36 Months of Treatment With Seladelpar Is Associated With Stable or Improved Liver Stiffness in Patients With Primary Biliary Cholangitis

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Conclusions

- Seladelpar treatment led to overall stable liver stiffness measurements (LSMs) in patients with primary biliary cholangitis (PBC)
- Patients at the highest risk of progression (LSM ≥16.9 kPa at baseline) showed a trend towards improvement in LSM with seladelpar treatment. Other subgroups demonstrated stability of LSM over time
- Most patients (85%) demonstrated either stable or improved LSM category at 36 months

Plain Language Summary

- Primary biliary cholangitis (PBC) is a long-term liver disease that gets worse over time
- Liver stiffness measurements can be used to understand if the disease is getting better, worse, or remains the same
- Seladelpar is a drug used to treat people with PBC
- This analysis looked at the impact of seladelpar on liver stiffness measurements in people with PBC
- The study showed that liver stiffness measurements remained the same or got better in most people treated with seladelpar over 36 months

References: **1.** Corpechot C, et al. *Hepatology*. 2012;56(1):198-208. **2.** Corpechot C, et al. *J Hepatol*. 2022;77(6):1545-53. **3.** Livdelzi. US prescribing information. Gilead Sciences, Inc.; 2024. **4.** Livdelzi. UK summary of product characteristics. Gilead Sciences, Inc.; 2024. **5.** Lyvdelzi. EMA prescribing information. Gilead Sciences, Inc.; 2025. **6.** Hirschfield GM, et al. *N Engl J Med*. 2024;390(9):783-94. **7.** Levy C, et al. *Am J Gastroenterol*. 2025. doi:10.14309/ajg.0000000000003603. Online ahead of print.

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Disclosures: Conflict of interest disclosures may be viewed using the QR code at the top right.

Introduction

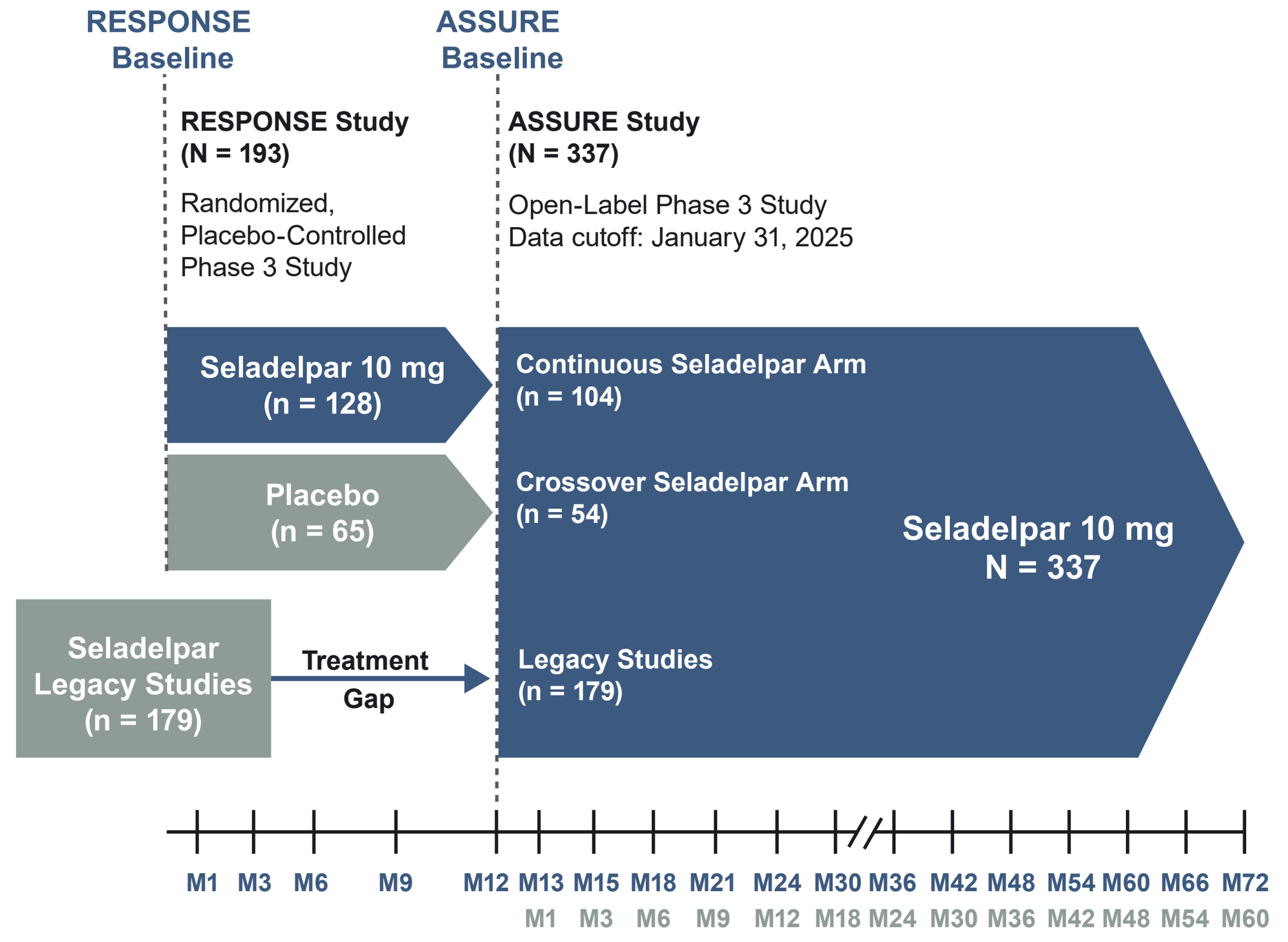
- Patients with primary biliary cholangitis (PBC) who have advanced fibrosis or cirrhosis tend to show progressive increases in liver stiffness measurements (LSMs) over time despite receiving first-line treatment with ursodeoxycholic acid (UDCA)[1]
- Elevated LSM is associated with increased risk of poor clinical outcomes, such as liver transplantation and death[2]
- Seladelpar is a first-in-class delpar (selective peroxisome proliferator–activated receptor delta [PPARδ] agonist) indicated for the treatment of PBC in combination with UDCA in adults who have an inadequate response to UDCA, or as monotherapy in patients who are unable to tolerate UDCA[3-5]
- Seladelpar treatment leads to improvement in cholestatic markers. Its long-term impact on LSM has not been previously evaluated[6,7]

