

Seladelpar Efficacy and Safety at 3 Months in Patients With Primary Biliary Cholangitis: ENHANCE, a Phase 3, Randomized, Placebo-controlled Study

Short title: Seladelpar treatment for primary biliary cholangitis

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SUPPLEMENTAL INFORMATION

Supplemental Tables

Supplemental Table S1. PBC response criteria

	Seladelpar		
	Placebo	5mg	10mg
Rotterdam criteria^a			
Month 1, n/N (%)	2/78 (3)	3/80 (4)	6/79 (8)
95% CI	0.3, 9.0	0.8, 10.6	2.8, 15.8
Month 3, n/N (%)	0/56 (0)	1/56 (2)	1/55 (2)
95% CI	0, 6.4	0, 9.6	0, 9.7
Month 6, n/N (%)	0/23 (0)	2/26 (8)	1/20 (5)
95% CI	0, 14.8	0.9, 25.1	0.1, 24.9
Barcelona criteria^b			
Month 1, n/N (%)	0/78 (0)	12/80 (15)	39/79 (49)
95% CI	0, 4.6	8.0, 24.7	37.9, 60.9
Month 3, n/N (%)	0/56 (0)	21/56 (38)	36/55 (66)
95% CI	0, 6.4	24.9, 51.5	51.4, 77.8
Month 6, n/N (%)	1/23 (4)	10/26 (39)	14/20 (70)
95% CI	0.1, 21.9	20.2, 59.4	45.7, 88.1
Paris I & II criteria			
Paris I criteria^c			
Month 1, n/N (%)	52/78 (67)	60/80 (75)	67/79 (85)
95% CI	55.1, 76.9	64.1, 84.0	75.0, 91.9

	Seladelpar		
	Placebo	5mg	10mg
Month 3, n/N (%)	36/56 (64)	45/56 (80)	48/55 (87)
95% CI	50.4, 76.6	67.6, 89.8	75.5, 94.7
Month 6, n/N (%)	17/23 (74)	19/26 (73)	17/20 (85)
95% CI	51.6, 89.8	52.2, 88.4	62.1, 96.8
Paris II criteria^d			
Month 1, n/N (%)	8/78 (10)	31/80 (39)	40/79 (51)
95% CI	4.5, 19.2	28.1, 50.3	39.1, 62.1
Month 3, n/N (%)	5/56 (9)	28/56 (50)	32/55 (58)
95% CI	3.0, 19.6	36.3, 63.7	44.1, 71.3
Month 6, n/N (%)	3/23 (13)	14/26 (54)	12/20 (60)
95% CI	2.8, 33.6	33.4, 73.4	36.1, 80.9
Toronto I criteria^e			
Month 1, n/N (%)	11/78 (14)	43/80 (54)	54/79 (68)
95% CI	7.3, 23.8	42.2, 65.0	56.9, 78.4
Month 3, n/N (%)	10/56 (18)	36/56 (64)	45/55 (82)
95% CI	8.9, 30.4	50.4, 76.6	69.1, 90.9
Month 6, n/N (%)	8/23 (35)	16/26 (62)	15/20 (75)
95% CI	16.4, 57.3	40.6, 79.8	50.9, 91.3
Toronto II criteria^f			
Month 1, n/N (%)	16/78 (21)	47/80 (59)	59/79 (75)
95% CI	12.2, 31.2	47.2, 69.6	63.6, 83.8

	Seladelpar		
	Placebo	5mg	10mg
Month 3, n/N (%)	14/56 (25)	40/56 (71)	45/55 (82)
95% CI	14.4, 38.4	57.8, 82.7	69.1, 90.9
Month 6, n/N (%)	9/23 (39)	17/26 (65)	16/20 (80)
95% CI	19.7, 61.5	44.3, 82.8	56.3, 94.3

Two-sided 95% exact (Clopper-Pearson) CIs are provided.

^aNormalization of abnormal total bilirubin and/or albumin

^bALP $\leq 1 \times \text{ULN}$ or $>40\%$ decrease

^cALP $< 3 \times \text{ULN}$, AST $< 2 \times \text{ULN}$, and total bilirubin $\leq 1 \text{mg/dL}$

^dALP $< 1.5 \times \text{ULN}$, AST $< 1.5 \times \text{ULN}$, and total bilirubin $\leq 1 \text{mg/dL}$

^eALP $\leq 1.67 \times \text{ULN}$

^fALP $\leq 1.76 \times \text{ULN}$

Abbreviations: ALP, alkaline phosphatase; AST, aspartate aminotransferase; CI, confidence interval; N, number of patients in the treatment group; n, number of patients in the category; ULN, upper limit of normal.

Supplemental Table S2. Proportion of patients who achieved individual composite endpoint components or ALP <1.5 × ULN through Month 6

	Placebo	Seladelpar	
		5mg	10mg
Month 1, N	78	80	79
ALP <1.67×ULN, n (%)	11 (14)	43 (54)	54 (68)
≥15% decrease in ALP, n (%)	12 (15)	74 (93)	76 (96)
Total bilirubin ≤ULN, n (%)	71 (91)	68 (85)	75 (95)
ALP <1.5×ULN, n (%)	8 (10)	37 (46)	47 (60)
Month 3, N	56	56	55
ALP <1.67×ULN, n (%)	10 (18)	36 (64)	45 (82)
≥15% decrease in ALP, n (%)	13 (23)	53 (95)	52 (95)
Total bilirubin ≤ULN, n (%)	51 (91)	48 (86)	51 (93)
ALP <1.5×ULN, n (%)	5 (9)	33 (59)	41 (75)
Month 6, N	23	26	20
ALP <1.67×ULN, n (%)	8 (35)	16 (62)	15 (75)
≥15% decrease in ALP, n (%)	7 (30)	22 (85)	17 (85)
Total bilirubin ≤ULN, n (%)	20 (87)	23 (89)	17 (85)
ALP <1.5×ULN, n (%)	3 (13)	15 (58)	13 (65)

Patients who discontinued treatment prior to time point due to reasons other than study termination and who did not have evaluable data at time point were considered nonresponders.

Abbreviations: ALP, alkaline phosphatase; N, number of patients in the treatment group; n, number of patients in the category; ULN, upper limit of normal.

Supplemental Table S3. Proportions of patients with pruritus NRS scores ≥ 4 or < 4 at baseline and post baseline

Post Baseline Pruritus NRS Score		< 4			≥ 4		
Baseline Pruritus NRS Score	Time point	Placebo	5mg	10mg	Placebo	5mg	10mg
≥ 4	Month 1	19.2 (5/26)	23.1 (6/26)	48.1 (13/27)	80.8 (21/26)	76.9 (20/26)	51.9 (14/27)
	Month 3	27.8 (5/18)	47.1 (8/17)	61.1 (11/18)	72.2 (13/18)	52.9 (9/17)	38.9 (7/18)
	Month 6	66.7 (4/6)	55.6 (5/9)	100 (7/7)	33.3 (2/6)	44.4 (4/9)	0 (0/7)
< 4	Month 1	93.3 (56/60)	98.4 (60/61)	93.5 (58/62)	6.7 (4/60)	1.6 (1/61)	6.5 (4/62)
	Month 3	97.5 (39/40)	97.6 (40/41)	92.7 (38/41)	2.5 (1/40)	2.4 (1/41)	7.3 (3/41)
	Month 6	95.2 (20/21)	94.7 (18/19)	95.2 (20/21)	4.8 (1/21)	5.3 (1/19)	4.8 (1/21)

Data are % (n/N). Shaded cells indicate no shift from baseline; unshaded cells indicate a shift from baseline.

Abbreviations: N, number of patients in the treatment group; n, number of patients in the category; NRS, numerical rating scale.

Supplemental Table S4. Proportions of patients with GGT levels $\geq 3.2 \times \text{ULN}$ or $< 3.2 \times \text{ULN}$ at baseline and post baseline

Post Baseline GGT Level		$< 3.2 \times \text{ULN}$			$\geq 3.2 \times \text{ULN}$		
Baseline GGT Level	Time point	Placebo	5mg	10mg	Placebo	5mg	10mg
$\geq 3.2 \times \text{ULN}$	Month 1	13.2 (7/53)	31.5 (17/54)	36.4 (20/55)	86.8 (46/53)	68.5 (37/54)	63.6 (35/55)
	Month 3	17.1 (6/35)	43.6 (17/39)	40.5 (15/37)	82.9 (29/35)	56.4 (22/39)	59.5 (22/37)
$< 3.2 \times \text{ULN}$	Month 1	100 (25/25)	100 (24/24)	100 (23/23)	0 (0/25)	0 (0/24)	0 (0/23)
	Month 3	95.2 (20/21)	100 (15/15)	100 (16/16)	4.8 (1/21)	0 (0/15)	0 (0/16)

Data are % (n/N). Shaded cells indicate no shift from baseline; unshaded cells indicate a shift from baseline.

