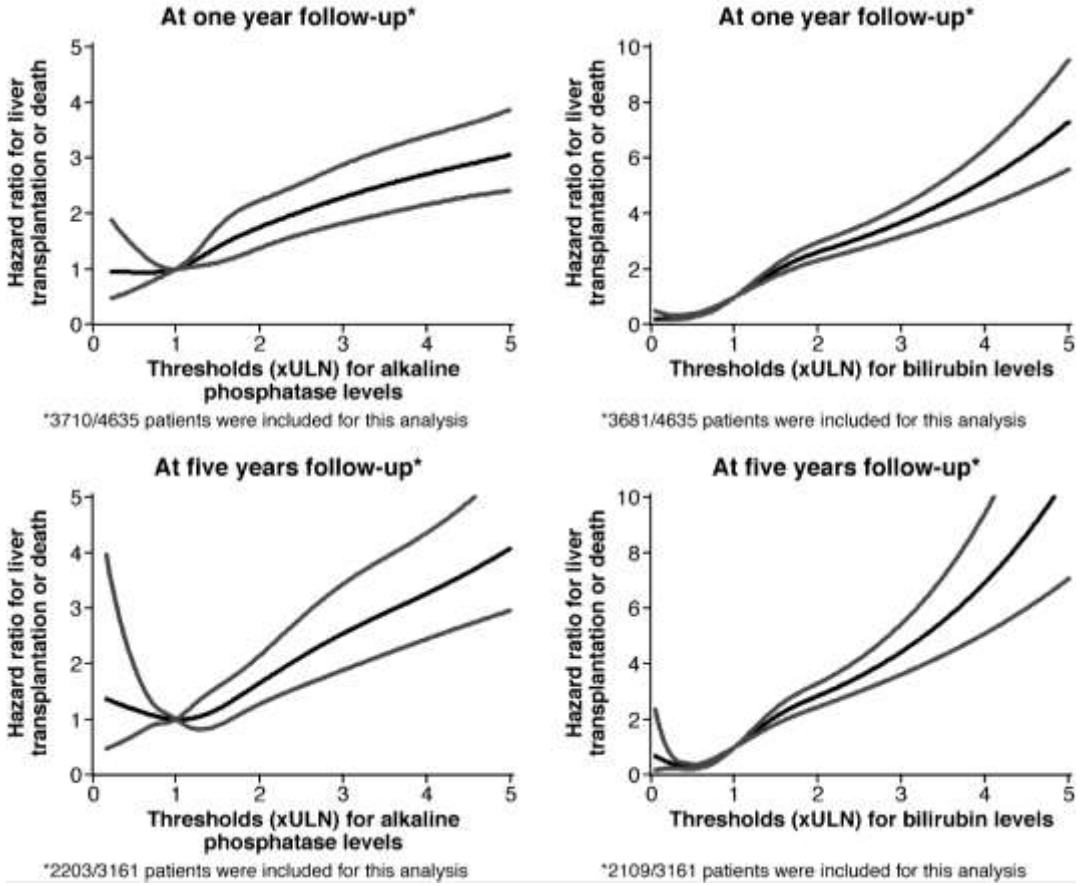
Capacidad pronóstica reforzada de la combinacion FAL y Bilirrubina a 10 años de seguimiento.

http://www.globalpbc.com/globe



Lammers WJ, et al. Gastroenterology. 2014;147:1338-1349..

Evaluar la respuesta al AUDC al año…Cuanto mas bajas son la FA y bilirrubina, mayor supervivencia.



HR: Hazard Ratio; LSN: Límite Superior de la Normalidad; FA: Fosfatasa Alcalina; BILI total: Bilirrubina total; AUDC: ácido ursodesoxicólico

Lammers WJ, et al. Gastroenterology. 2014;147:1338-1349.

Criterios	Meses después de empezar AUDC	Criterios de respuesta incompleta
Escalas binarias		**Variables**
Rochester	6	ALP> 2XULN
Barcelona	12	ALP>ULN or less than 40% decrease in ALP
Paris-I	12	ALP >3ULN, AST >2 ULN, or T.Bili>ULN
Paris-II	12	ALP>1.5XULN, AST>1.5XULN or TB>1 mg/dl
Rotterdam	12	TB>ULN or Albumin<LLN
Toronto	24	ALP>1.67 X ULN
Escalas continuas		**Variables**
GLOBE-PBC	12	TB, ALP, Albumin and platelet count after 12 months of ursodiol. Age at baseline
UK-PBC	12	TB, ALP, and AST (or ALT) after 12 months of ursodiol use. Albumin and platelets at baseline

Criteria [a]	Derivation cohort (n = 2488)					Validation cohort (n = 1631)				
	HR	95% CI	P value	C-statistic	95% CI	HR	95% CI	P value	C-statistic	95% CI
Barcelona	1.69	1.39–2.06	<.0001	0.58	0.55–0.61	1.84	1.42–2.38	<.0001	0.57	0.54–0.61
Paris-1	3.64	3.03–4.36	<.0001	0.69	0.66–0.71	4.61	3.61–5.90	<.0001	0.70	0.67–0.73
Rotterdam	4.11	3.32–5.08	<.0001	0.69	0.66–0.71	4.10	3.11–5.42	<.0001	0.68	0.65–0.71
Toronto	2.13	1.76–2.56	<.0001	0.61	0.58–0.63	2.46	1.90–3.18	<.0001	0.62	0.59–0.65
Paris-2	2.82	2.29–3.47	<.0001	0.63	0.61–0.65	2.89	2.17–3.85	<.0001	0.63	0.61–0.66
GLOBE score	—	—	—	0.81	0.79–0.83	—	—	—	0.82	0.79–0.84

Lammers WJ et al Gastroenterology 2015; 2015;149:1804-1812.

Table 4. Multivariable analyses of risk prediction scores at 1 year of UDCA therapy (N = 905)

	Univariate analyses			Multivariable analyses		
Prognostic score	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
MRS 1989	2.40	3.14–2.70	<0.001			
MRS 1994	1.98	1.81–2.17	<0.001	1.28	1.06–1.55	0.01
MELD	1.15	1.12–1.18	<0.001	1.02	0.97–1.07	0.37
UK-PBC	2.10	1.86–2.37	<0.001	0.99	0.82–1.21	0.99
GLOBE	3.34	2.83–3.95	<0.001	2.36	1.71–3.27	<0.001

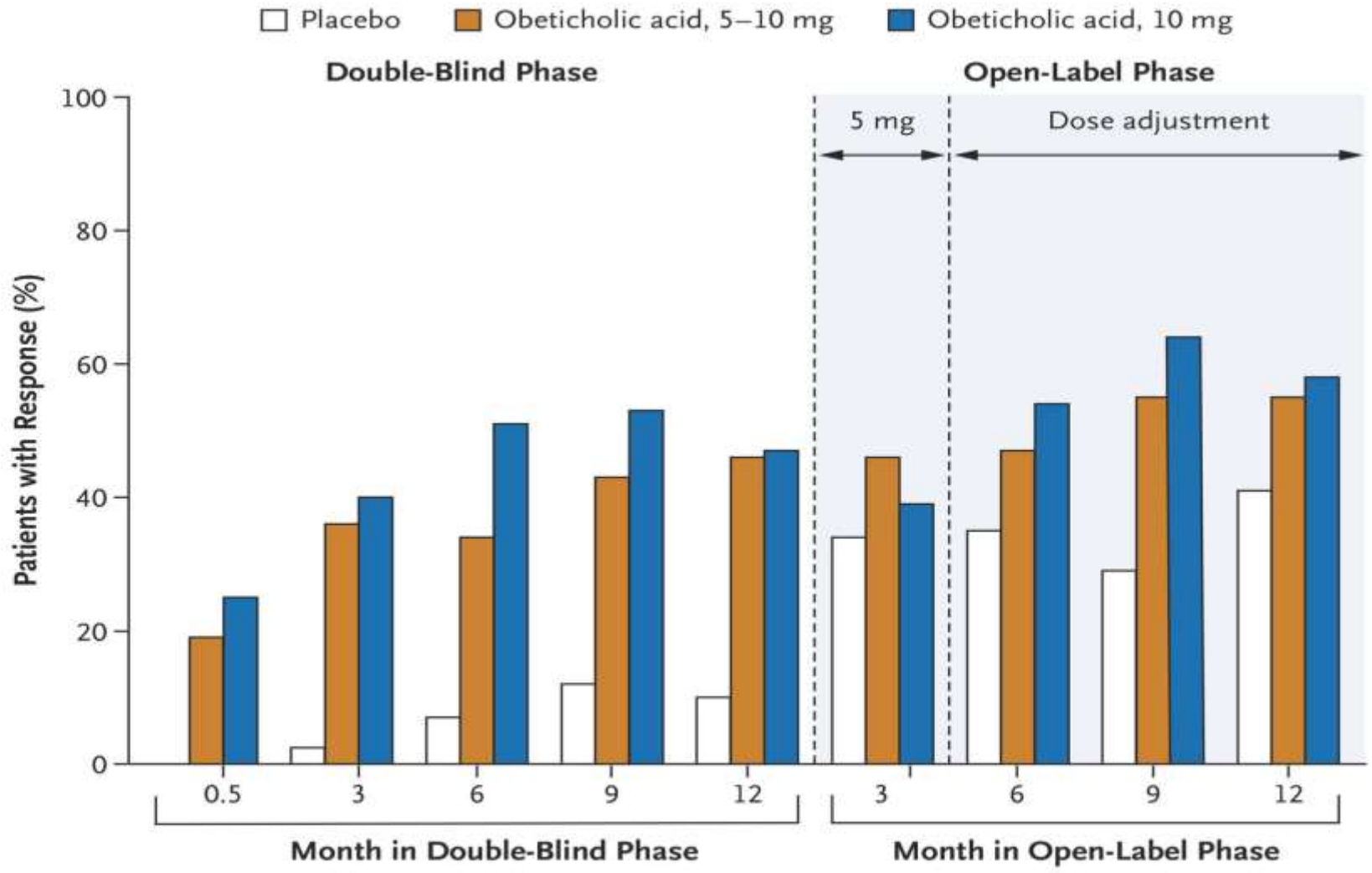
CI, confidence interval; MELD, Model for End-stage Liver Disease; MRS, Mayo Risk Score; UDCA, ursodeoxycholic acid.

Goet J et al: Am J Gastroenterol, 2021; 116:1514-1522

Tratamientos de segunda linea

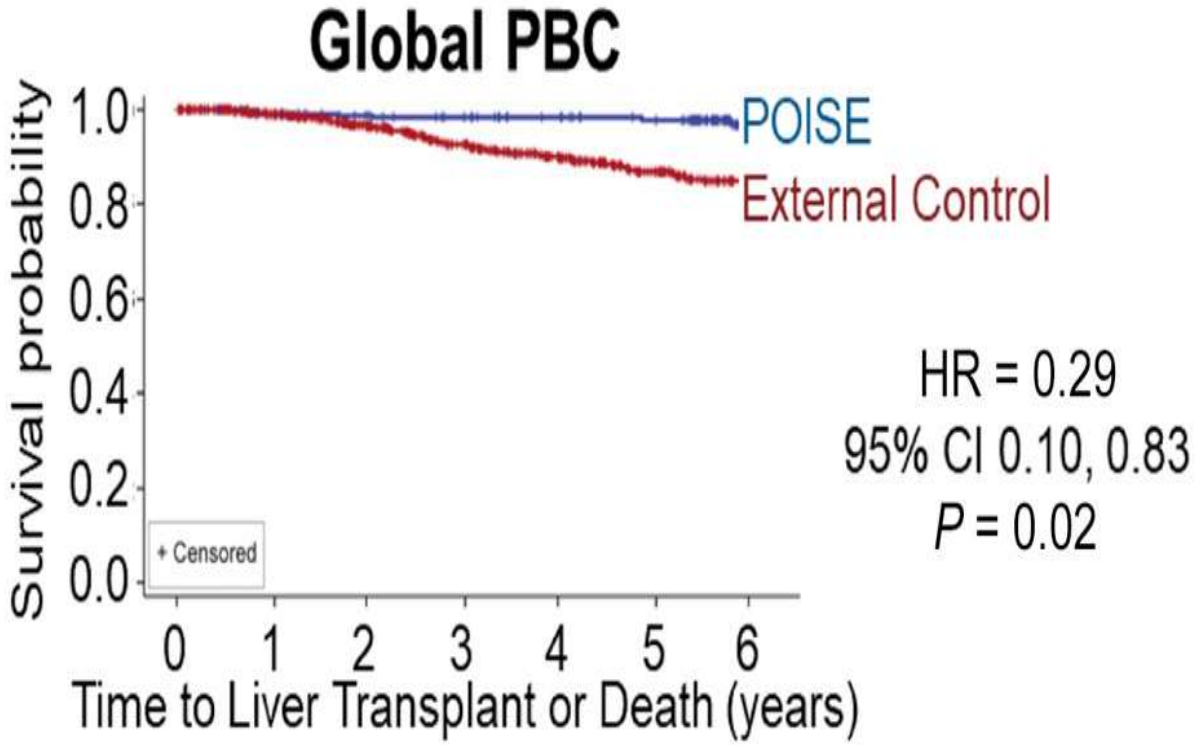
1. Agonistas FxR: Acido Obeticólico (OCA)
2. Agonistas PPAR: Bezafibrato
3. Nuevos agonistas PPAR (Elafibranor y Seladelpar)
4. Inhibidores de al NADPH Oxidasa (NOX1 y NOX4):
   Senataxib (Fase 2b-3).
5. Triple terapia.