Objectives

- ASSURE is an ongoing, open-label Phase 3 study (NCT03301506) providing long-term efficacy and safety data on seladelpar 10 mg (Figure 1)
- This interim analysis reports longitudinal trends in LSMs in patients treated with seladelpar through January 31, 2025 (up to 3 years of treatment)

Methods

Figure 1. ASSURE Study Design


RESPONSE Study Baseline
ASSURE Baseline
RESPONSE Study (N = 193)
Randomized, Placebo-Controlled Phase 3 Study
ASSURE Study (N = 337)
Open-Label Phase 3 Study
Data cutoff: January 31, 2025
Seladelpar 10 mg (n = 128)
Continuous Seladelpar Arm (n = 104)
Placebo (n = 65)
Crossover Seladelpar Arm (n = 54)
Seladelpar 10 mg N = 337
Seladelpar Legacy Studies (n = 179)
Treatment Gap
Legacy Studies (n = 179)
M1 M3 M6 M9 M12 M13 M15 M18 M21 M24 M30 M36 M42 M48 M54 M60 M66 M72
M1 M3 M6 M9 M12 M18 M24 M30 M36 M42 M48 M54 M60

Phase 2 dose-ranging study (NCT02955602), Phase 3 long-term safety study (NCT03301506), Phase 3 ENHANCE study (NCT03602560), Phase 1b hepatic impairment study (NCT04950764), Phase 3 placebo-controlled RESPONSE study (NCT04620733), and Phase 3, open-label ASSURE study (NCT03301506). The Phase 2 and 3 parent studies required an inadequate response or intolerance to first-line UDCA. Data cutoff: January 31, 2025. In ASSURE, clinic visits were at 1, 3, and 6 months and every 6 months thereafter. In the pooled population, baseline was at seladelpar initiation. Data from the RESPONSE study were added to the ASSURE data. In ASSURE, 2 patients initiated seladelpar at 5 mg and were excluded from the analysis.
M, month; UDCA, ursodeoxycholic acid.