Abbreviations: GGT, gamma glutamyl transferase; N, number of patients in the treatment group; n, number of patients in the category; ULN, upper limit of normal.

Supplemental Table S5. Mean absolute values and LS mean relative (percent) change from baseline in 7 α -hydroxy-4-cholesten-3-one (C4) and immunoglobulin M (IgM) through Month 6

	Seladelpar		
	Placebo	5mg	10mg
C4			
Baseline, N	87	89	89
Mean (SD), ng/mL	27.3 (25.0)	23.1 (23.6)	20.7 (18.9)
Month 1, N	22	27	19
Mean (SD), ng/mL	24.1 (17.7)	19.6 (16.7)	16.1 (12.2)
LS mean (SE) change from baseline, %	21.3 (18.0)	6.9 (15.4)	-25.0 (18.1)
Month 3, N	55	52	51
Mean (SD), ng/mL	25.8 (20.5)	17.8 (15.6)	19.0 (27.2)
LS mean (SE) change from baseline, %	3.6 (9.6)	-17.5 (9.8)	-24.8 (10.0)
Month 6, N	0	1	1
Mean (SD), ng/mL	--	10.2 (--)	21.2 (--)
Mean (SD) change from baseline, %	--	4.6 (--)	-20.4 (--)

IgM

Baseline, N	87	88	89
Mean (SD), mg/dL	357.9 (264.2)	331.6 (201.8)	316.5 (181.3)
Month 1, N	78	77	78
Mean (SD), mg/dL	341.7 (227.0)	314.5 (189.6)	290.7 (168.1)
LS mean (SE) change from baseline, %	-2.6 (1.4)	-5.7 (1.4)	-7.3 (1.4)
Month 3, N	55	53	53
Mean (SD), mg/dL	312.1 (221.7)	305.1 (196.5)	267.1 (151.2)
LS mean (SE) change from baseline, %	-5.7 (2.1)	-10.2 (2.1)	-12.4 (2.1)
Month 6, N	23	24	18
Mean (SD), mg/dL	314.7 (261.2)	301.4 (243.6)	301.1 (229.8)
LS mean (SE) change from baseline, %	-3.4 (4.8)	-8.7 (4.4)	-12.2 (4.6)

Abbreviations: C4, 7 α -hydroxy-4-cholesten-3-one; IgM, immunoglobulin M; LS, least squares; N, number of patients in the treatment group; n, number of patients in the category; SD, standard deviation; SE, standard error.

Supplemental Table S6. Summary of treatment-emergent adverse events in patients with and without cirrhosis at baseline

	Patients With Cirrhosis			Patients Without Cirrhosis		
	Seladelpar			Seladelpar		
	Placebo (N=7)	5 mg (N=9)	10 mg (N=13)	Placebo (N=80)	5 mg (N=80)	10 mg (N=76)
TEAE, n (%)						
≥1 TEAE	7 (100)	5 (56)	8 (62)	57 (71)	51 (64)	50 (66)
≥1 serious TEAE	0	0	0	3 (4)	3 (4)	1 (1)
≥1 Grade ≥3 TEAE	0	0	0	6 (8)	3 (4)	5 (7)
≥1 TEAE leading to study drug discontinuation	1 (14)	0	1 (8)	1 (1)	2 (3)	1 (1)
≥1 treatment-related TEAE	4 (57)	2 (22)	1 (8)	12 (15)	23 (29)	14 (18)
≥1 serious treatment-related TEAE	0	0	0	0	0	0
TEAE						
≥1 treatment-related TEAE	0	0	0	0	0	0
Grade ≥3						
Deaths	0	0	0	0	0	0

	Patients With Cirrhosis			Patients Without Cirrhosis		
	Seladelpar			Seladelpar		
	Placebo (N=7)	5 mg (N=9)	10 mg (N=13)	Placebo (N=80)	5 mg (N=80)	10 mg (N=76)
TEAEs occurring in ≥ 2 patients with cirrhosis in any treatment cohort						
Arthralgia	1 (14)	1 (11)	2 (15)	4 (5)	4 (5)	2 (3)
Fatigue	2 (29)	0	2 (15)	6 (8)	2 (3)	2 (3)
Pruritus (qualitative)	1 (14)	0	2 (15)	10 (13)	3 (4)	8 (11)
Abdominal pain upper	0	1 (11)	2 (15)	3 (4)	7 (9)	4 (5)
Headache	0	0	3 (23)	1 (1)	5 (6)	4 (5)
Dry eye	0	1 (11)	2 (15)	2 (3)	2 (3)	1 (1)
Nausea	0	0	2 (15)	4 (5)	5 (6)	5 (7)
Vomiting	0	0	2 (15)	3 (4)	0	1 (1)
Musculoskeletal chest pain	0	0	2 (15)	0	0	1 (1)

All values are n (%) for patients in the safety population.

Adverse events were coded using MedDRA[®] version 21.0. MedDRA, Medical Dictionary for Regulatory Activities; n, number in category; N, number in treatment cohort; TEAE, treatment-emergent adverse event.

Supplemental Table S7. Mean absolute values and mean relative (percent) change from baseline in serum creatinine and creatine kinase through Month 6

	Seladelpar		
	Placebo	5mg	10mg
Serum creatinine			
Baseline, N	87	89	89
Mean (SD), mg/dL	0.71 (0.12)	0.70 (0.15)	0.72 (0.14)
Month 1, N	78	78	78
Mean (SD), mg/dL	0.73 (0.12)	0.73 (0.16)	0.76 (0.15)
Mean (SD) change from baseline, %	2.7 (7.9)	4.4 (10.5)	6.0 (10.8)
Month 3, N	56	54	53
Mean (SD), mg/dL	0.70 (0.11)	0.74 (0.16)	0.79 (0.16)
Mean (SD) change from baseline, %	4.0 (12.3)	5.0 (10.0)	7.2 (10.8)
Month 6, N	23	24	18
Mean (SD), mg/dL	0.68 (0.12)	0.81 (0.16)	0.84 (0.17)
Mean (SD) change from baseline, %	9.1 (10.3)	13.4 (13.3)	12.3 (10.2)

Creatine kinase

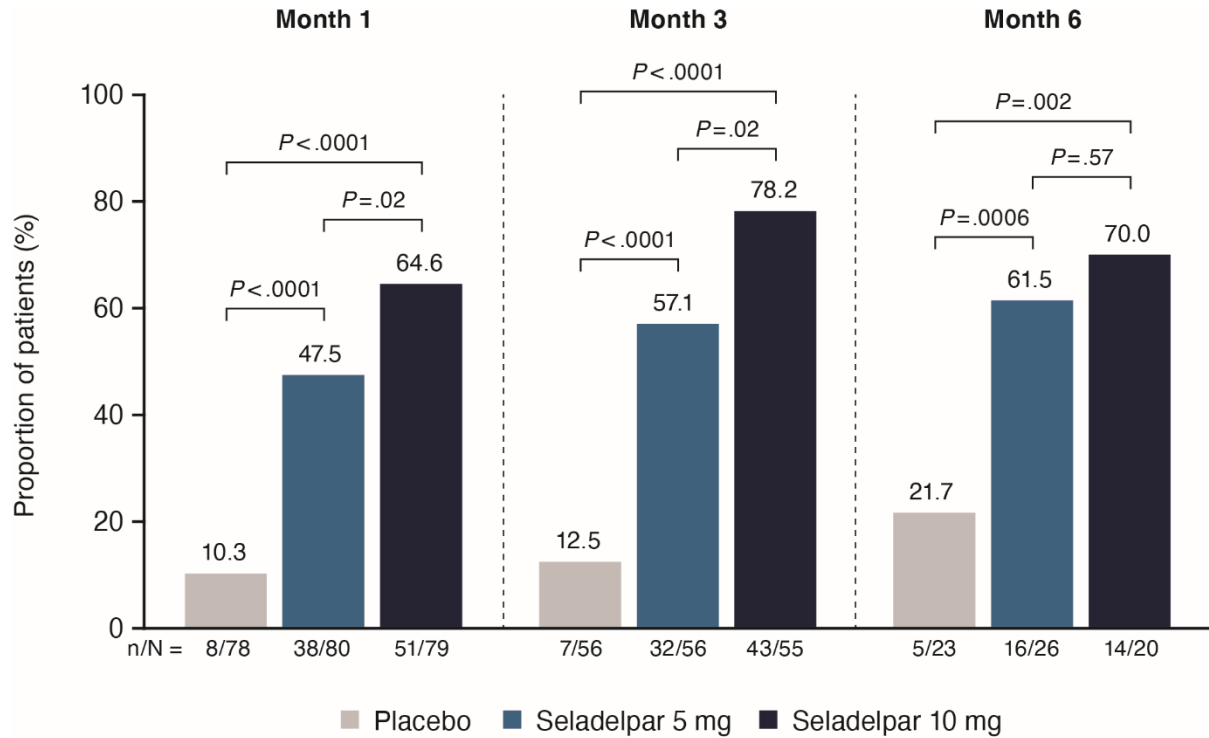
Baseline, N	87	89	89
Mean (SD), U/L	70.8 (34.9)	78.3 (41.1)	80.3 (42.8)
Month 1, N	78	78	78
Mean (SD), U/L	81.7 (53.5)	81.4 (54.8)	92.1 (78.4)
Mean (SD) change from baseline, %	14.2 (55.8)	4.8 (50.7)	20.5 (78.5)
Month 3, N	56	54	53
Mean (SD), U/L	69.8 (32.2)	94.0 (104.4)	84.8 (46.1)
Mean (SD) change from baseline, %	5.4 (29.9)	8.1 (50.4)	10.8 (36.7)
Month 6, N	23	24	18
Mean (SD), U/L	75.3 (39.2)	67.0 (31.6)	75.1 (33.9)
Mean (SD) change from baseline, %	2.0 (23.7)	-1.3 (21.3)	17.2 (59.2)

Serum creatinine ULN for females is 1.2mg/dL. Creatine kinase ULN is 210U/L.