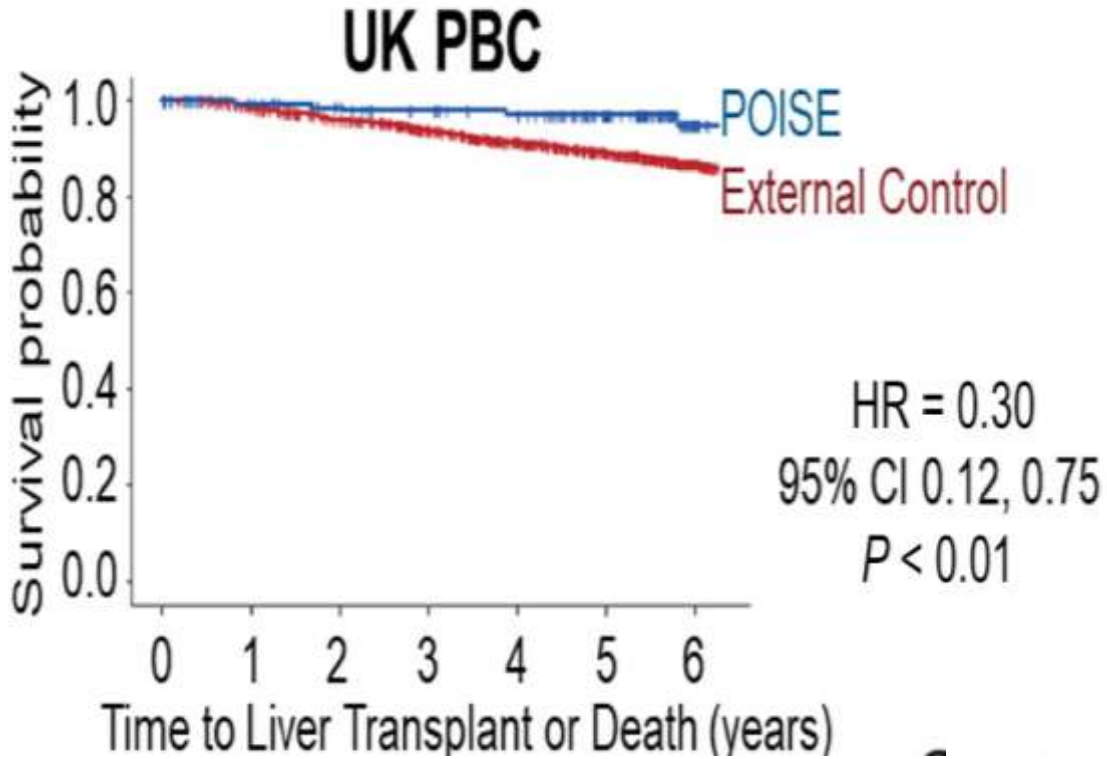
Descenso de FA a
≤1,67 LSN y Δ-15%
Bilirrubina normal



No. of Patients									
Placebo	73	73	73	73	73	64	60	59	59
Obeticholic acid, 5–10 mg	70	70	70	70	70	63	62	62	60
Obeticholic acid, 10 mg	73	73	73	73	73	64	59	61	59

Nevens F, et al *N Engl J Med*. 2016;375:631–643.





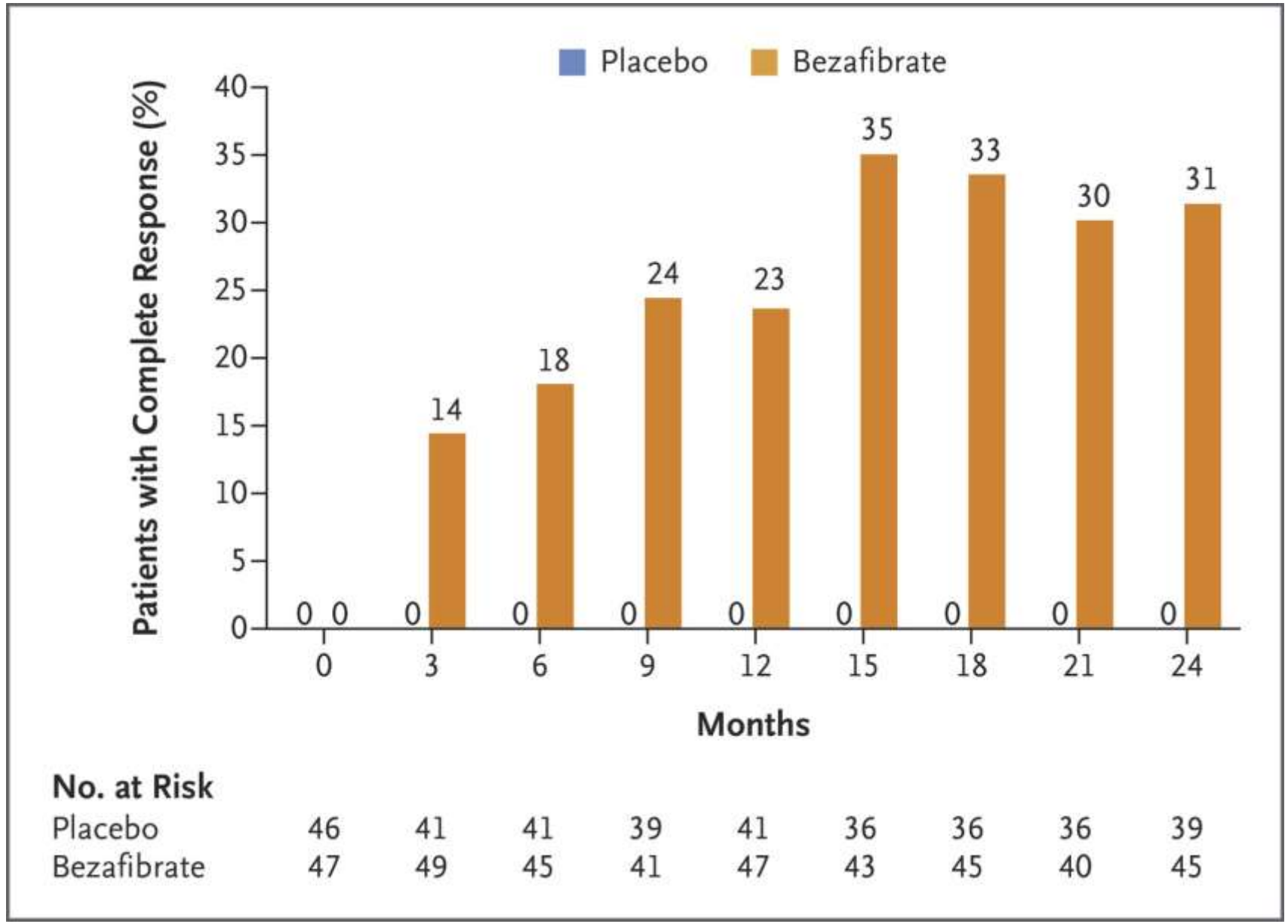
IPTW

Murillo-Perez CF et al Gastroenterology 2022 1631630-1642

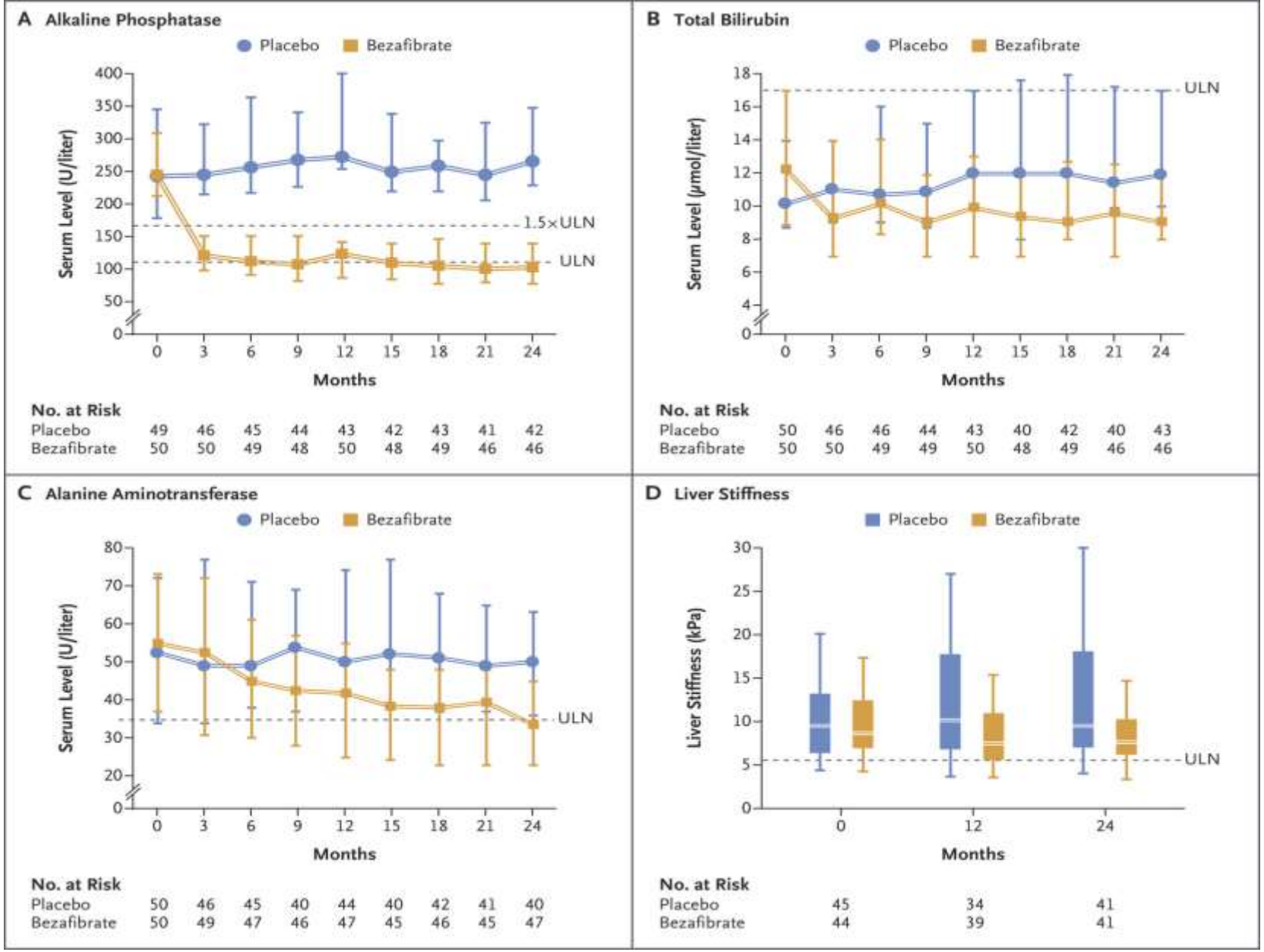
Efectos adversos.

- El prurito es el EA mas frecuente con OCA[1]. El mecanismo de acción es desconocido, y dosis dependiente. Afectó al 68% del grupo de 10 mg y 56% en el de 5–10 mg en el ensayo POISE[1].
- La hepatotoxicidad secundaria a OCA parece dosis-dependiente en pacientes con hepatopatia mas avanzada[2,3] . Por lo que OCA esta contraindicada en cirrosis CPT-B y existe una advertencia de la FDA[4].
- Se recomienda monitorizacion estrecha en estos pacientes[5].