- Study population (N = 311)
  - All patients in ASSURE who received open-label seladelpar 10 mg with at least one post-baseline LSM were included, including exposure in RESPONSE for patients who were randomized to seladelpar in the pivotal study
- Assessment of liver stiffness
  - LSM was assessed using vibration-controlled transient elastography (FibroScan) as an exploratory endpoint, with local reads at screening and every 12 months
- For the current analyses:
  - Baseline was defined as the time of seladelpar initiation
  - Data are reported from an interim cutoff date of January 31, 2025
  - LSM values with an IQR/LSM ratio >30% were excluded to ensure data reliability
  - Subgroups by baseline LSM categories were defined post hoc based on established diagnostic thresholds for fibrosis stages in PBC[1]:
    - <10.7 kPa (F0–F2)
    - ≥10.7 and <16.9 kPa (F3)
    - ≥16.9 kPa (F4)
  - Changes in LSM were assessed at 12, 24, and 36 months, and median change and percent change were summarized
  - Patients with shifts in LSM category were summarized, and patients with >30% improvement or worsening were assessed for pattern of change or clinical characteristics

Results

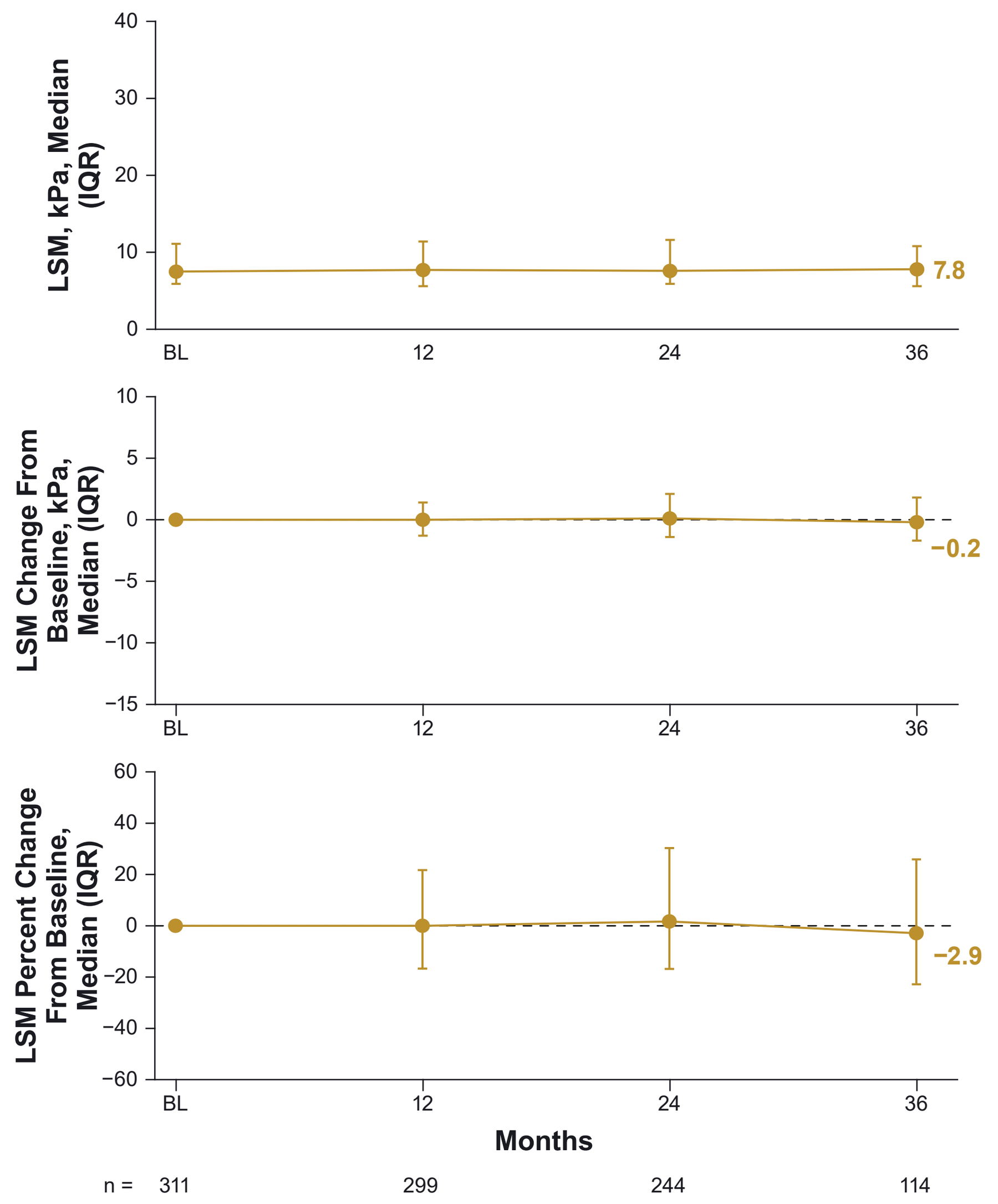
Table 1. Demographics and Clinical Characteristics at Baseline