Abbreviations: LS, least squares; N, number of patients in the treatment group; n, number of patients in the category; SD, standard deviation.

Supplemental Figures

Supplemental Figure S1. Composite endpoint through Month 6



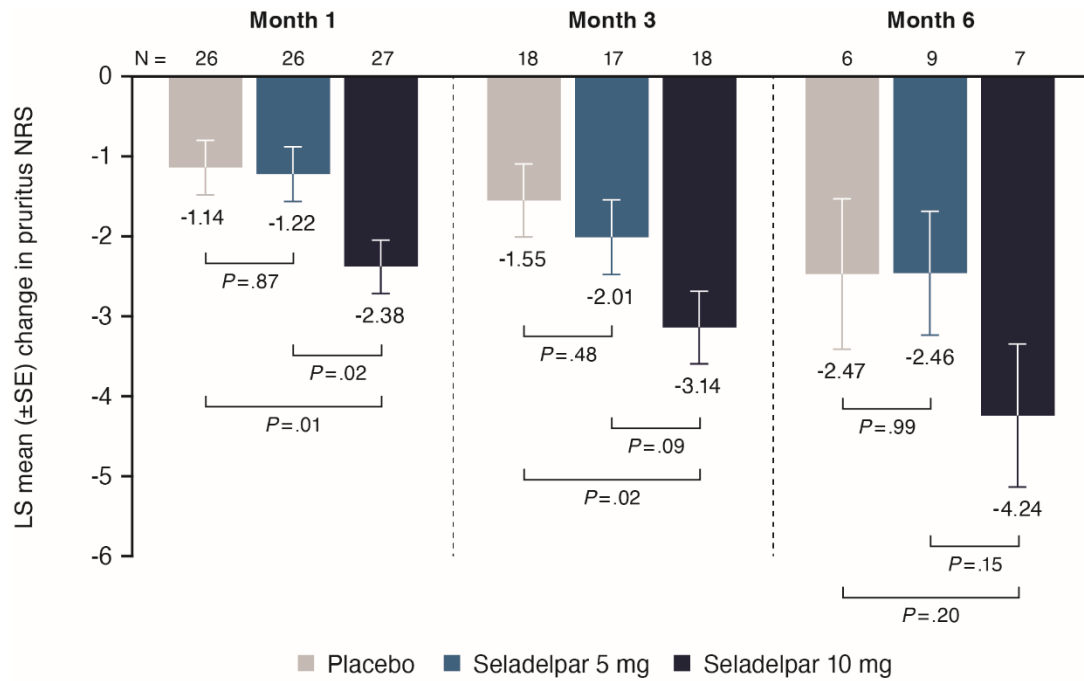
Composite endpoint was defined as ALP serum levels $<1.67 \times \text{ULN}$, $\geq 15\%$ decrease in ALP serum levels, and total bilirubin serum levels $\leq \text{ULN}$.

P-values are based on the Cochran-Mantel-Haenszel test adjusted for both randomization stratification variables.

Note: Patients who discontinued treatment prior to time point due to reasons other than study termination and who did not have evaluable data at time point were considered nonresponders.

Abbreviations: ALP, alkaline phosphatase; N, number of patients in the treatment group; n, number of patients in the category; ULN, upper limit of normal.

Supplemental Figure S2. NRS change from baseline through Month 6



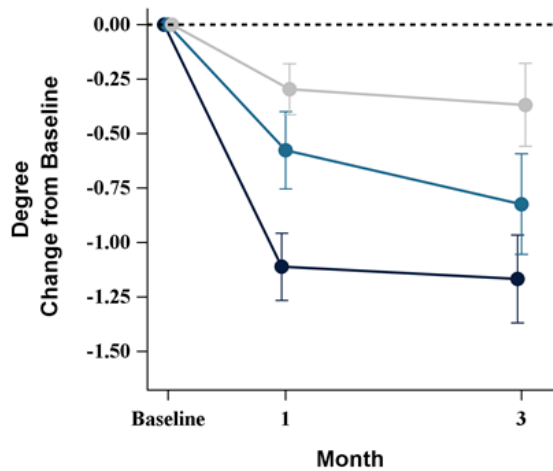
Population included only patients with pruritus NRS ≥ 4 at baseline.

Change from baseline was estimated by an ANCOVA model with treatment group and randomization ALP stratification factors as fixed effects and baseline pruritus score as a covariate.

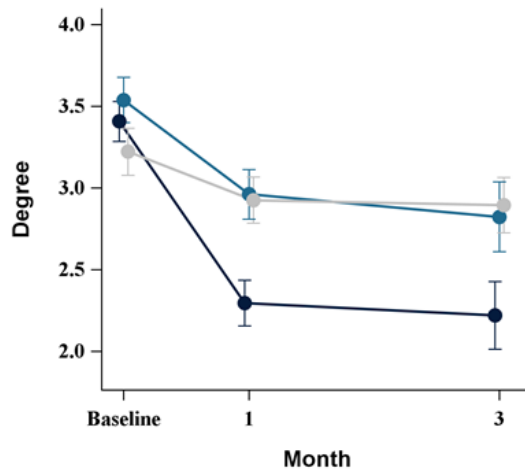
Abbreviations: ALP, alkaline phosphatase; ANCOVA, analysis of covariance; LS, least squares; N, number of patients in the treatment group; NRS, numerical rating scale; SE, standard error.

Supplemental Figure S3. 5-D itch scale. Mean change from baseline and absolute scores through Month 3 for the 5-D itch scale degree domain (A-B), duration domain (C-D), direction domain (E-F), sleep domain (G-H), highest disability domain (I-J), and total score (K-L) among patients with baseline pruritus NRS ≥ 4

A



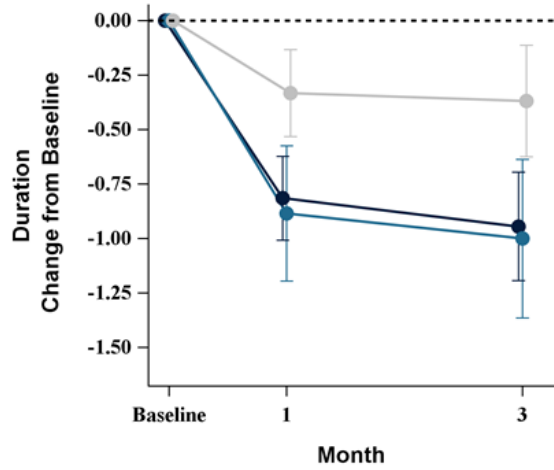
B



	Baseline	1	3	Baseline	1	3
N= Placebo	27	27	19	27	27	19
5 mg	26	26	17	26	26	17
10 mg	27	27	18	27	27	18