1. Nevens F, et al *N Engl J Med*. 2016;375:631–643 ; 2. Eaton JE et al. Liver injury in patients with cholestatic liver disease treated with obeticholic acid. *Hepatology*. 2020;71:1511–1514; 3. Aschenbrenner DS. Excessive Dosing of Obeticholic Acid May Increase Risk of Liver Damage. Am J Nurs. 2018 Feb;118(2):46
4. US Food and Drug Administration. *FDA Adds Boxed Warning to Highlight Correct Dosing of Ocaliva (Obeticholic Acid) for Patients with a Rare Chronic Liver Disease*. US Food and Drug Administration; 2018;
5. Siddiqui MS et al. *J Hepatol*. 2020;72:25–33



BEZURSO Trial. Corpechot Ch et al N Engl J Med 2018;378:2171-2181

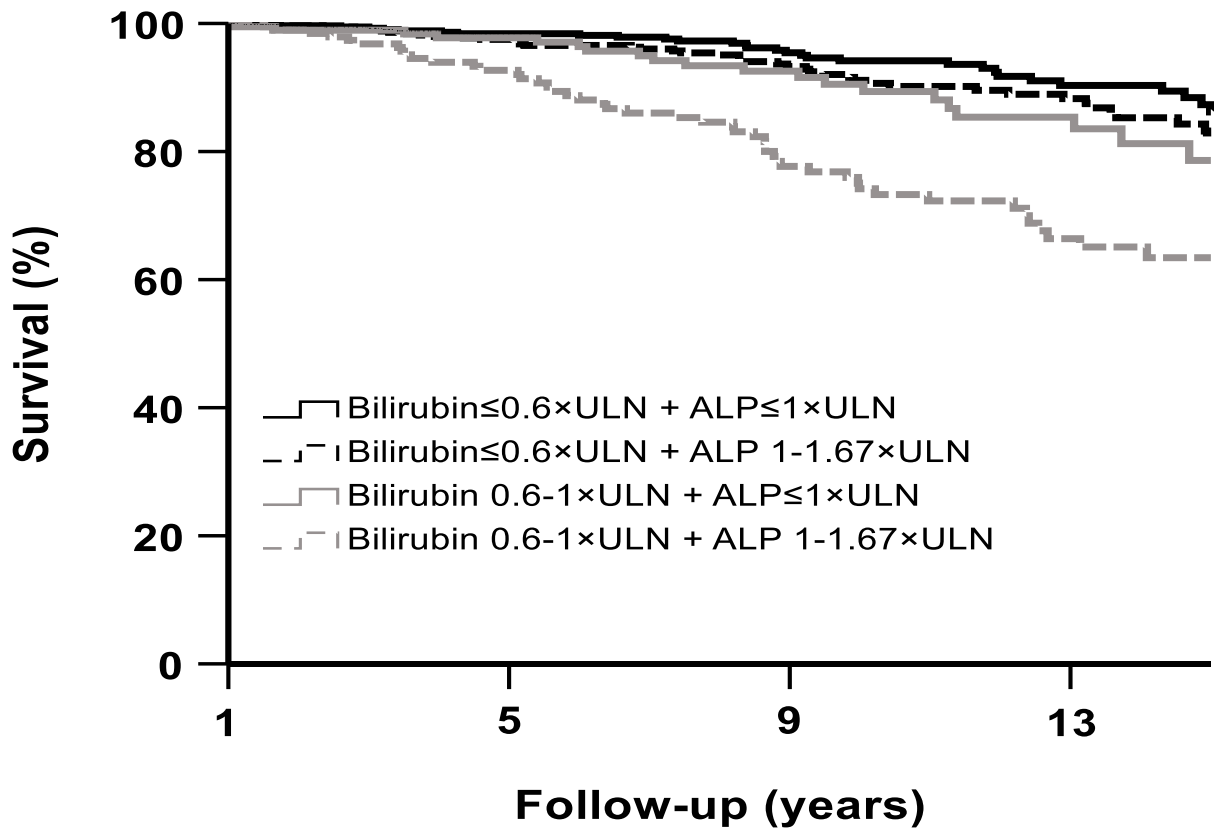


Corpechot Ch et al N Engl J Med 2018;378:2171-2181

Drugs Currently in Phase 2-3 Clinical Trials for the Management of PBC

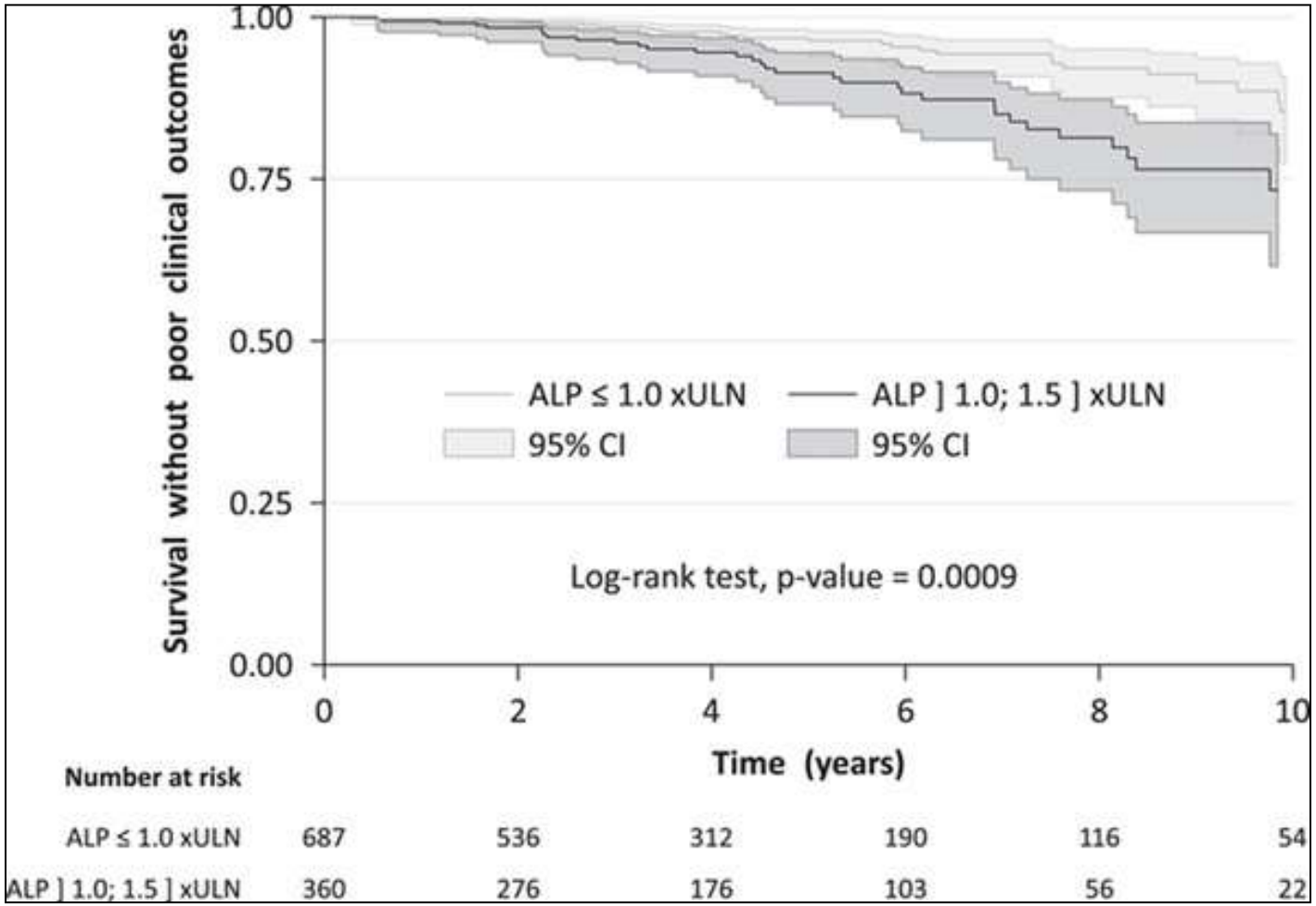
Drug	NCT	Mechanism of Action	Primary Endpoint/Coments
Seladelpar	NCT04620733	PPAR-δ agonist	•ALP<1.67 ULN •>15% reduction in ALP •Total bilirubin <ULN
Saroglitazar	NCT05133336	PPAR α and γ agonist	•ALP<1.67 ULN •>15% reduction in ALP •Total bilirubin <ULN
Elafibranor	NCT04526665	PPAR-α and δ agonist	•ALP<1.67 ULN •>15% reduction in ALP •Total bilirubin <ULN
Setanaxib	NCT05014672	NOX 1 and 4 inhibitors	•ALP<1.67 ULN •>15% reduction in ALP •Total bilirubin <ULN
Linerixibat	NCT04950127	ASBT inhibitors	•Monthly itch scores over 24 weeks
Non-bile FXR agonists	NCT02943447	FxR agonists	No data on GLOBE scores. It is likely that the real impact on long-term survival is not reflected by GLOBE scores because of the ability of FXR agonists to induce ALP transcription
Aldafermin	NCT02026401	Subcutaneously administered analog of FGF-19	•No data on GLOBE scores, but will likely improve it based on improvement in the ALP levels noted

Nuevos objetivos bioquímicos.



a	579	407	243	123
b	552	416	238	126
c	194	148	97	48
d	198	143	97	51

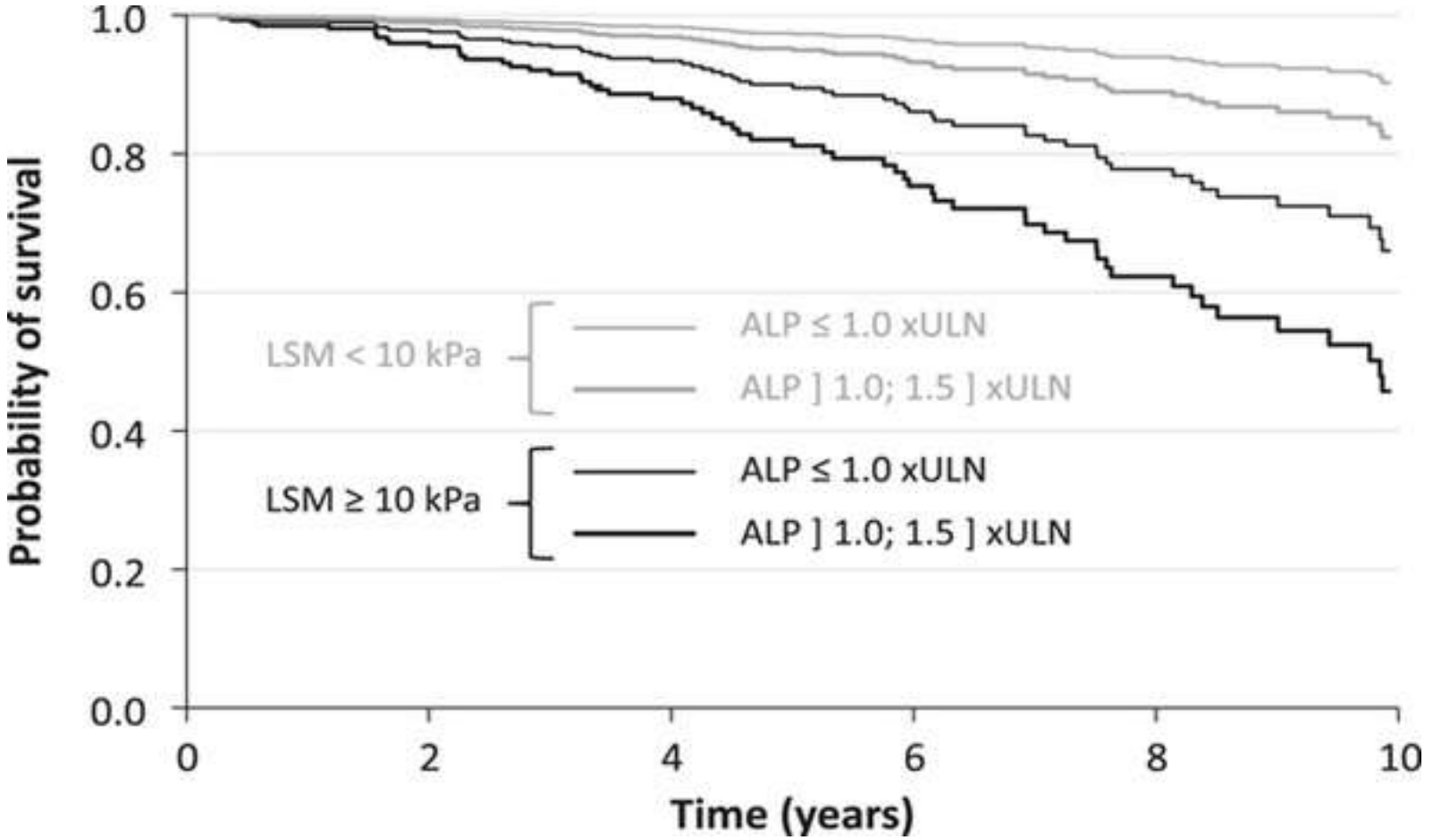
Murillo Pérez C et al AJG 2020 **115:1066-1074**



Adequate versus deep response to ursodeoxycholic acid in primary biliary cholangitis: To what extent and under what conditions is normal alkaline phosphatase level associated with complication-free survival gain?.

Corpechot Ch et al Hepatology. 2024; 79:39-48.

N=1047 pacientes que cumplían criterios de respuesta al AUDC (Paris II)



Normal serum ALP values (but not normal GGT, ALT, AST or total bilirubin < 0.6 ×ULN, were associated with a significant absolute complication-free survival gain at 10 years (mean 7.6 months, 95% CI: 2.7 - 12.6 mo.; p = 0.003). In subgroup analysis, **this association was significant in patients with a LSM ≥ 10 kPa and/or age ≤ 62 years, with a 10-year absolute complication-free survival gain of 52.8 months (95% CI: 45.7-59.9, p < 0.001) when these 2 conditions were met.**

Corpechot Ch et al Hepatology. 2024; 79:39-48.