	Total (N = 311)	BL LSM <10.7 kPa (n = 227)	BL LSM ≥10.7 and <16.9 kPa (n = 51)	BL LSM ≥16.9 kPa (n = 33)
Age[a], years, mean (SD)	58 (9.6)	58 (9.3)	58 (11.7)	60 (8.1)
Age <50 years at PBC diagnosis, n (%)	166 (53)	118 (52)	29 (57)	19 (58)
Female, n (%)	294 (95)	217 (96)	50 (98)	27 (82)
BMI ≥30 kg/m², n (%)	86 (28)	57 (25)	19 (37)	10 (30)
LSM, kPa, median (IQR)	7.5 (5.9, 11.1)	6.6 (5.5, 8.0)	12.6 (11.6, 13.6)	21.1 (18.9, 28.4)
ELF, mean (SD)	10 (1.03)	9.7 (0.85)	10.7 (0.86)	11.0 (1.19)
ALP, U/L, mean (SD)[b]	287 (128.2)	281 (119.2)	307 (168.6)	295 (116.8)
Total bilirubin, mg/dL, mean (SD)[c]	0.74 (0.33)	0.68 (0.27)	0.85 (0.35)	1.02 (0.44)
ALT, U/L, mean (SD)[d]	42.7 (23.3)	41.0 (23.1)	49.9 (25.0)	43.2 (20.3)
AST, U/L, mean (SD)[e]	37.7 (16.5)	35.3 (15.5)	44.7 (17.3)	43.9 (17.2)
GGT, U/L, mean (SD)[f]	227 (197.1)	210 (196.1)	269 (160.0)	275 (240.0)
Albumin, g/dL, mean (SD)[g]	4.1 (0.27)	4.2 (0.25)	4.1 (0.28)	4.0 (0.34)
Platelets, 10³/µL, mean (SD)[h]	241 (78.8)	255 (74.0)	201 (82.1)	201 (72.4)
Patients with cirrhosis at baseline, n (%)[i]	49 (16)	9 (4)	14 (27)	26 (79)
Child-Pugh Class A, n (%)[j]	46 (94)	9 (100)	14 (100)	23 (88)
Child-Pugh Class B, n (%)[j]	3 (6)	0	0	3 (12)

BL was defined at the time of seladelpar initiation. Subgroup cutoffs are based on previously established diagnostic thresholds for liver stiffness: F1 at 7.1 kPa, F2 at 8.8 kPa, F3 at 10.7 kPa, and F4 (cirrhosis) at 16.9 kPa.[1]
[a]Age at enrollment. [b]The ULN for ALP is 116 U/L in men and women. [c]The ULN for total bilirubin is 1.10 mg/dL in men and women. [d]The ULN for ALT is 41 U/L in men and women. [e]The ULN for AST is 34 U/L in men and women. [f]The ULN for GGT is 52 U/L in men and 38 U/L in women. [g]The normal range for albumin is 3.5–5.5 g/dL. [h]The normal range for platelet count is 140–400 × 10³ /uL. [i]In this analysis, cirrhosis was defined as: a history of liver biopsy showing cirrhosis (eg, Ludwig stage 4 or Ishak stage 5); current or a history of decompensated liver disease; liver stiffness >16.9 kPa by FibroScan; the combination of a platelet count <140 × 10³ cells/µL with a serum albumin level <3.5 g/dL, an INR >1.3 (not due to antithrombotic agent use), or a total bilirubin level >1.0 × ULN; the presence of radiologic evidence of cirrhosis (a nodular liver) with concurrent splenomegaly; or clinical determination by the investigator. [j]Percent of patients with cirrhosis.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BL, baseline; BMI, body mass index; ELF, enhanced liver fibrosis; GGT, gamma-glutamyl transferase; INR, international normalized ratio; LSM, liver stiffness measurement; ULN, upper limit of normal.