—●— Placebo —●— Seladelpar 5 mg —●— Seladelpar 10 mg

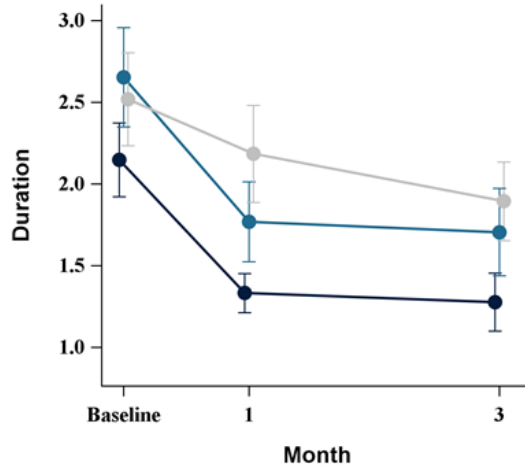
C



N= Placebo	27	27	19
5 mg	26	26	17
10 mg	27	27	18

—●— Placebo —●— Seladelpar 5 mg —●— Seladelpar 10 mg

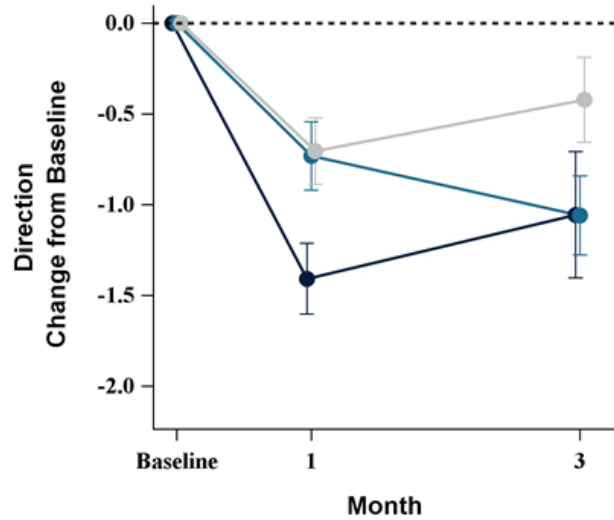
D



	27	27	19
	26	26	17
	27	27	18

—●— Placebo —●— Seladelpar 5 mg —●— Seladelpar 10 mg

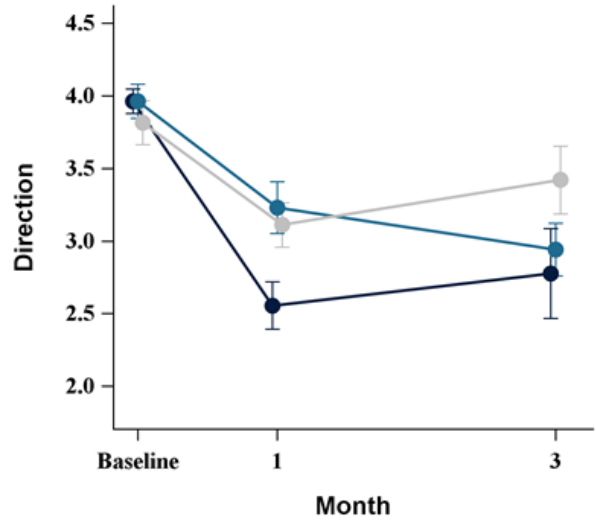
E



N= Placebo	27	27	19
5 mg	26	26	17
10 mg	27	27	18

—●— Placebo —●— Seladelpar 5 mg —●— Seladelpar 10 mg

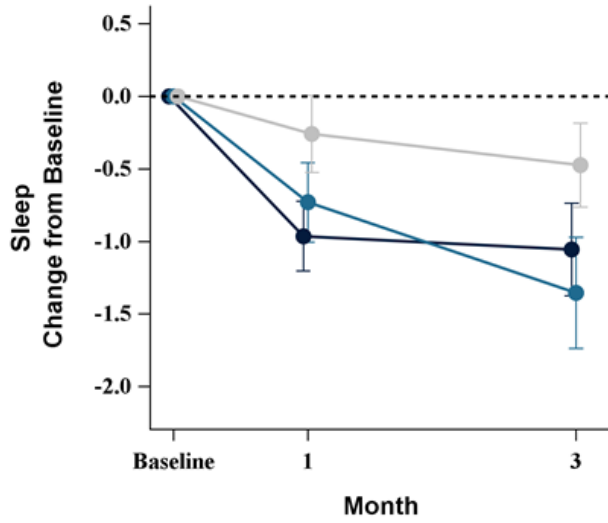
F



	27	27	19
	26	26	17
	27	27	18

—●— Placebo —●— Seladelpar 5 mg —●— Seladelpar 10 mg

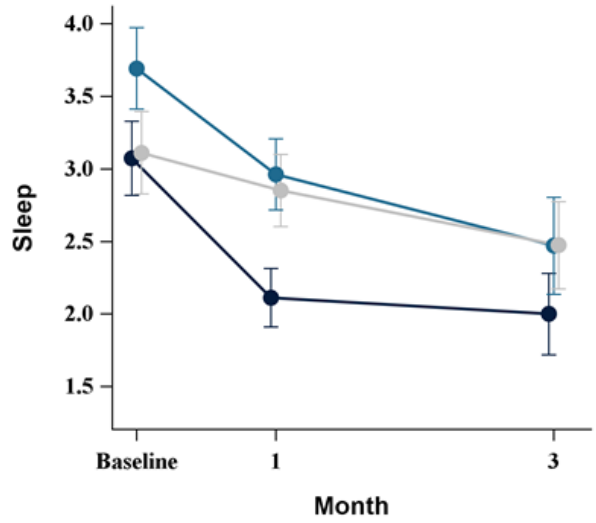
G



N= Placebo	27	27	19
5 mg	26	26	17
10 mg	27	27	18

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

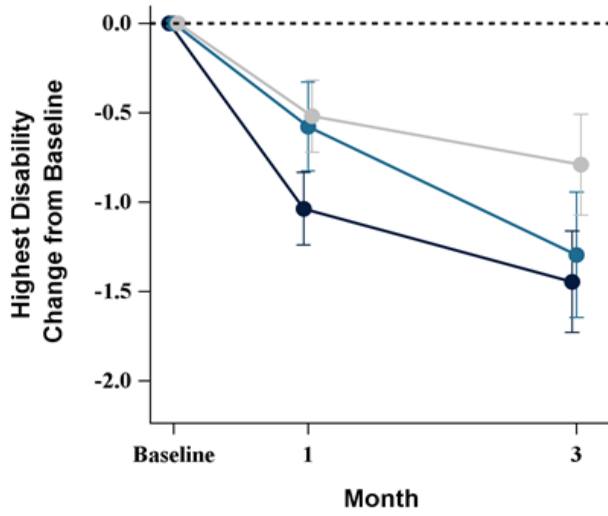
H



N= Placebo	27	27	19
5 mg	26	26	17
10 mg	27	27	18

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

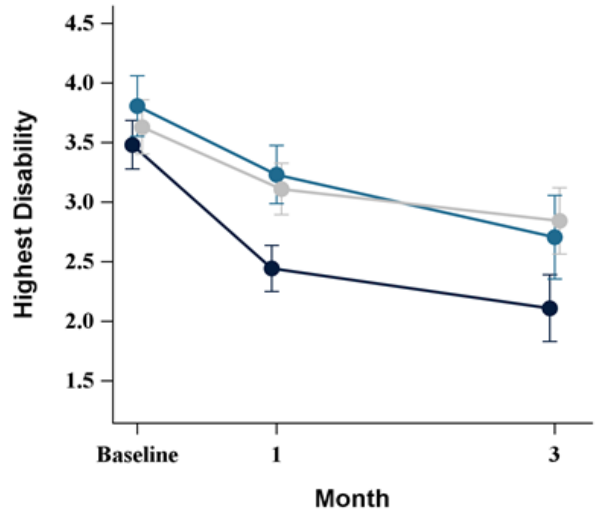
I



N= Placebo	27	27	19
5 mg	26	26	17
10 mg	27	27	18

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

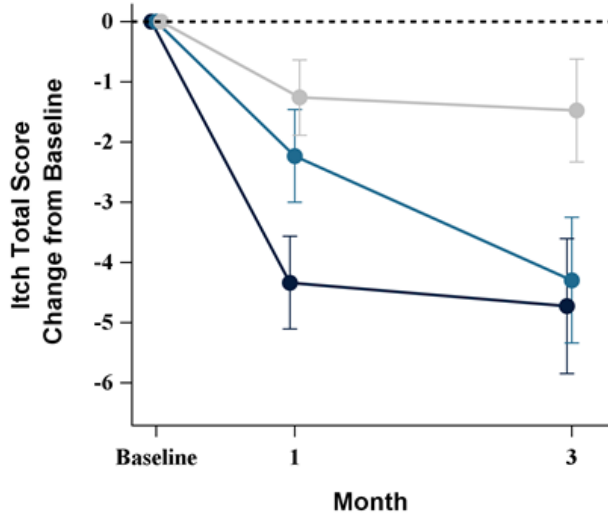
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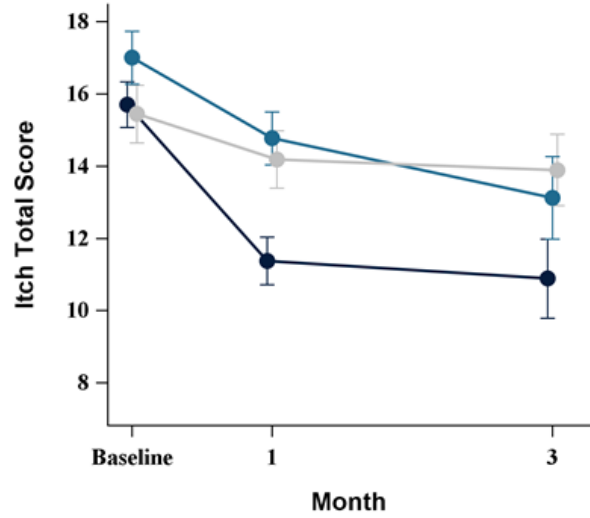
N= Placebo	27	27	19
5 mg	26	26	17
10 mg	27	27	18