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The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

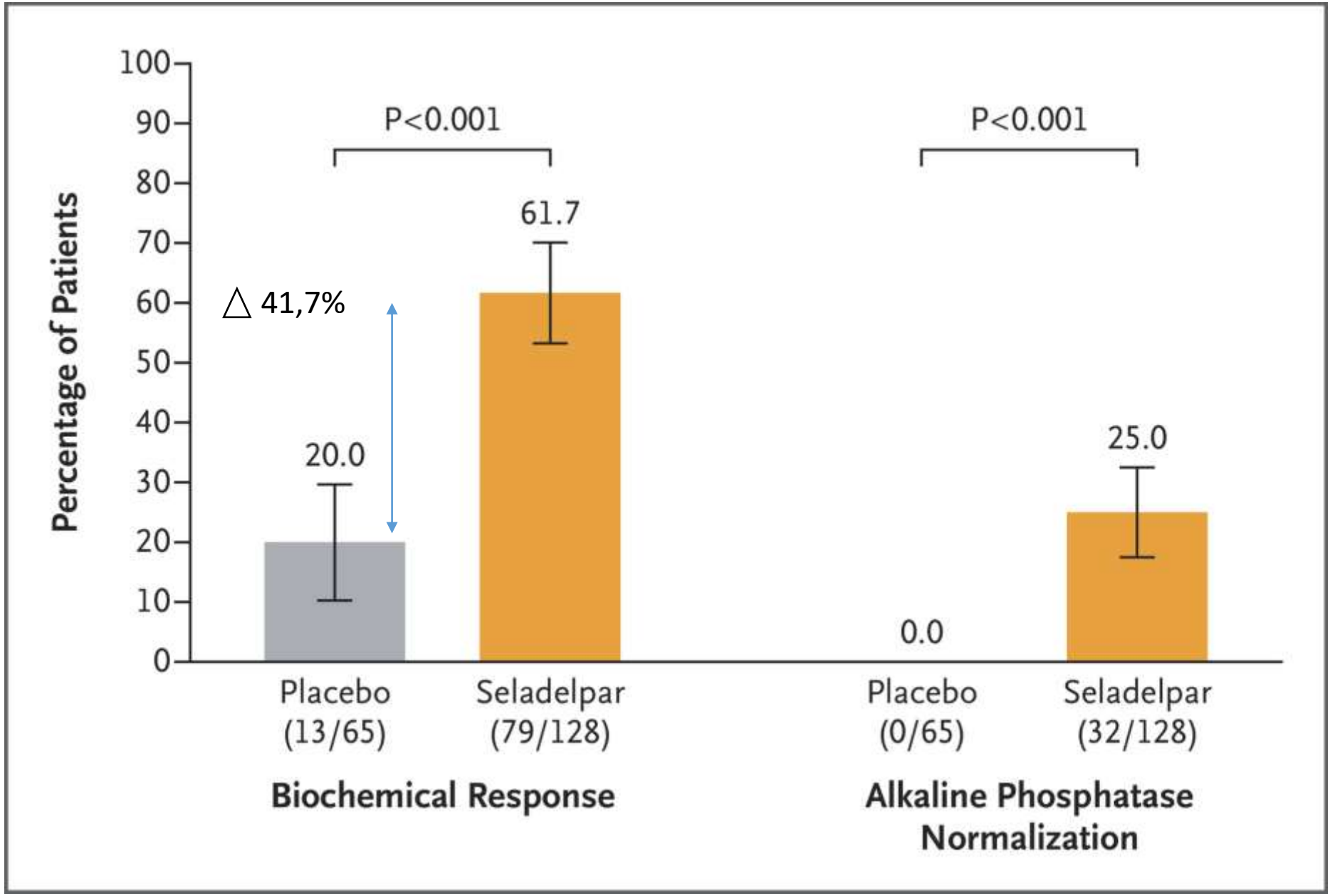
A Phase 3 Trial of Seladelpar in Primary Biliary Cholangitis

Hirschfield GM et al. DOI: 10.1056/NEJMoa2312100

Characteristic	Placebo (N=65)	Seladelpar (N=128)
Age — yr	57.0±9.2	56.6±10.0
Age at diagnosis — yr	49.3±10.9	49.2±9.9
Female sex — no. (%)	60 (92.3)	123 (96.1)
Race or ethnic group — no. (%)†		
White	56 (86.2)	114 (89.1)
Asian	4 (6.2)	7 (5.5)
Black	2 (3.1)	2 (1.6)
American Indian or Alaska Native	3 (4.6)	3 (2.3)
Hispanic or Latino	27 (41.5)	29 (22.7)
Duration of disease — yr	8.6±6.5	8.2±6.7
Positive for antimitochondrial antibodies — no. (%)‡	55 (84.6)	106 (82.8)
Ursodeoxycholic acid		
History of unacceptable side effects — no. (%)	4 (6.2)	8 (6.2)
Daily dose — mg/kg§	14.9±3.3	15.0±3.1
Alkaline phosphatase level — U/liter¶	313.8±117.7	314.6±123.0
≥350 U/liter 3×ULN — no. (%)	18 (27.7)	35 (27.3)
Total bilirubin level — mg/dl‖	0.74±0.3	0.77±0.3
>ULN — no. (%)	5 (7.7)	20 (15.6)
ALT level — U/liter**	48.2±22.8	47.4±23.5
AST level — U/liter††	41.7±16.0	39.6±16.1
γ-glutamyltransferase — U/liter‡‡	287.5±249.6	269.0±240.0
Albumin level — g/dl	4.1±0.2	4.2±0.3
Platelet count — $\times 10^3$/mm^3§§	241.9±84.5	241.7±78.9
History of pruritus — no. (%)	48 (73.8)	91 (71.1)
Pruritus NRS score¶¶	3.0±3.0	3.0±2.8
≥4 — no. (%)	23 (35.4)	49 (38.3)
≥4 — mean score	6.6±1.4	6.1±1.4
Liver stiffness — kPa‖‖	8.7±4.2	9.8±6.2
Cirrhosis — no. (%)***	9 (13.8)	18 (14.1)
Portal hypertension	3 (4.6)	0

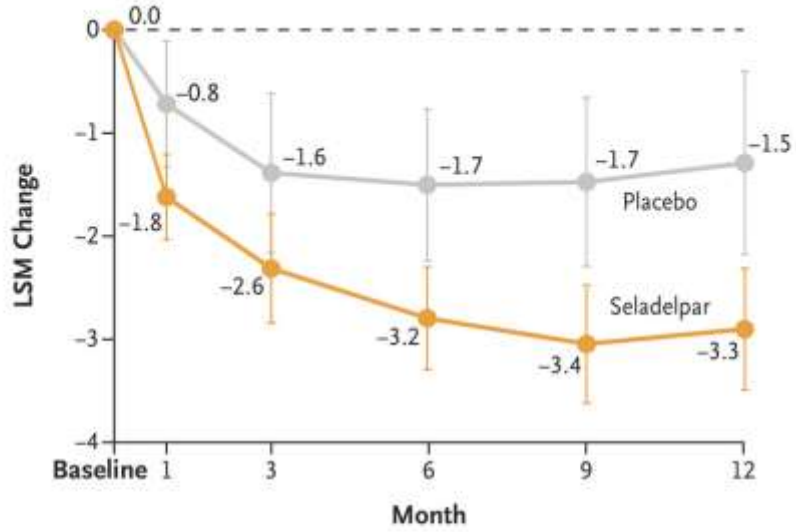
RESPONSE Trial (Fase III) **Baseline Demographic and Clinical Characteristics.***

Hirschfield GM, Bowlus CL, Mayo MJ, et al. A phase 3 trial of seladelpar in primary biliary cholangitis. N Engl J Med 2024;390:783-794.



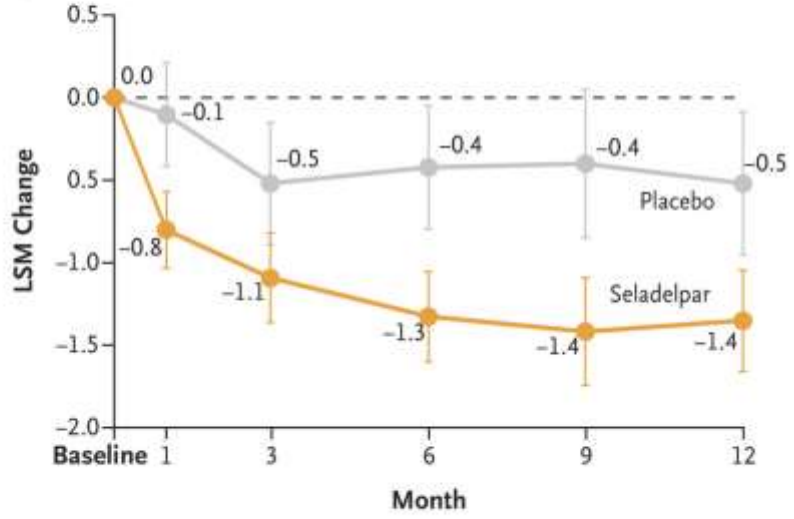
Hirschfield GM, Bowlus CL, Mayo MJ, et al. A phase 3 trial of seladelpar in primary biliary cholangitis. N Engl J Med 2024;390:783-794

A Patients with a Baseline Pruritus NRS Score ≥4



No. at Risk						
Placebo	23	22	22	20	20	16
Seladelpar	49	48	46	45	36	39

B Overall Population



No. at Risk						
Placebo	65	64	63	61	56	48
Seladelpar	128	127	124	121	108	105

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ORIGINAL ARTICLE

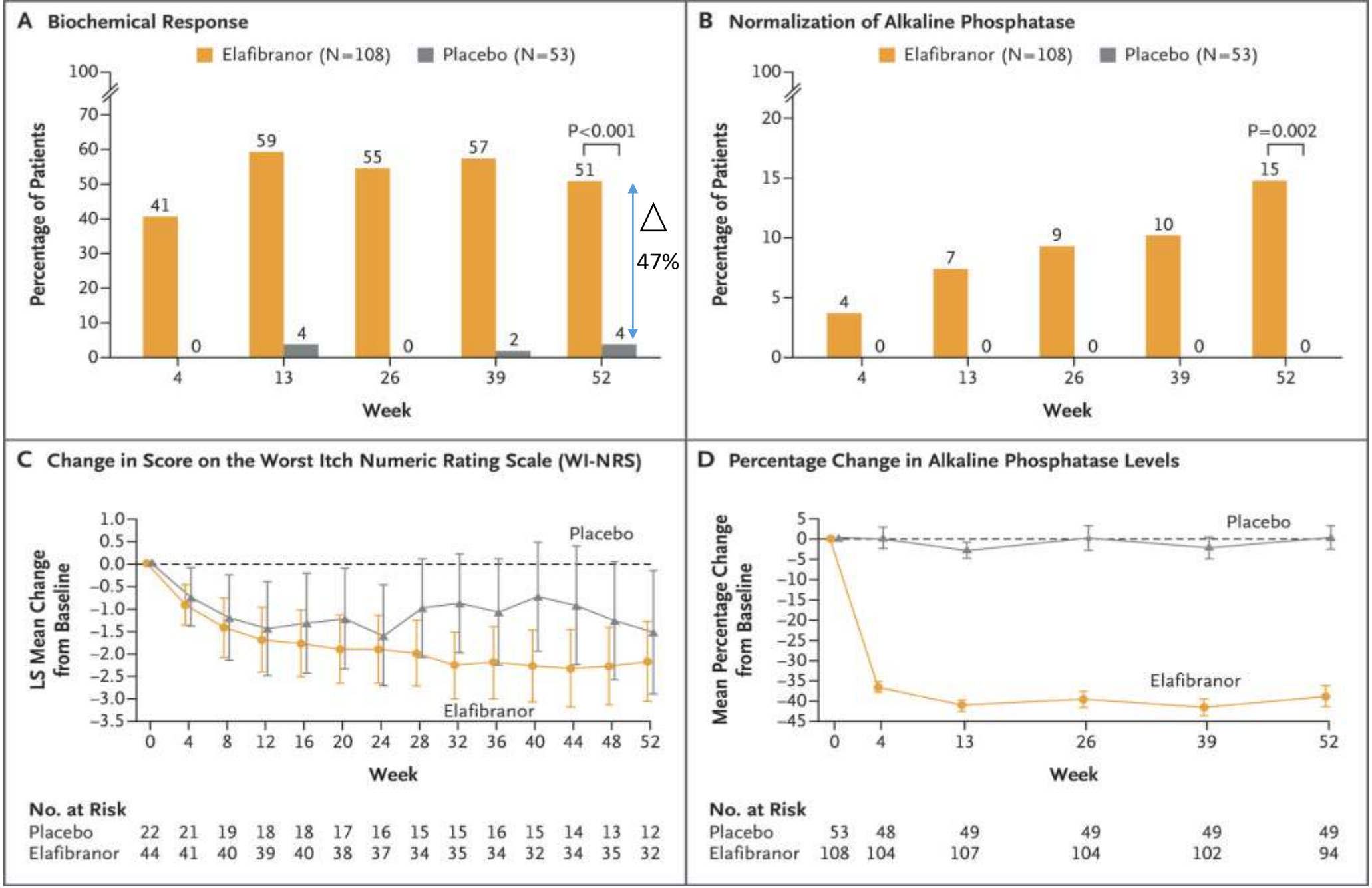
Efficacy and Safety of Elafibranor in Primary Biliary Cholangitis