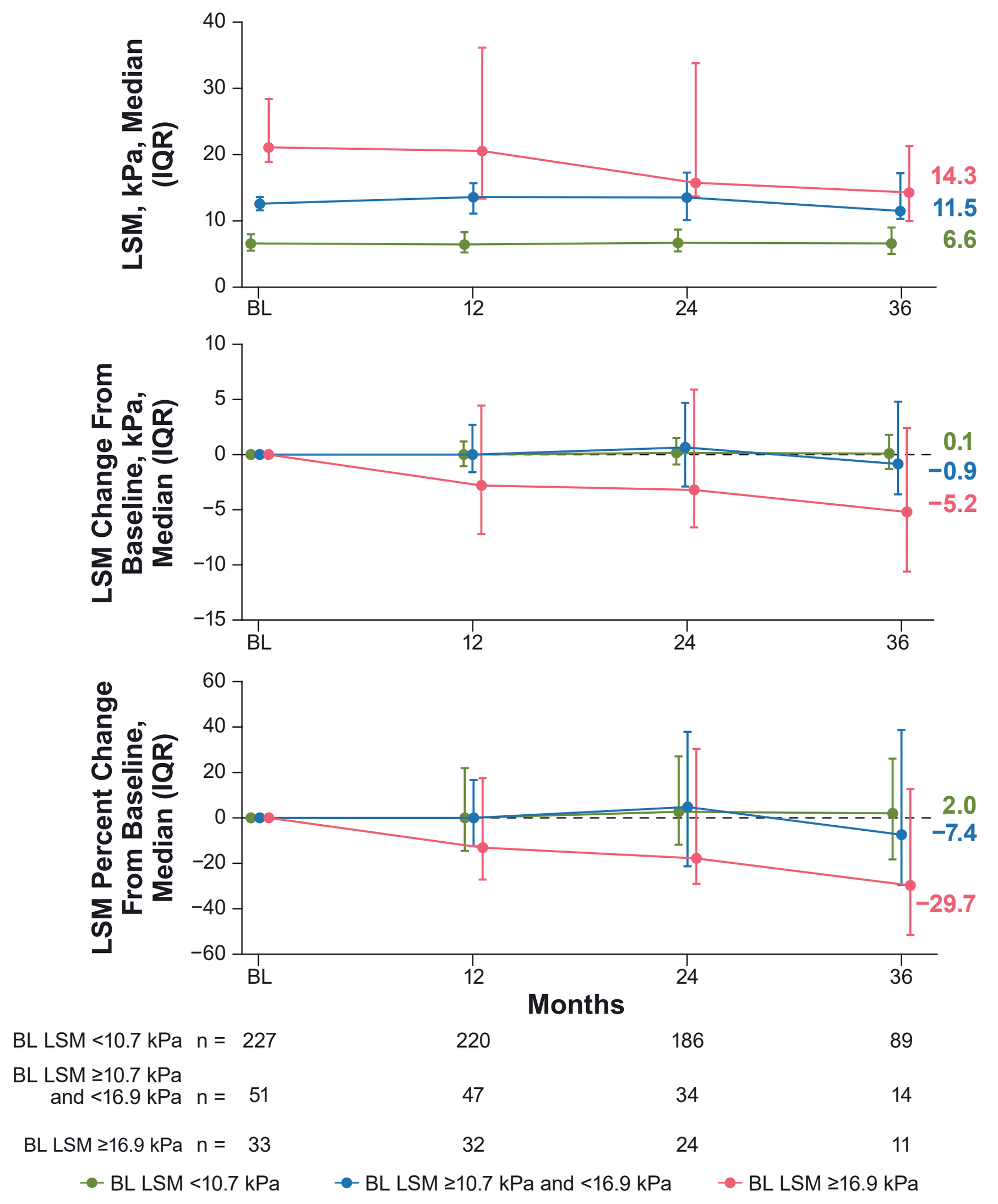
- A total of 311 patients were included in the analysis, and LSM values at 36 months were available in 114 patients (Table 1)
- 79% of the patients with baseline LSM ≥16.9 kPa had confirmed cirrhosis at baseline

Figure 2. Changes in Liver Stiffness in the Overall Population (N = 311)



BL was defined at the time of seladelpar initiation.
n = the number of patients evaluable at each time point.
BL, baseline; LSM, liver stiffness measurement.