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

K



L



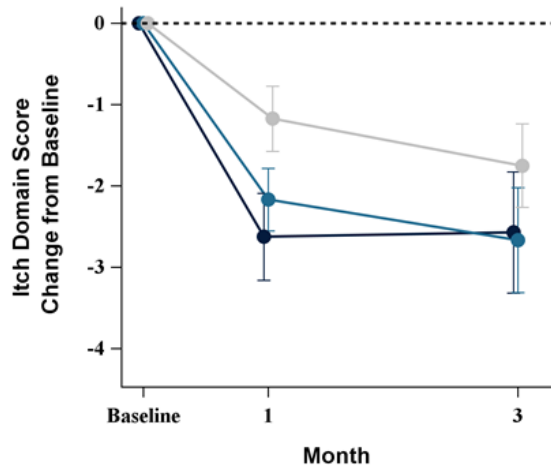
N=	Placebo	27	27	19	27	27	19
	5 mg	26	26	17	26	26	17
	10 mg	27	27	18	27	27	18

● Placebo
 ● Seladelpar 5 mg
 ● Seladelpar 10 mg

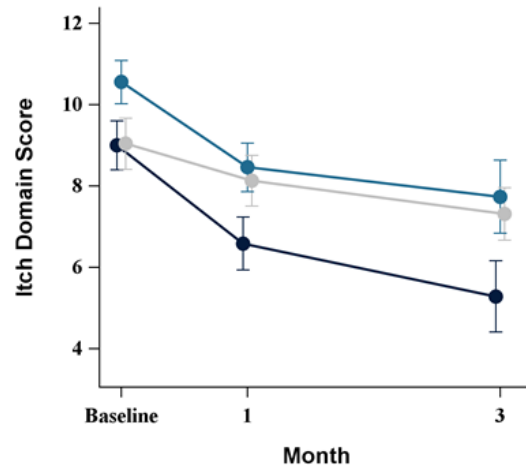
Abbreviations: BL, baseline; M, month; NRS, numerical rating scale; SE, standard error.

Supplemental Figure S4. PBC-40 questionnaire. Mean change from baseline and absolute scores through Month 3 in the PBC-40 questionnaire itch domain (A-B), cognitive domain (C-D), emotional domain (E-F), fatigue domain (G-H), symptoms domain (I-J), social domain (K-L), and total score (M-N) among patients with baseline pruritus NRS ≥ 4

A



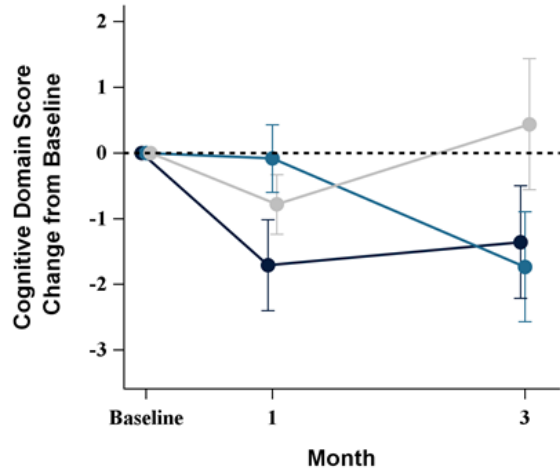
B



	Baseline	1	3	Baseline	1	3
N= Placebo	26	23	16	26	23	16
5 mg	27	24	15	27	24	15
10 mg	27	24	14	27	24	14

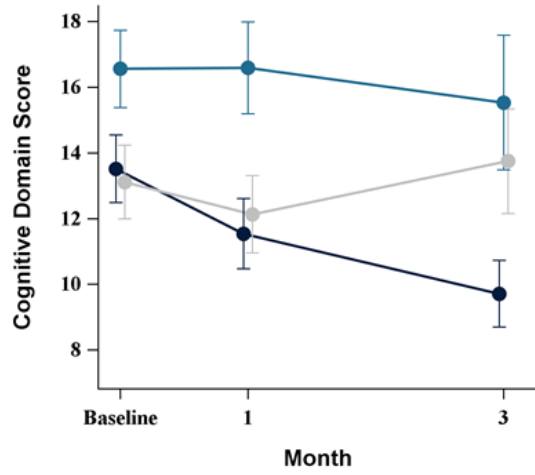
● Placebo
 ● Seladelpar 5 mg
 ● Seladelpar 10 mg

C



N=	Placebo	26	23	16
5 mg	27	24	15	
10 mg	27	24	14	

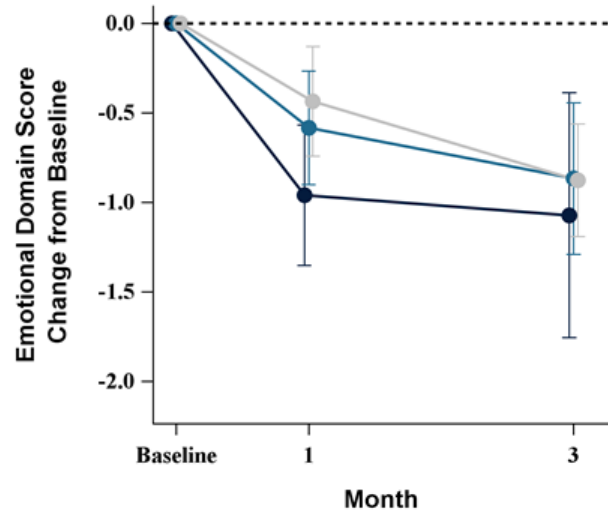
D



N=	Placebo	26	23	16
5 mg	27	24	15	
10 mg	27	24	14	

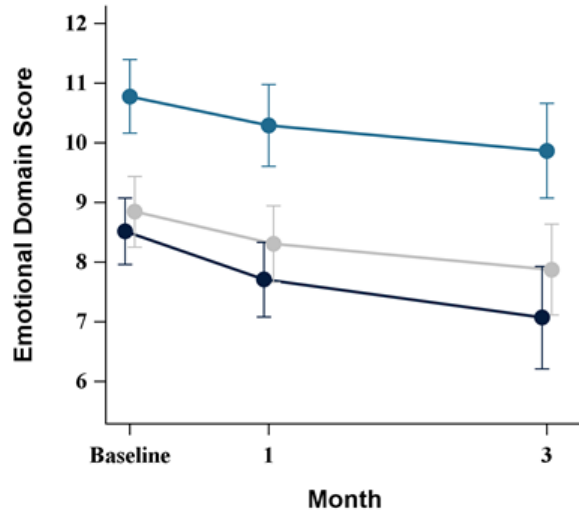
● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