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Elafibranor Group (N=108)	Placebo Group (N=53)	Total (N=161)
Age — yr	57.5±8.4	56.4±9.3	57.1±8.7
Female sex — no. (%)	102 (94)	52 (98)	154 (96)
White race — no. (%)†	101 (94)	46 (87)	147 (91)
Time since diagnosis — yr	7.9±5.9	8.3±6.8	8.0±6.2
Alkaline phosphatase			
Mean — U/liter	321.3±121.9	323.1±198.6	321.9±150.9
>3× ULN — no. (%)‡	43 (40)	20 (38)	63 (39)
Total bilirubin — μmol/liter§	9.7±5.1	9.4±5.0	9.6±5.1
Aspartate aminotransferase — U/liter	45.0±24.2	47.2±32.8	45.7±27.2
Alanine aminotransferase — U/liter	49.3±29.4	50.3±38.7	49.6±32.6
γ-Glutamyltransferase — U/liter	213.3±186.1	220.0±220.3	215.5±197.4
Concurrent ursodeoxycholic acid — no. (%)	102 (94)	51 (96)	153 (95)
WI-NRS score¶			
Mean	3.3±2.8	3.2±2.9	3.3±2.8
Moderate-to-severe pruritus — no. (%)‖	44 (41)	22 (42)	66 (41)
Liver stiffness**			
Mean — kPa	9.9±7.8	10.7±8.9	10.1±8.2
>10.0 kPa — no./total no. (%)	31/104 (30)	17/50 (34)	48/154 (31)
Bridging fibrosis or cirrhosis — no./total no. (%)††	12/31 (39)	8/16 (50)	20/47 (43)
Liver stiffness >10 kPa or bridging fibrosis (or both) or cirrhosis — no./total no. (%)**††	35/104 (34)	19/50 (38)	54/154 (35)

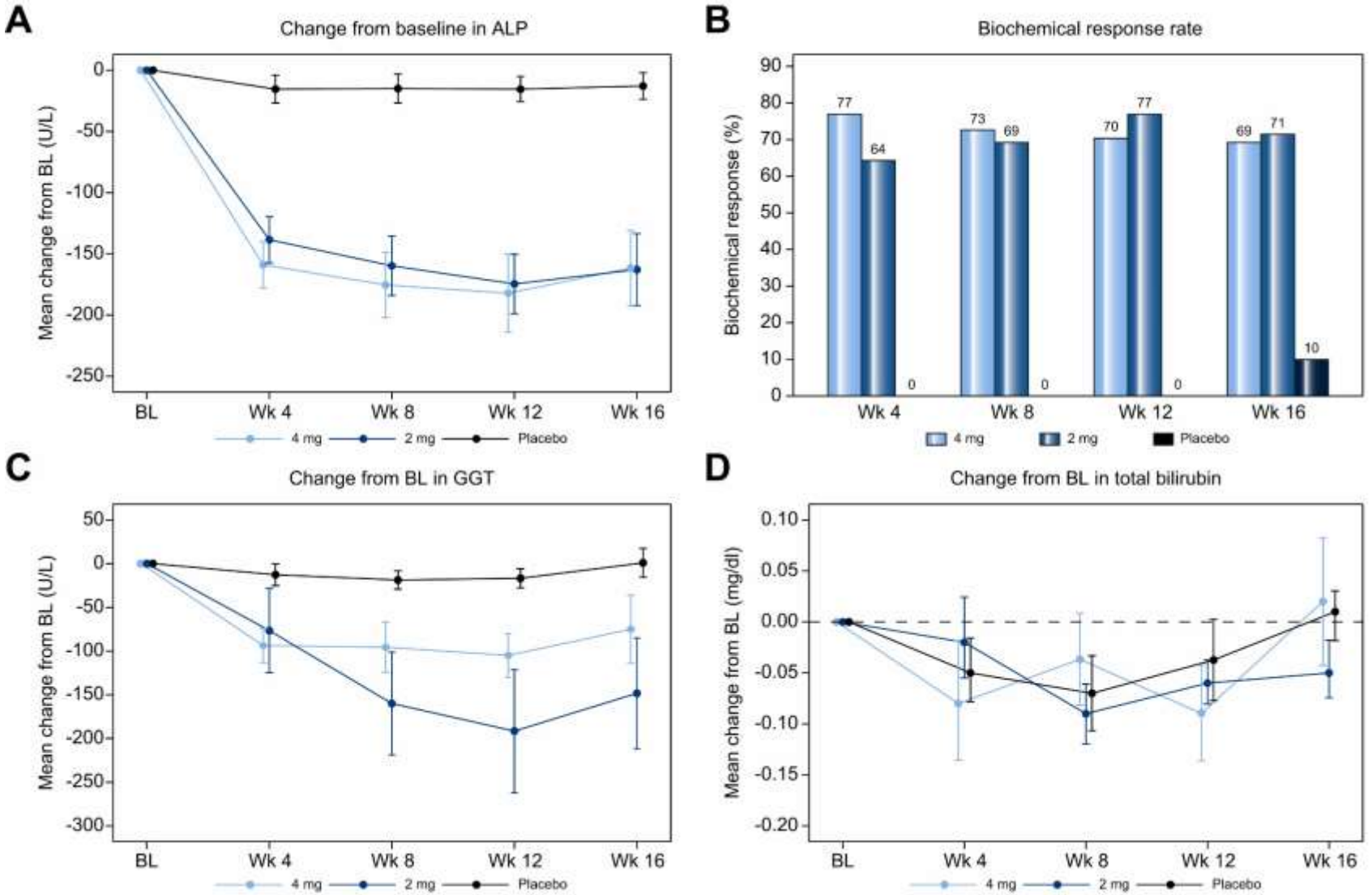
ELATIVE Trial (Fase III) **Baseline Demographic and Clinical Characteristics.***

Kowdley KV et al N Engl J Med. 2023 Nov 13. doi: 10.1056/NEJMoa2306185. Epub ahead of print. PMID: 37962077.



Kowdley KV et al N Engl J Med. 2023 Nov 13. doi: 10.1056/NEJMoa2306185. Epub ahead of print. PMID: 37962077.

Saroglitazar



Vuppalanchi R et al Journal of Hepatology, 2022; 76: 75-85

Results from a planned interim analysis of a randomized, double-blind, active-controlled trial evaluating the effects of obeticholic acid and bezafibrate on serum biomarkers in primary biliary colangitis

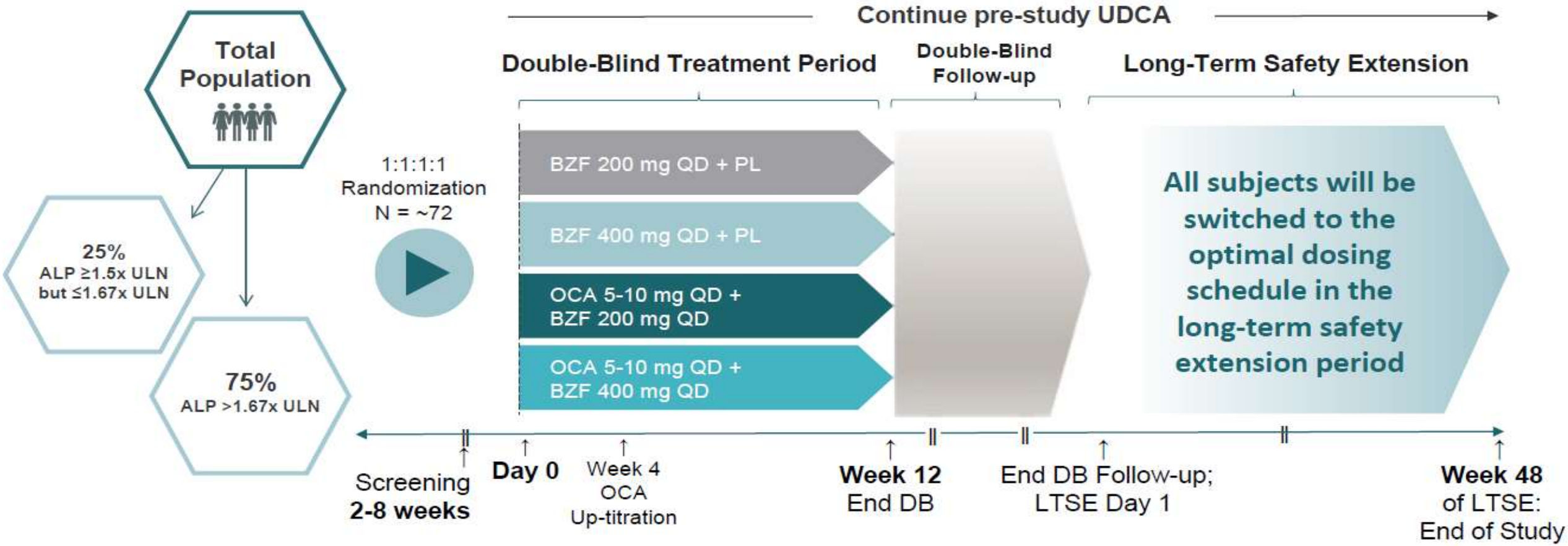
Hejda V et al EASL Vienna, 2023.

Dose-Range Exploration for the Fixed-Dose Combination of Obeticholic Acid and Bezafibrate

The global research program to date includes:

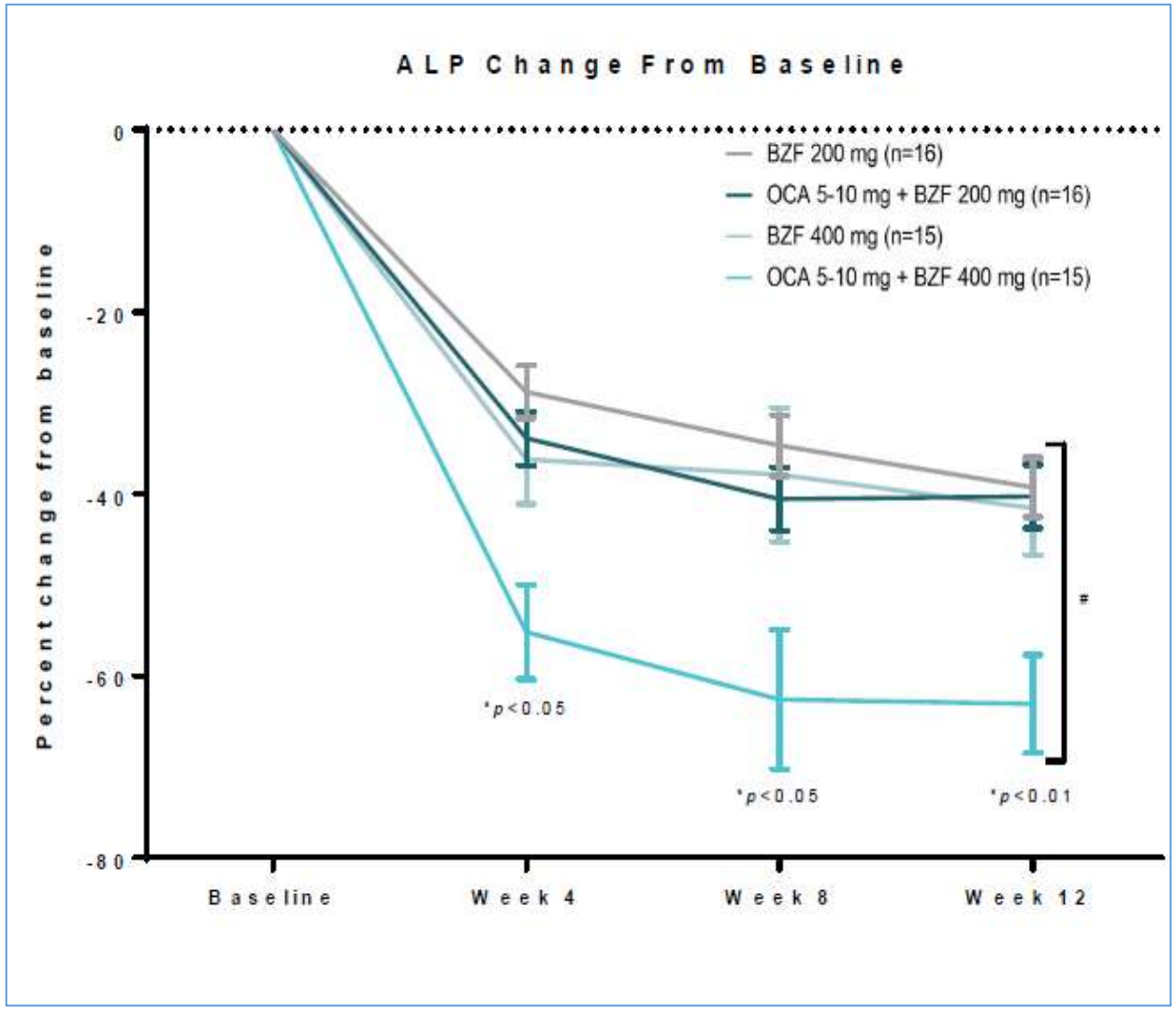
- Study 123: explored a range of doses of obeticholic acid and bezafibrate in healthy adult subjects using cross-over methodology
- Study 213: Phase 2 (n=~72 patients), predominantly in Europe
- Study 214: Phase 2 (n=62 patients), predominantly in the United States, Argentina, and Turkey