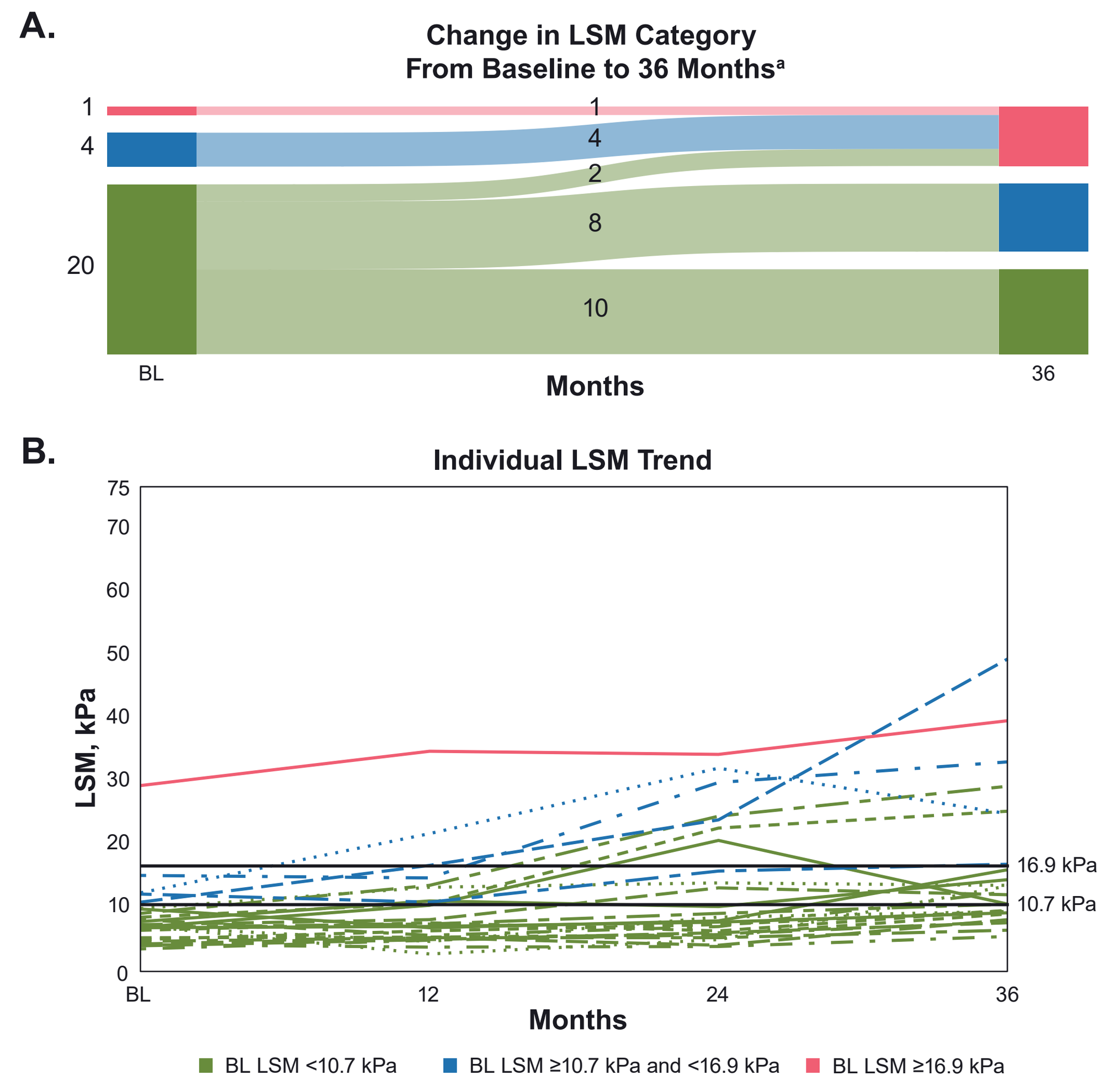
Figure 3. Changes in Liver Stiffness by Baseline Liver Stiffness Subgroup


LSM, kPa, Median (IQR)
14.3
11.5
6.6
LSM Change From Baseline, kPa, Median (IQR)
0.1
−0.9
−5.2
LSM Percent Change From Baseline, Median (IQR)
2.0
−7.4
−29.7
BL
12
24
36
Months
BL LSM <10.7 kPa n = 227 220 186 89
BL LSM ≥10.7 kPa and <16.9 kPa n = 51 47 34 14
BL LSM ≥16.9 kPa n = 33 32 24 11
BL LSM <10.7 kPa
BL LSM ≥10.7 kPa and <16.9 kPa
BL LSM ≥16.9 kPa

BL was defined at the time of seladelpar initiation.
n = the number of patients evaluable at each time point.
BL, baseline; LSM, liver stiffness measurement.