E



N=	Placebo	26	23	16
5 mg	27	24	15	
10 mg	27	24	14	

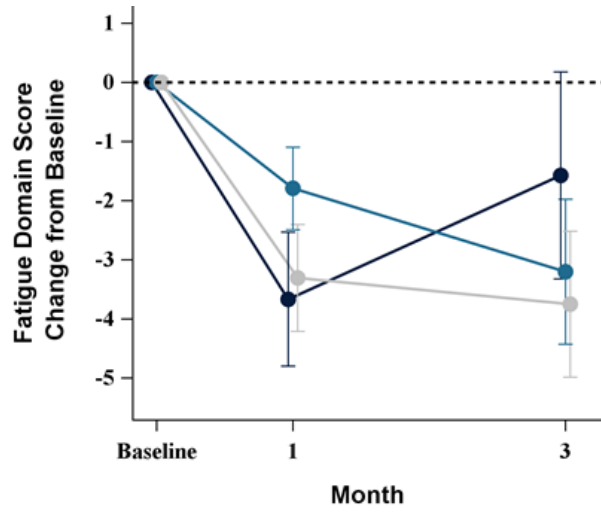
F



N=	Placebo	26	23	16
5 mg	27	24	15	
10 mg	27	24	14	

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

G

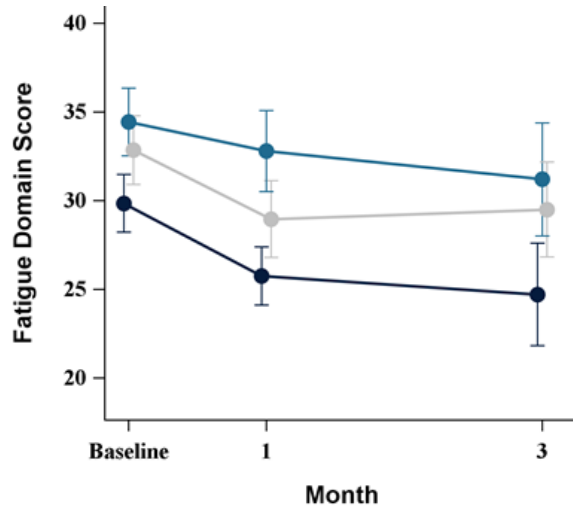


N= Placebo 26
5 mg 27
10 mg 27

23 24 24
16 15 14

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

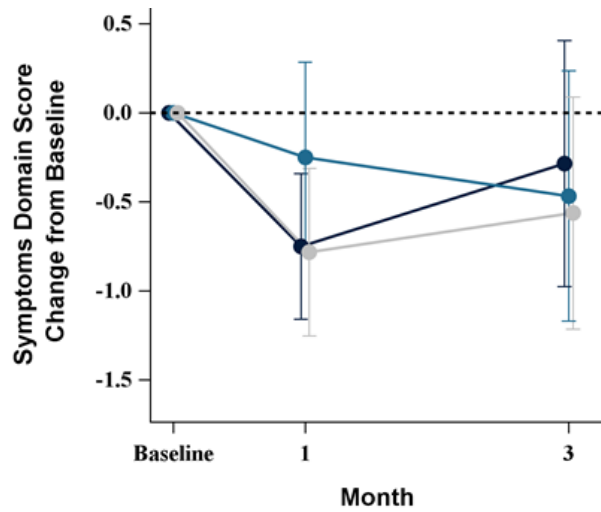
H



26 27 27
23 24 24
16 15 14

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

I

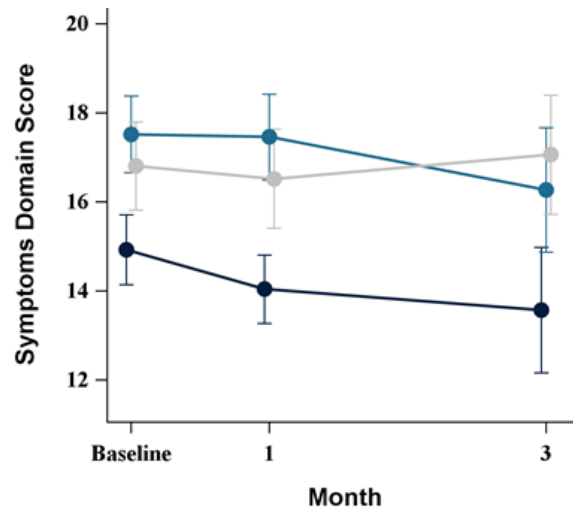


N= Placebo 26
5 mg 27
10 mg 27

23 24 24
16 15 14

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

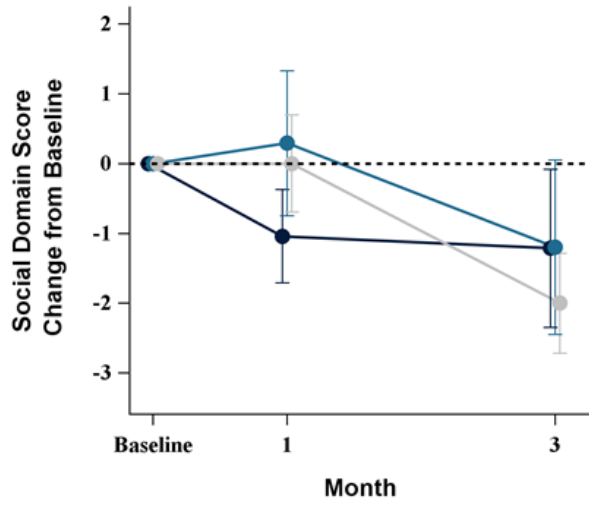
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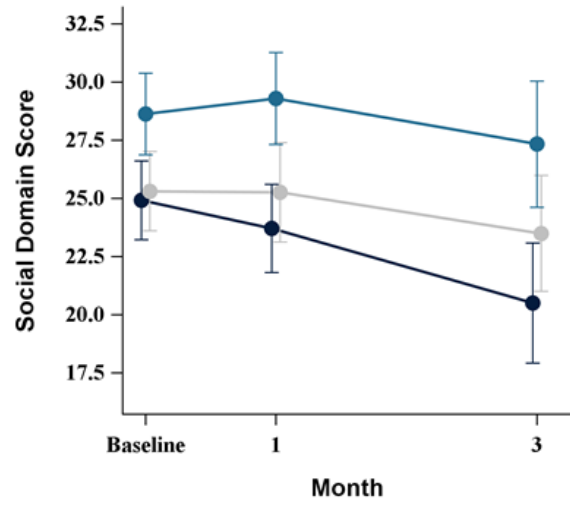
26 27 27
23 24 24
16 15 14

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

K



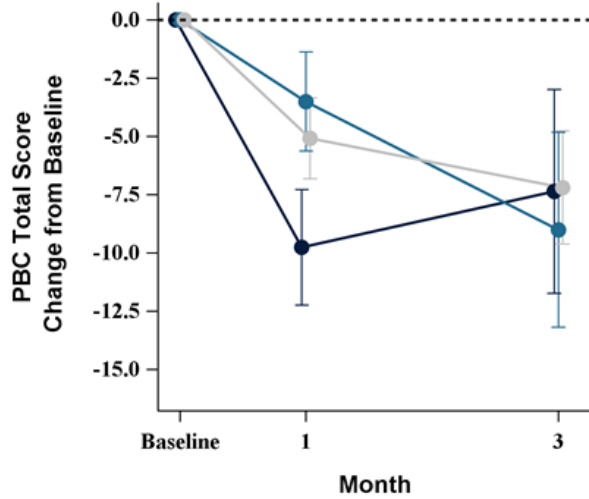
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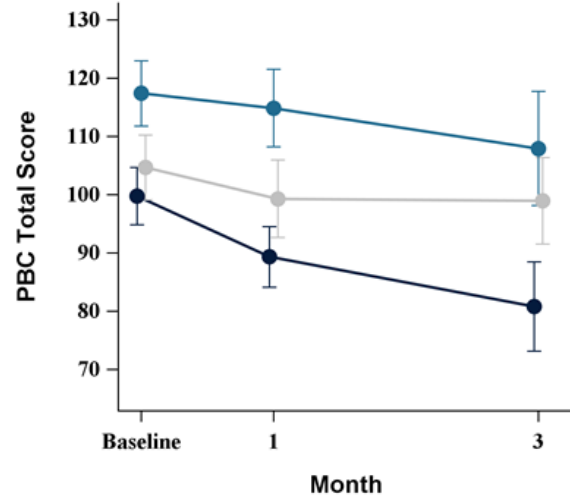
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N= Placebo	26	23	16	26	23	16	26	23	16
5 mg	27	24	15	27	24	15	27	24	15
10 mg	27	24	14	27	24	14	27	24	14