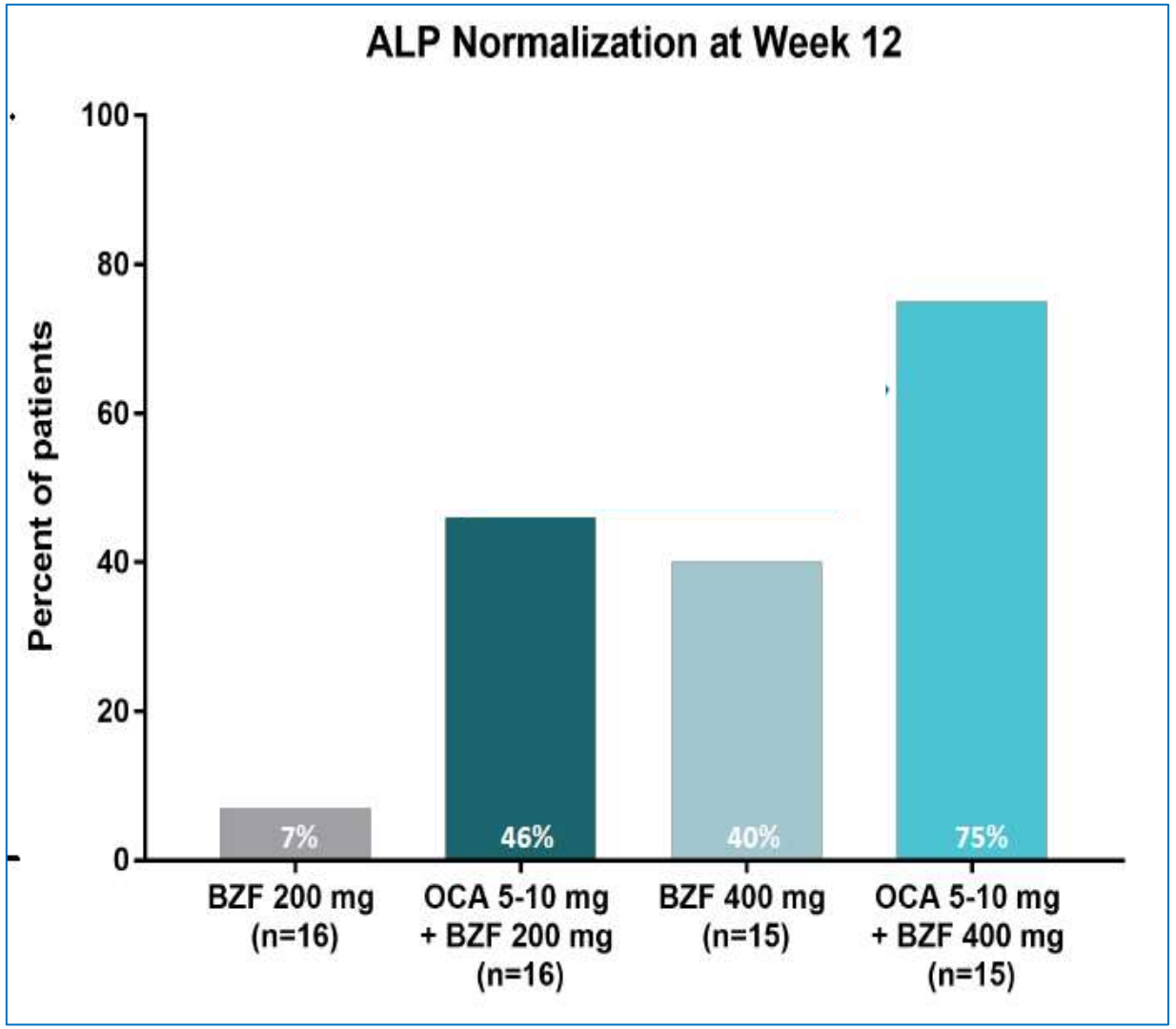
Study 213 Design: Active Comparator



Abbreviations: ALP, alkaline phosphatase; BZF, bezafibrate; DB, double-blind; PL, placebo; LTSE, long-term safety extension; OCA, obeticholic acid; QD, daily; UDCA, ursodeoxycholic acid; ULN, upper limit of normal.

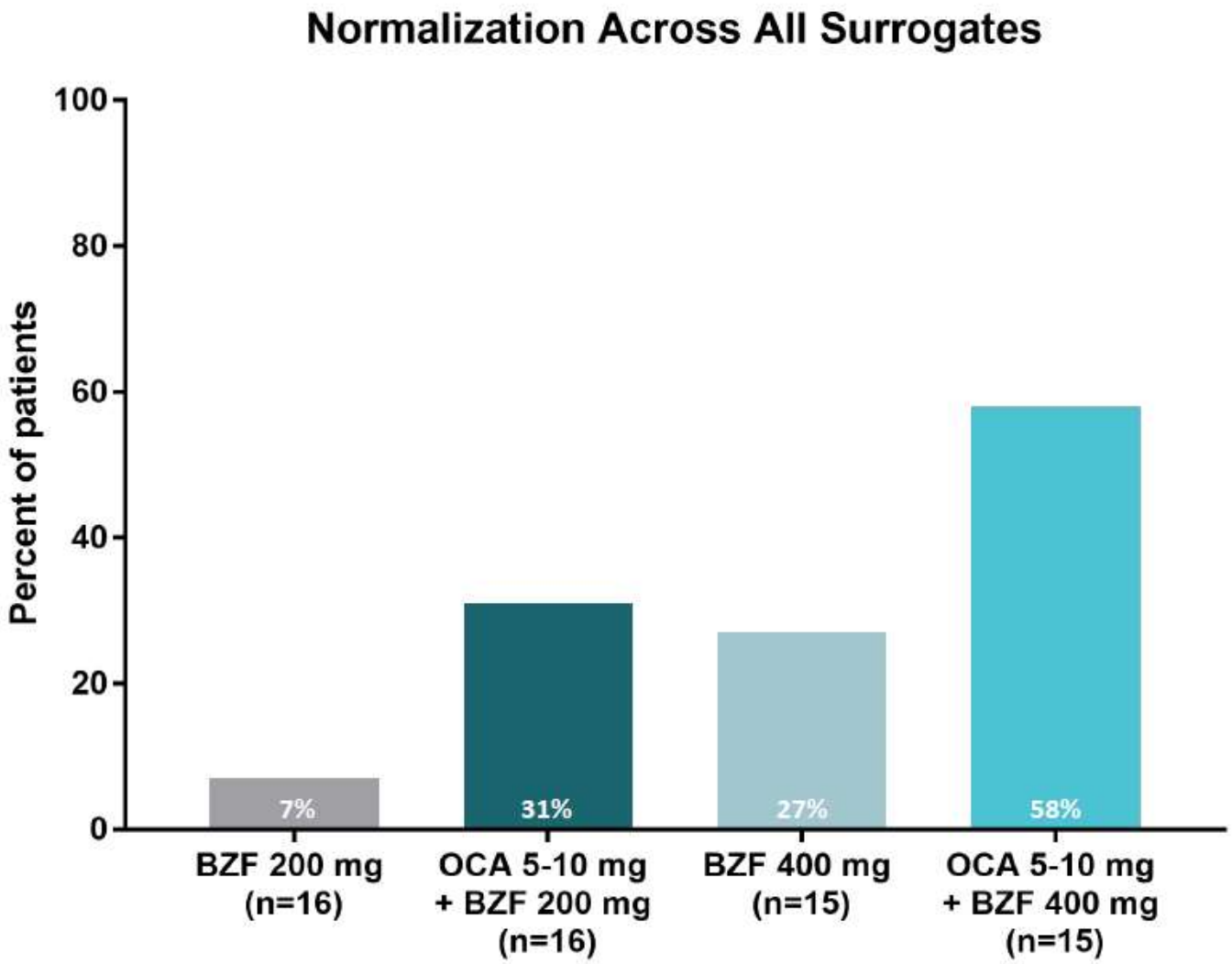
Normalización de la FA con triple terapia



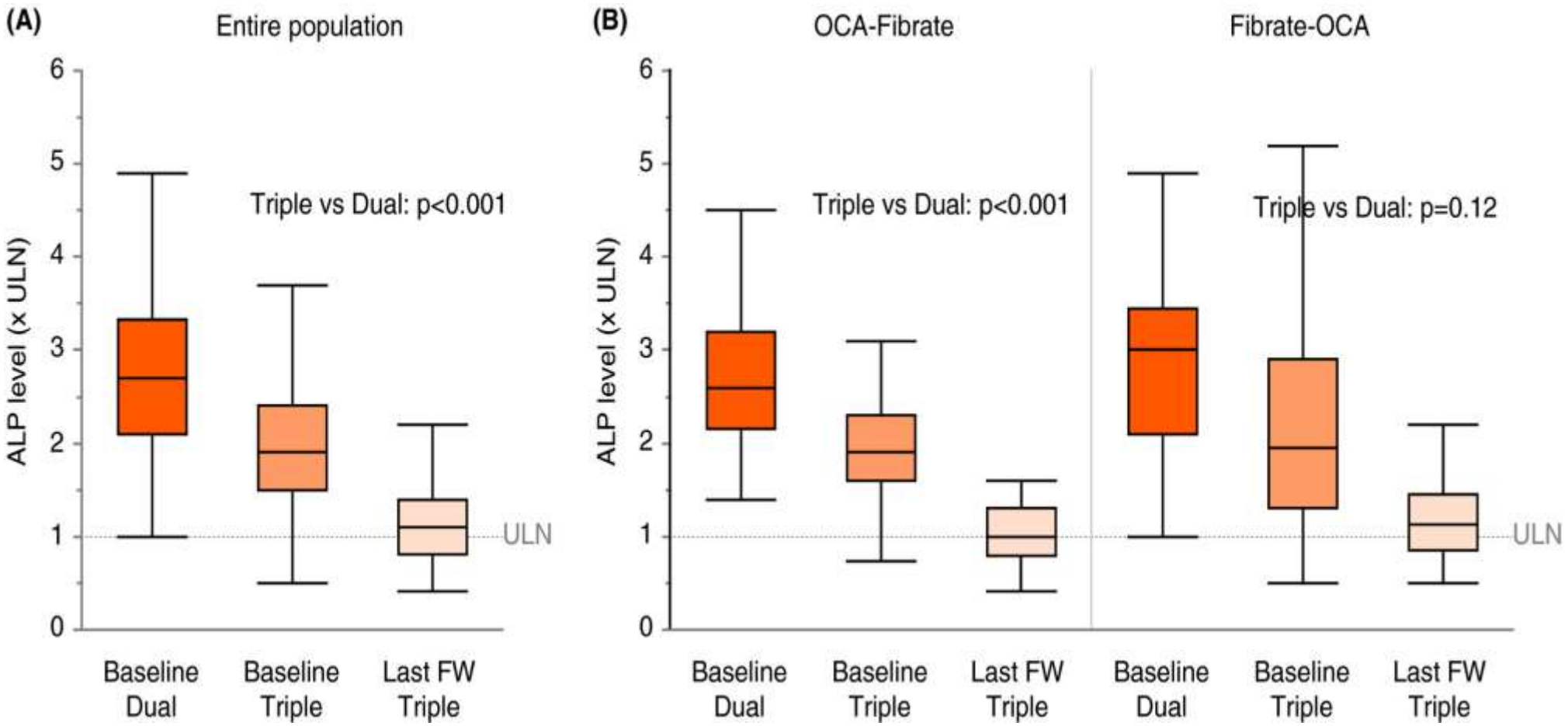


Hejda V et al EASL Vienna, 2023

OCA 5-10mg + BZF 400mg mostraron una Remisión Bioquímica en el 58% de los pacientes