- LSM remained stable over time with seladelpar treatment (median change from baseline, −0.2 kPa; median percent change from baseline, −2.9%; Figure 2)
- There was a trend towards improvement in LSM for patients with LSM ≥16.9 kPa (median change from baseline, −5.2 kPa; median percent change from baseline, −29.7%; Figure 3)
- LSM remained stable over time in patients with baseline LSM <10.7 kPa (median change from baseline, 0.1 kPa; median percent change from baseline, 2.0%) and those with baseline LSM ≥10.7 and <16.9 kPa (median change from baseline, −0.9 kPa; median percent change from baseline, −7.4%)

Figure 4. Patients With Liver Stiffness Worsening of >30% at 36 Months (N = 25)



LSM values range from 0 to 75 kPa.
[a]n values correspond to patients with >30% increase in LSM at 36 months, with available data at both BL and 36 months; patients without available data at these time points were excluded.
BL, baseline; LSM, liver stiffness measurement.

- Among the patients who had LSM worsening of >30%, the majority of patients (80% [20/25]) were from the baseline LSM <10.7 kPa group, and half of these patients remained in the <10.7 kPa category at 36 months of seladelpar treatment (Figure 4)

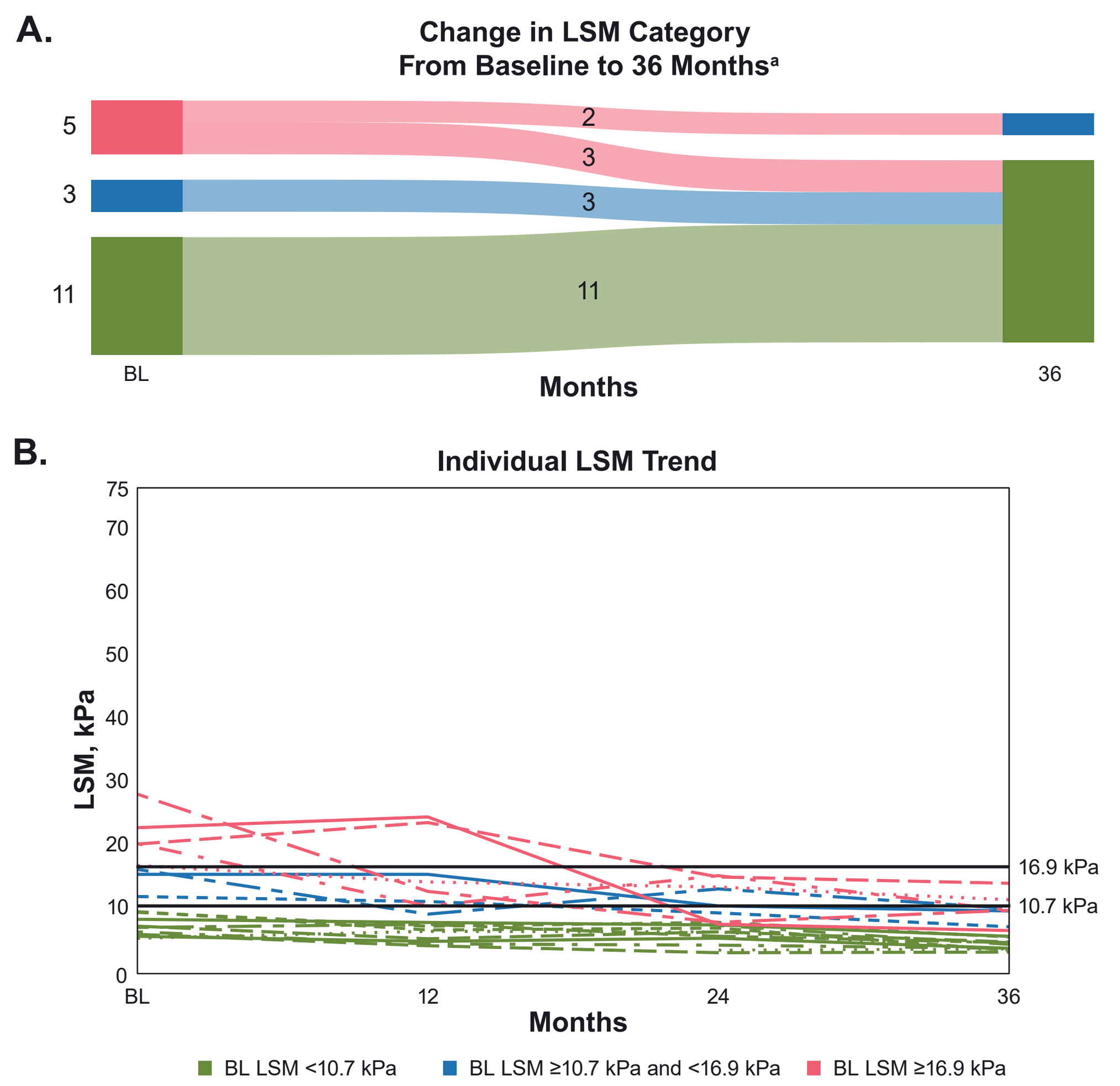
Table 2. Shift in Liver Stiffness Category at 36 Months