Legend: ● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

M



N

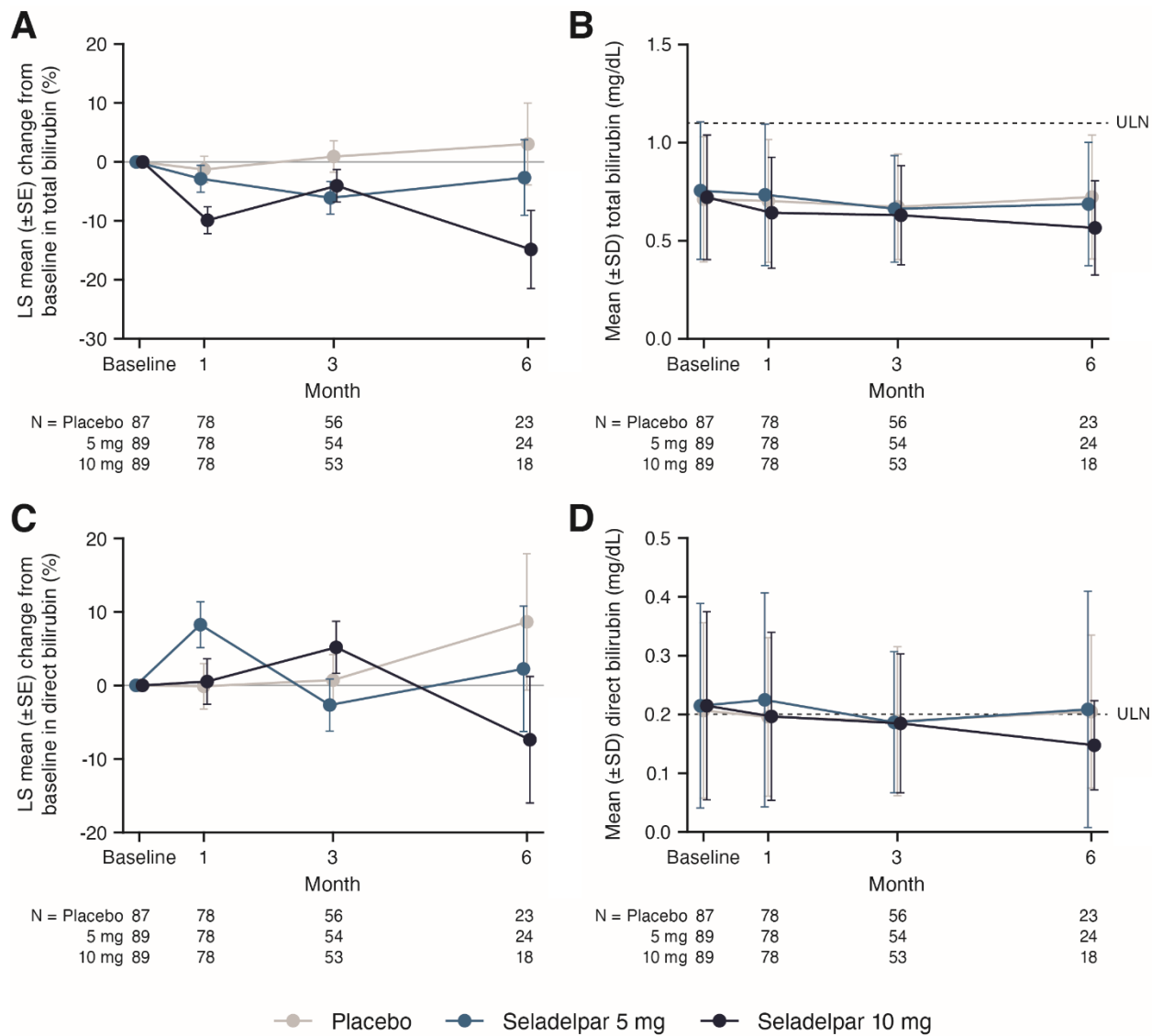


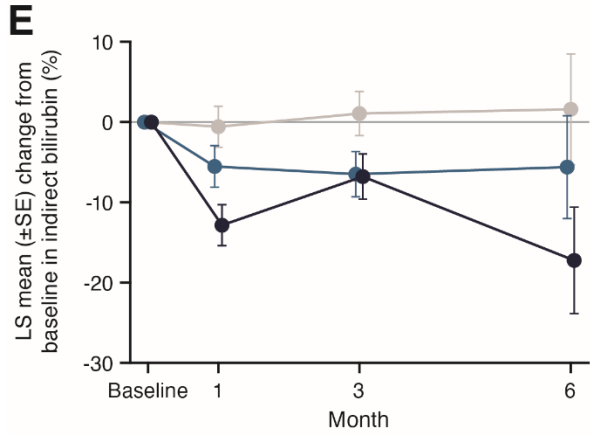
	Baseline	1	3	Baseline	1	3	Baseline	1	3
N= Placebo	26	23	16	26	23	16	26	23	16
5 mg	27	24	15	27	24	15	27	24	15
10 mg	27	24	14	27	24	14	27	24	14

Legend: ● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg

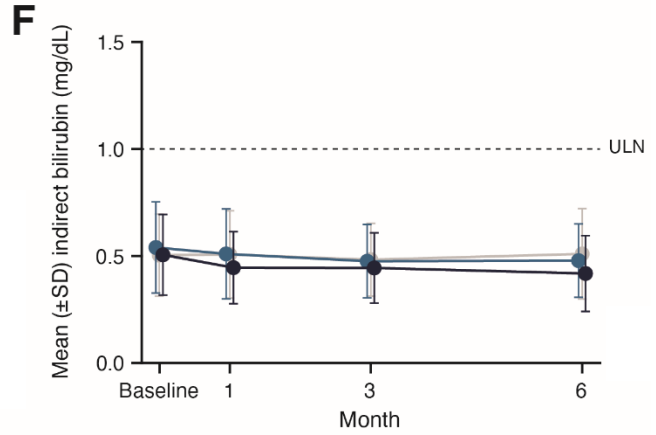
Abbreviations: BL, baseline; M, month; NRS, numeric rating scale; PBC, primary biliary cholangitis; SE, standard error.

Supplemental Figure S5. Relative changes from baseline and absolute serum levels of total (A-B), direct (C-D), and indirect bilirubin (E-F); AST (G-H); GGT (I-J); triglycerides (K-L); total cholesterol (M-N); LDL-C (O-P); and HDL-C (Q-R) through Month 6

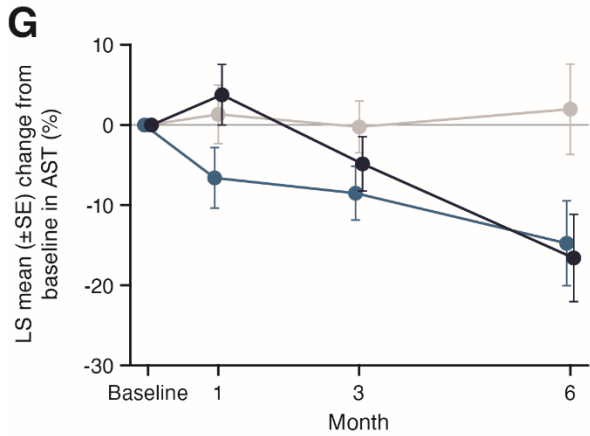




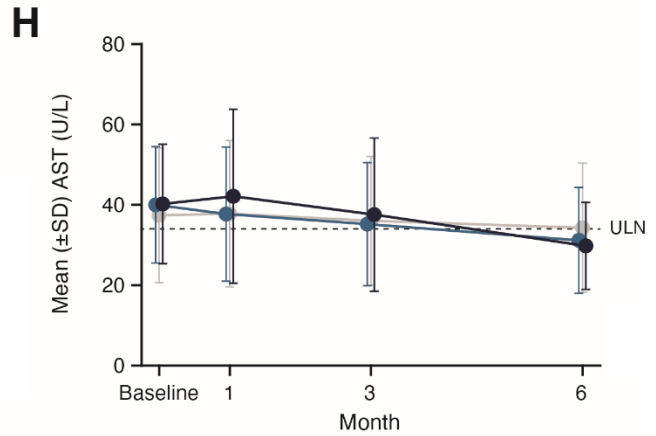
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5 mg	89	78	54	24
10 mg	89	78	53	18



N =	Placebo	78	56	23
5 mg	89	78	54	24
10 mg	89	78	53	18

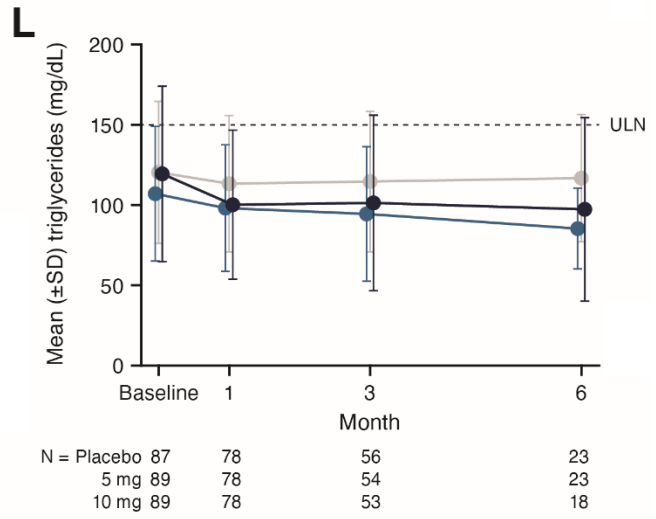
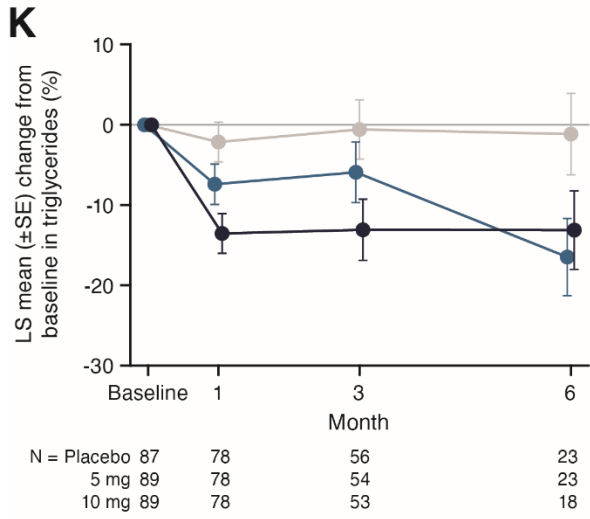
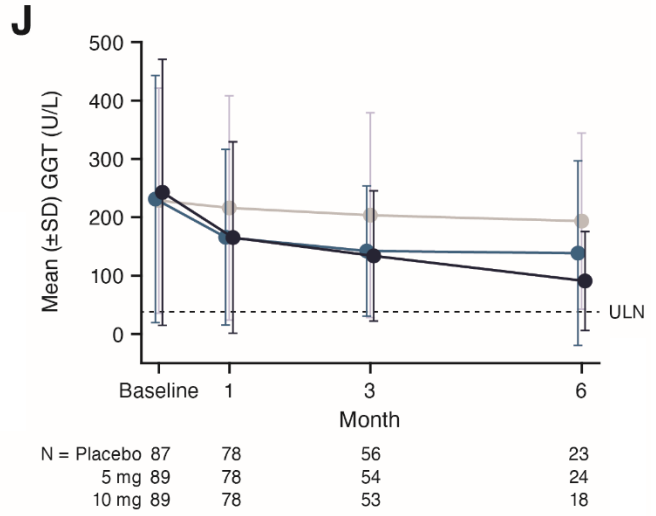
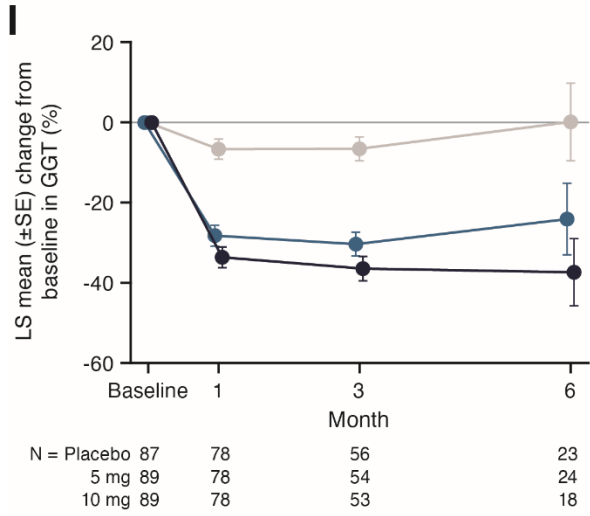