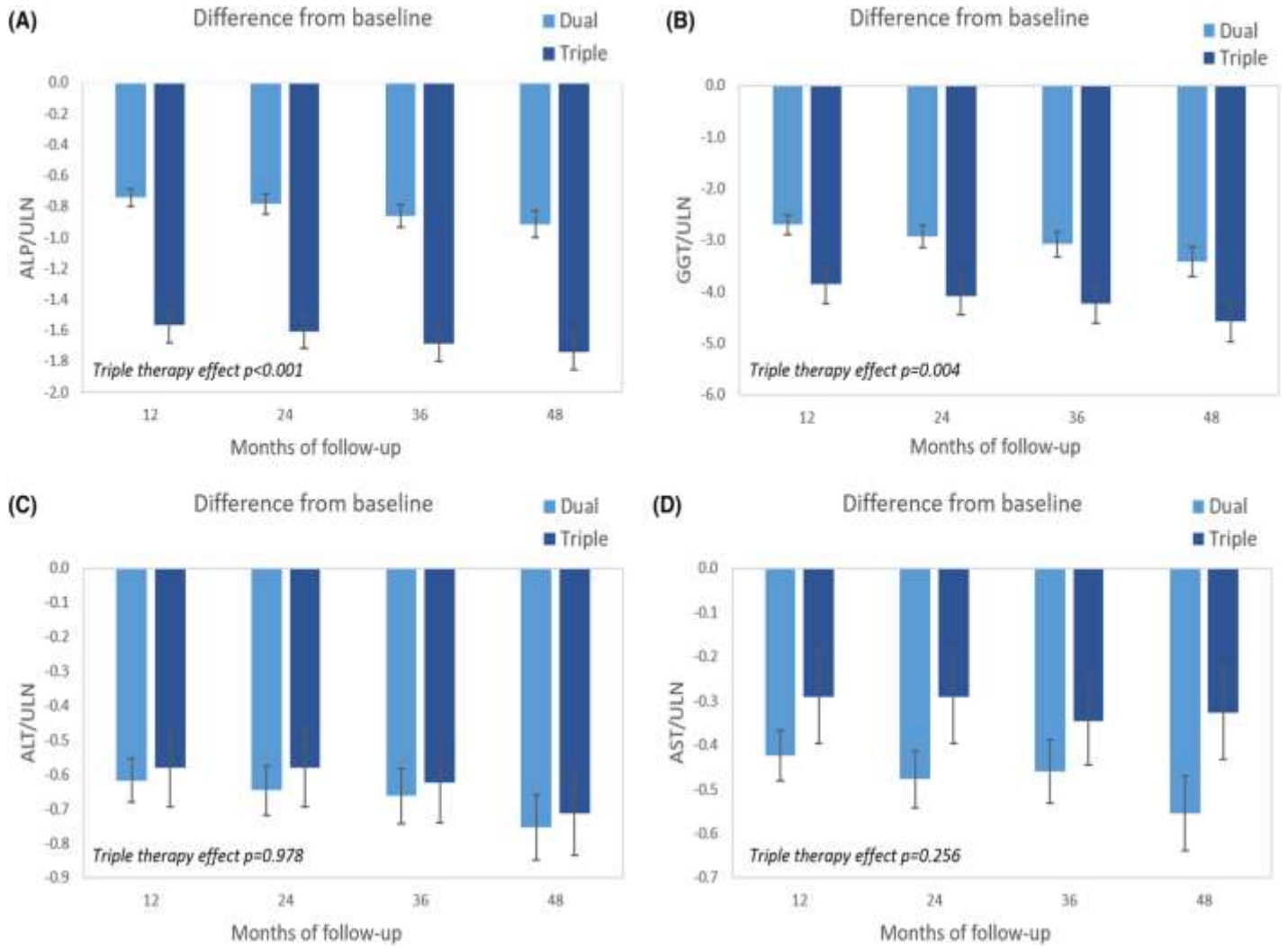


Hejda V et al EASL Vienna, 2023

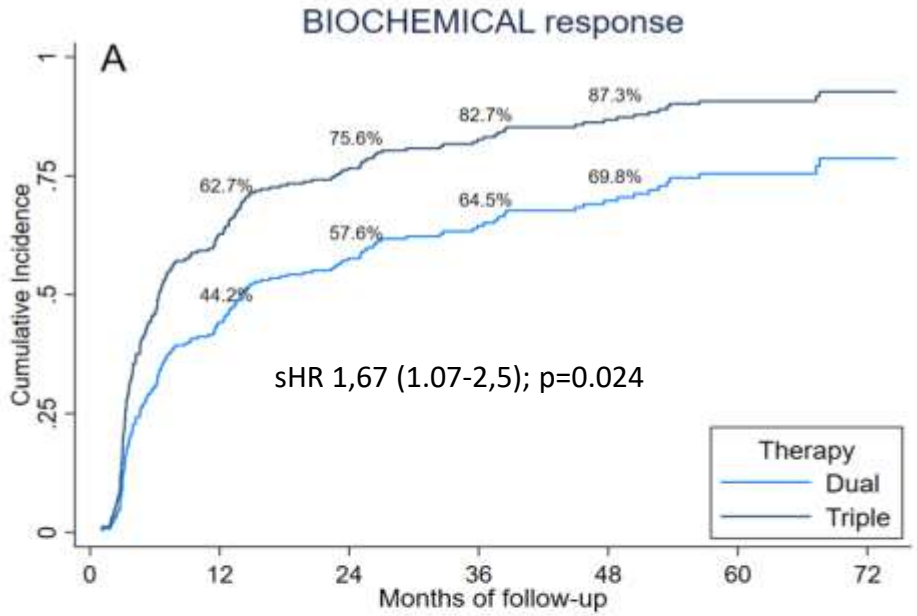


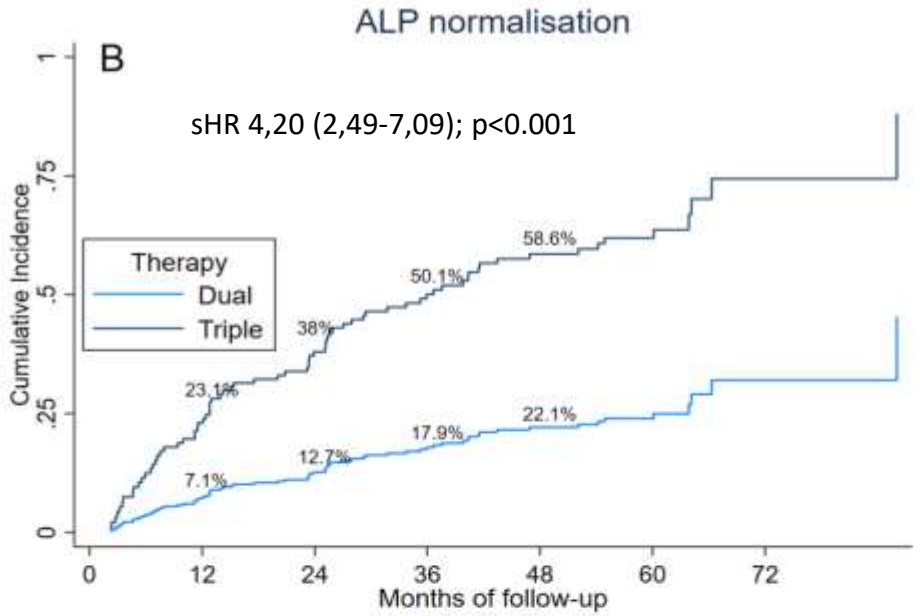
Aliment Pharmacol Ther, Volume: 53, Issue: 10, Pages: 1138-1146, First published: 25 March 2021, DOI: (10.1111/apt.16336)

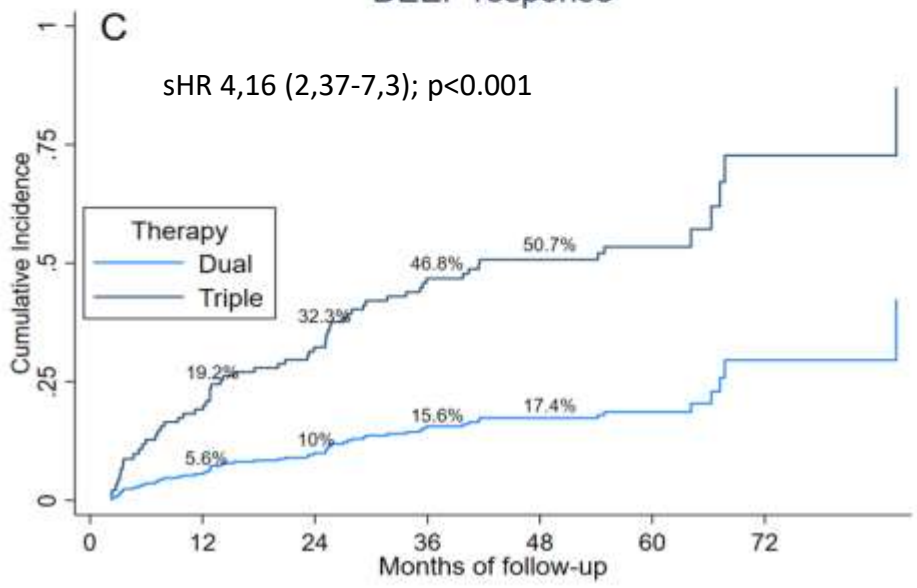
Longitudinal outcomes of obeticholic acid therapy in ursodiol-nonresponsive primary biliary cholangitis: Stratifying the impact of add-on fibrates in real-world practice

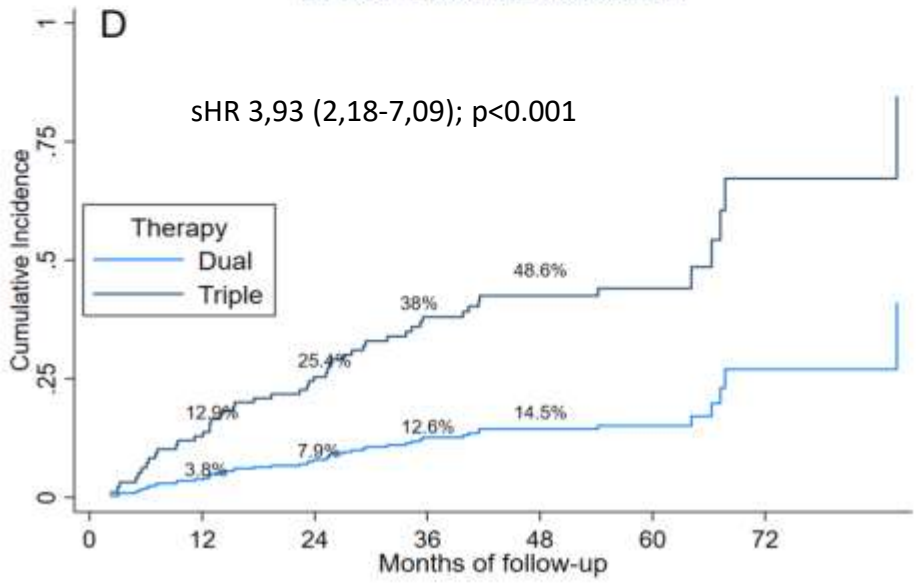


Aliment Pharmacol Ther, First published: 01 May 2024, DOI: (10.1111/apt.18004)









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Síndrome de solapamiento CBP-HAI

Criterios diagnosticos de Paris, 2 de 3:

1. ALT >5x LSN
2. IgG al menos x 2 LSN y/o Ac ML +.
3. BH con hepatitis de la interfase moderada o severa[1]

Chazouillères O et al. Primary biliary cirrhosis-autoimmune hepatitis overlap syndrome: clinical features and response to therapy. Hepatology. 1998;28:296-301.

Caso Clínico.

Mujer de 38 años sin AP de interés, 2 embarazos normales. No bebe alcohol, ni toma fármacos. Derivada por alteración de la bioquímica hepática y HBsAg y Ac VHC negativos con ANA +

ALT	110 U/ml(≤30)
FA	240 (≤104 U/mL)
ANA	+ 1:160 (Ac-gp210)
AMA	Negativos
IgG	2000 mg/dl (≤1600 mg/dL)
A_1AT	Normal
Ceruloplasmina y Ferritina	Normales
BH	11 espacios porta. Infiltrado linfoplasmocitario portal y lobulillar. Sin lesión ductal florida.

Component	Result	Score
Biochemical category		
AST or ALT above ULN	>2	+3
	1.5-2	+2
	1-1.5	+1
	<1	0
ALP above ULN	>1	+2
	0.75-1	+1
	<0.75	0
Serum globulin above ULN	>1.5	+2
	1-1.5	+1
	<1	0
Immunologic category		
ANA, ASMA, or LKM1	>1:80	+3
	1:80	+2
	1:40	+1
	<1:40	0
or		
Anti-SLA, pANCA	Positive	+2
AMA	Positive	+3
Histologic category		
	Interface hepatitis	+3
	Lymphoplasmacytic	+1
	Hepatic rosettes	+1
	Biliary damage	
	Granulomas	+3
	Florid ductal lesion	+1
	Ductular proliferation	+1
	Bile duct loss	+1
Others category		
Viral markers	Positive	–3
	Negative	+3
Drugs	Yes	–4
	No	+1
Alcohol	<25 g/day	+2
	>60 g/day	–2
Interpretation of scores	Definitive	≥21
	Probable	19 or 20
	Rejected	<19

+3

+1

+1

+3

+3

+1

Proposed Scoring Classification for Overlap Syndrome (Zhang W, et al Hepatol Commun. 2018 20;2:245-253.