Category at Baseline	Category at 36 Months: LSM <10.7 kPa	Category at 36 Months: LSM ≥10.7 and <16.9 kPa	Category at 36 Months: LSM ≥16.9 kPa
LSM <10.7 kPa (n = 89)	**76/89 (85%)**	**11/89 (12%)**	**2/89 (2%)**
LSM ≥10.7 and <16.9 kPa (n = 14)	**5/14 (36%)**	**5/14 (36%)**	**4/14 (29%)**
LSM ≥16.9 kPa (n = 11)	**3/11 (27%)**	**4/11 (36%)**	**4/11 (36%)**

Baseline was defined at the time of seladelpar initiation.
Patients with values at both baseline and 36 months are included in this analysis.
Green shading indicates stability or improvement of liver stiffness measurement category.

- Most patients (85% [97/114]) demonstrated either stable or improved LSM category at 36 months (Table 2)

Figure 5. Patients With Liver Stiffness Improvement of >30% at 36 Months (N = 19)



LSM values range from 0 to 75 kPa.
[a]n values correspond to patients with >30% decrease in LSM at 36 months, with available data at both BL and 36 months; patients without available data at these time points were excluded.
BL, baseline; LSM, liver stiffness measurement.

- Among the patients with LSM improvement of >30%, 89% (17/19) of patients had LSM <10.7 kPa at 36 months of seladelpar treatment (Figure 5)

Table 3. Baseline Characteristics Associated With Significant Worsening of Liver Stiffness

	>30% Worsening From Baseline in LSM at 36 Months (N = 25)	≤30% Change From Baseline in LSM at 36 Months (N = 89)	*P*-value for 2-sided test
Age[a], years, mean	55.4	60.1	**0.0275***
Age at PBC diagnosis, years, mean	46.4	49.5	0.1620
Female, n (%)	23 (92)	84 (94)	0.6625
BMI ≥30 kg/m², n (%)	6 (24)	32 (36)	0.2646
LSM, kPa, mean	8.7	9.1	0.8185
≥10 kPa, n (%)	7 (28)	24 (27)	0.9186
ELF, mean	9.7	9.7	0.7039
AST, U/L, mean	37.8	34.1	0.3308
ALT, U/L, mean	48.1	39.4	0.1955
ALP, U/L, mean	289.8	260.2	0.3588
>1.0 to ≤1.5 x ULN, n (%)	0	17 (19)	**0.0122***
>1.5 to ≤2.0 x ULN, n (%)	12 (48)	21 (24)	
>2.0 x ULN, n (%)	13 (52)	51 (57)	
Total bilirubin, mg/dL, mean	0.8	0.7	0.1418
≤1.0 x ULN, n (%)	22 (88)	82 (92)	0.5203
GGT, U/L, mean	233.9	205.6	0.219
Albumin, g/dL, mean	4.2	4.2	0.9344
Platelets, 10³/µL, mean	232.2	243.3	0.3509
Cirrhosis: Yes, n (%)	2 (8)	14 (16)	0.3276
Child-Pugh Class A, n (%)[b]	2 (100)	14 (100)	–

Baseline was defined at the time of seladelpar initiation.
[a]Age at enrollment. [b]Percent of patients with cirrhosis. *Significant at a *P* <0.05 threshold.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; ELF, enhanced liver fibrosis; GGT, gamma-glutamyl transferase; LSM, liver stiffness measurement; PBC, primary biliary cholangitis; ULN, upper limit of normal.

- Younger age at seladelpar initiation and higher baseline alkaline phosphatase category were both significantly associated with a greater than 30% increase in LSM at 36 months (Table 3)