N =	Placebo	78	56	23
5 mg	89	78	54	24
10 mg	89	78	53	18

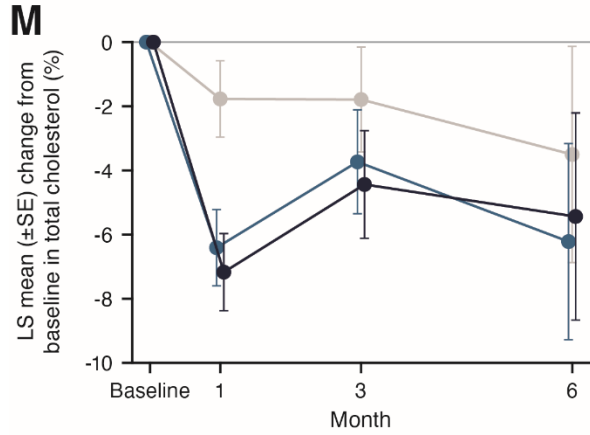


N =	Placebo	78	56	23
5 mg	89	78	54	24
10 mg	89	78	53	18

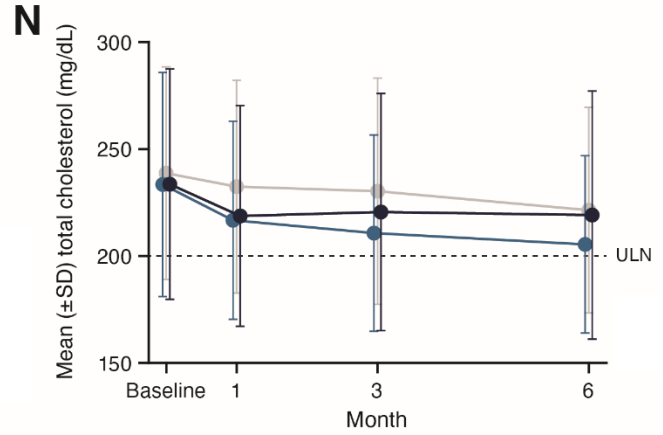
● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg



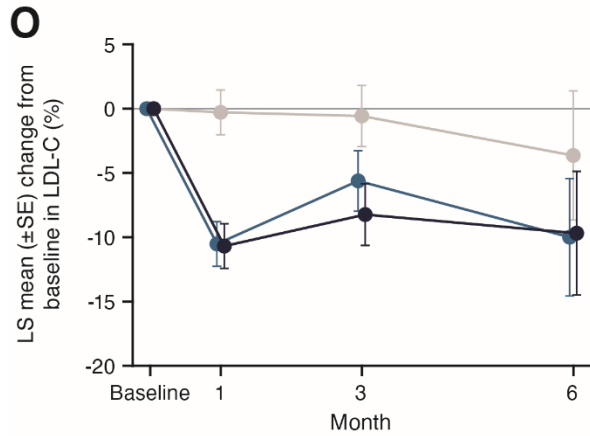
● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg



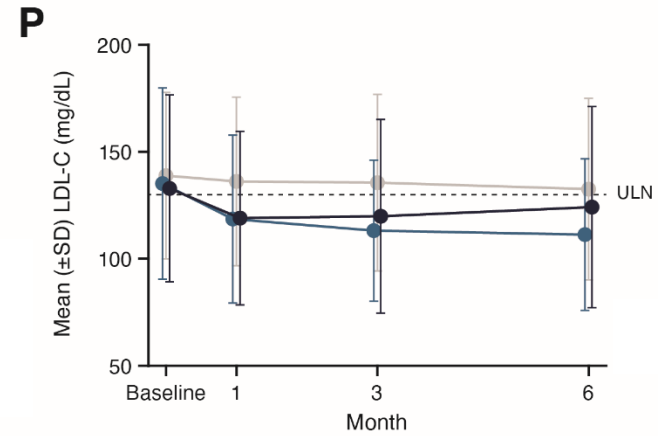
	Baseline	1	3	6
N = Placebo	87	78	56	23
5 mg	89	78	54	23
10 mg	89	78	53	18



	Baseline	1	3	6
N = Placebo	87	78	56	23
5 mg	89	78	54	23
10 mg	89	78	53	18

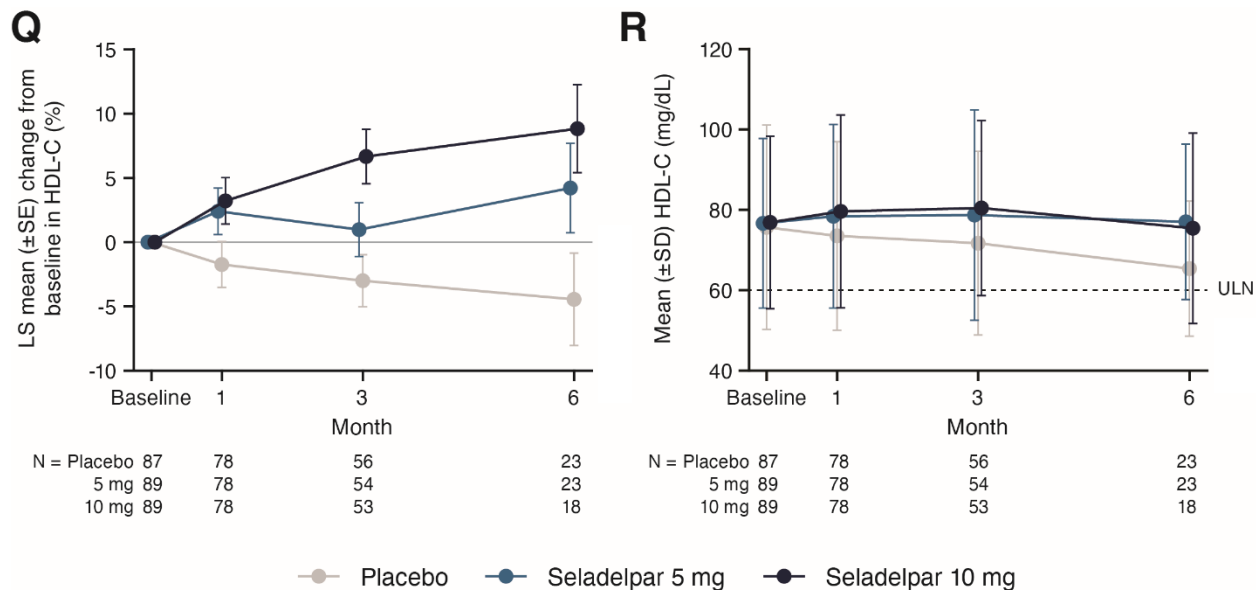


	Baseline	1	3	6
N = Placebo	87	78	56	23
5 mg	89	78	54	23
10 mg	89	78	53	18



	Baseline	1	3	6
N = Placebo	87	78	56	23
5 mg	89	78	54	23
10 mg	89	78	53	18

● Placebo ● Seladelpar 5 mg ● Seladelpar 10 mg



Percent change from baseline was estimated by ANCOVA with percent change from baseline as the dependent variable, treatment group and randomization stratification factors as fixed effects, and baseline as a covariate.

Abbreviations: ANCOVA, analysis of covariance; AST, aspartate aminotransferase; GGT, gamma glutamyl transferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; N, number of patients in the treatment group; SD, standard deviation; SE, standard error.