+3

+1

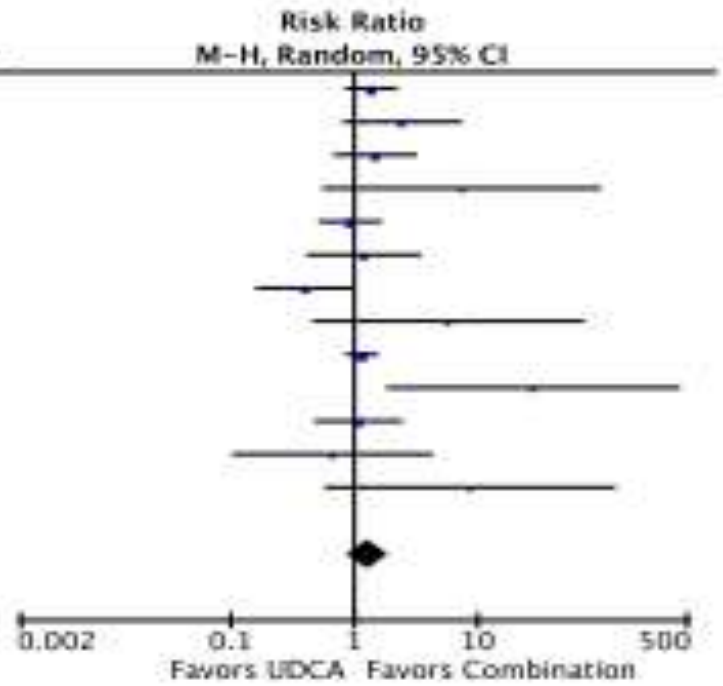
+2

Total= 18

Study or Subgroup	Combination Events	Total	UDCA Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Gunsar et al.	4	4	8	12	14.2%	1.38 [0.84, 2.25]	2002
Chazouilleres et al.	4	6	3	11	7.4%	2.44 [0.80, 7.48]	2006
Saito et al.	6	6	2	3	10.6%	1.49 [0.68, 3.26]	2006
Wu et al.	6	6	0	3	2.1%	7.43 [0.55, 100.11]	2006
Poupon et al.	8	10	2	2	12.8%	0.93 [0.51, 1.69]	2006
Heurgue et al.	3	5	3	6	7.8%	1.20 [0.41, 3.51]	2007
Ozaslan et al.	3	9	3	3	9.1%	0.40 [0.16, 1.01]	2010
Yokokawa et al.	13	13	0	2	2.1%	5.79 [0.46, 72.80]	2010
Ozaslan et al.	49	67	19	30	16.4%	1.15 [0.85, 1.57]	2014
Liu C et al.	12	14	0	16	1.9%	28.33 [1.83, 438.84]	2014
Efe et al.	15	18	1	1	10.1%	1.09 [0.48, 2.49]	2014
Park et al,.	1	3	2	4	3.6%	0.67 [0.10, 4.35]	2015
Yang et al.	13	27	0	8	1.9%	8.68 [0.57, 131.87]	2016
Total (95% CI)		**188**		**101**	**100.0%**	**1.32 [0.89, 1.95]**	
Total events	137		43				

Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 27.71$, df = 12 (P = 0.006); $I^2 = 57\%$

Test for overall effect: Z = 1.36 (P = 0.17)



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Chazouilleres et al.	4	6	3	11	6.1%	2.44 [0.80, 7.48]	2006
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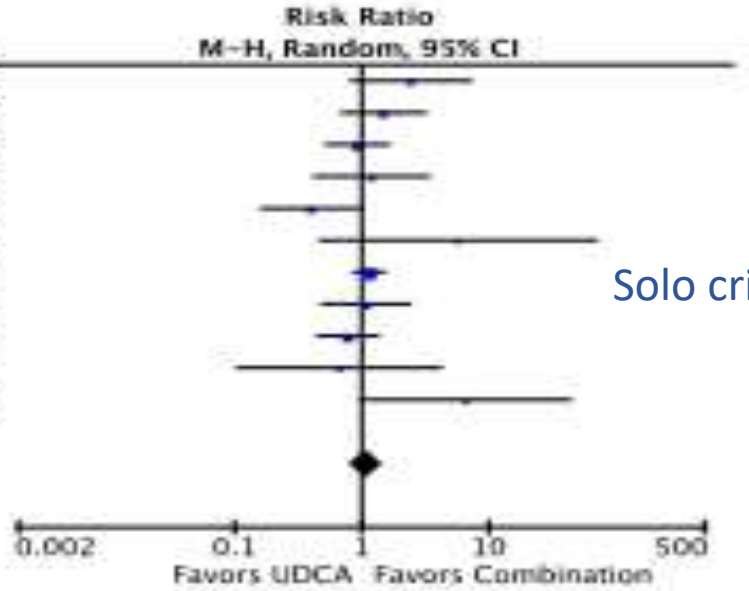
Efe et al.	15	18	1	1	9.6%	1.09 [0.48, 2.49]	2014
Levy et al.	10	21	11	18	14.8%	0.78 [0.44, 1.39]	2014
Park et al,.	1	3	2	4	2.5%	0.67 [0.10, 4.35]	2015
Fan et al.	6	10	1	11	2.3%	6.60 [0.95, 45.75]	2018
Total (95% CI)		**168**		**91**	**100.0%**	**1.09 [0.80, 1.48]**	
Total events	118		47				

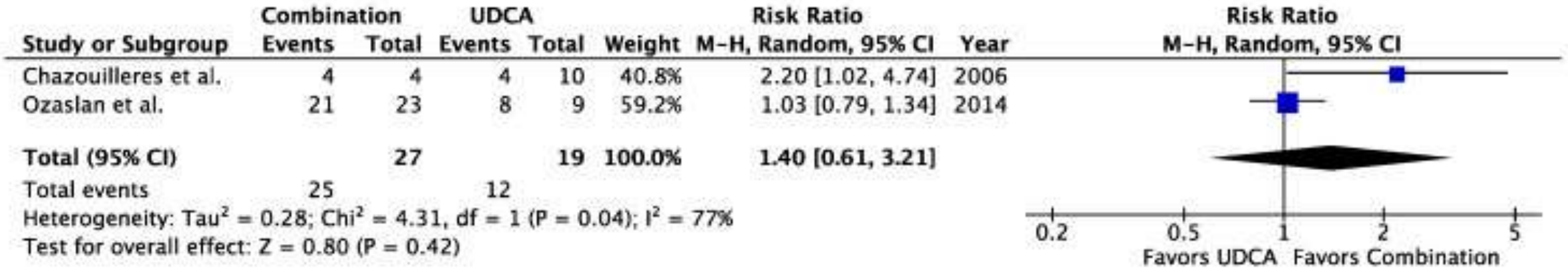
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 15.08$, df = 10 (P = 0.13); $I^2 = 34\%$

Test for overall effect: Z = 0.54 (P = 0.59)

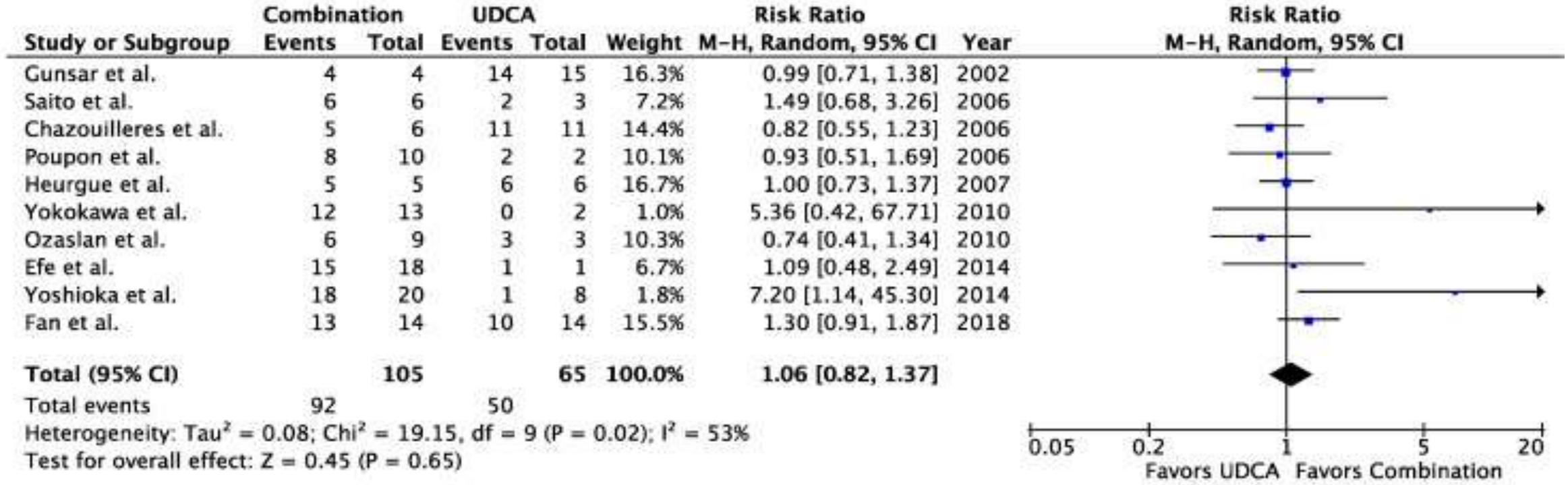


Solo criterios de Paris

Freedman BL et al. J Clin Med. 2020 May 13;9(5):1449. doi: 10.3390/jcm9051449. PMID: 32414025; PMCID: PMC7291241



Non-progression of liver fibrosis in AIH-PBC. Combination therapy vs. UDCA alone, Combination = UDCA + corticosteroids ± AZA



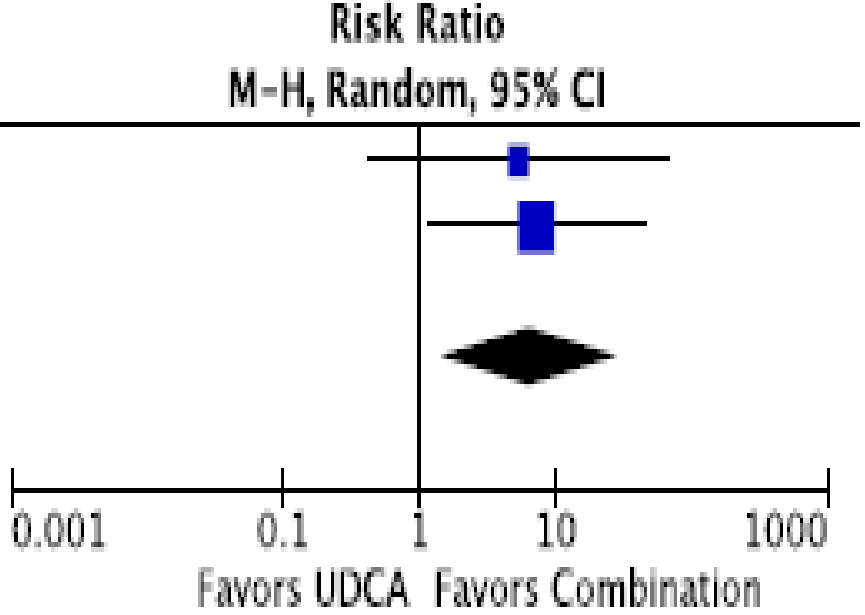
Transplant-free survival in AIH-PBC patients treated with combination therapy vs. UDCA alone. UDCA = ursodeoxycholic acid, Combination = UDCA + [corticosteroids and/or antimetabolites]

Freedman BL et al. J Clin Med. 2020 May 13;9(5):1449. doi: 10.3390/jcm9051449. PMID: 32414025; PMCID: PMC7291241

Study or Subgroup	Combination Events	Total	UDCA Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Yokokawa et al.	12	13	0	2	34.5%	5.36 [0.42, 67.71]	2010
Yoshioka et al.	18	20	1	8	65.5%	7.20 [1.14, 45.30]	2014
Total (95% CI)		**33**		**10**	**100.0%**	**6.50 [1.47, 28.83]**	
Total events	30		1				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.03$, $df = 1$ ($P = 0.85$); $I^2 = 0\%$

Test for overall effect: $Z = 2.46$ ($P = 0.01$)



SLT en CBP-HAI tratados con combinación frente a AUDC, incluyendo solo estudios con mediana de seguimiento > 90 meses. Combinacion: Corticosteroides ± Azatioprina

Freedman BL et al. J Clin Med. 2020 May 13;9(5):1449. doi: 10.3390/jcm9051449. PMID: 32414025; PMCID: PMC7291241

Guía AASLD 2018[2]

Clearly, there is a need for better long-term analysis regarding the natural history of PBC with features of AIH in order to determine whether PBC/AIH overlap is a distinct clinical entity.

In addition, the clinical benefit and harm of adding immunosuppressive medications to PBC patients with AIH features require further study.

Lindor K; Bowlus CL; Boyer J; Levy C; Mayo M. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. Hepatology 2018; 69: 394-419.

Conclusiones.

1. La terapia de segunda línea actual en CBP mejora los marcadores indirectos de supervivencia.
2. La baja respuesta en marcadores más restrictivos refuerza la necesidad de nuevos tratamientos, estudios sobre combinaciones incluyendo triple terapia, y deberá individualizarse, considerando la edad, la fibrosis y la intensidad de la colestasis.
3. En el síndrome de solapamiento CBP-HAI, no hay diferencias claras entre los regímenes de tratamiento (AUDC vs AUDC+ Corticoides ± inmunosupresores, aunque se necesita evidencia de mayor calidad.
4. Mientras tanto, se deben seguir las recomendaciones de las sociedades científicas y opiniones de expertos.