Seladelpar Leads to Sustained, Clinically Meaningful Improvement in Pruritus: Results From the ASSURE Study up to 30 Months

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Author Disclosures

GMH reports having consulted for Advanz Pharma; CymaBay Therapeutics; Falk; Gilead Sciences, Inc.; GSK; Intercept Pharmaceuticals; Ipsen; Kowa; Mirum Pharma; and Pliant Therapeutics. **AEK** reports receiving grants or contracts from Gilead Sciences, Inc.; Intercept Pharmaceuticals; and Roche; consulting fees from AbbVie; Advanz Pharma; Alentis Therapeutics; Alfasigma; Astellas; AstraZeneca; Attovia Therapeutics; Avior Bio; Bayer; Bristol Myers Squibb; Boehringer Ingelheim; CymaBay Therapeutics; Gilead Sciences, Inc.; GSK; Guidepoint; Intercept Pharmaceuticals; Ipsen; Mirum Pharma; Merck Sharp & Dohme; Novo Nordisk; Rectify Pharma; Roche; and Takeda; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from AbbVie; Advanz Pharma; AOP Orphan Pharmaceuticals; Bayer; Bristol Myers Squibb; CymaBay Therapeutics; Falk; Gilead Sciences, Inc.; GSK; Intercept Pharmaceuticals; Ipsen; Johnson & Johnson; Medscape; Mirum Pharma; Merck Sharp & Dohme; NewBridge Pharmaceuticals; Novartis; Roche; Vertex Pharmaceuticals; and Viofor; support for attending meetings and/or travel from Gilead Sciences, Inc.; participation on a data safety monitoring board with AbbVie; Advanz Pharma; Alentis Therapeutics; Alfasigma; AstraZeneca; Avior Bio; Bayer; Bristol Myers Squibb; CymaBay Therapeutics; Escient Pharmaceuticals; Falk; Gilead Sciences, Inc.; GSK; Guidepoint; Intercept Pharmaceuticals; Ipsen; Mirum Pharma; Merck Sharp & Dohme; Novo Nordisk; Roche; and Takeda; and a leadership or fiduciary role in other board, society, committee, or advocacy groups (paid or unpaid) with PBC Foundation, Swiss Association for the Study of the Liver (SASL), Swiss Gastroenterology Society (SGG), Swiss Hepa, and Swiss Transplant Society (STS). **CL** reports receiving research grants paid to her institution from Calliditas Therapeutics; CymaBay Therapeutics; Escient Pharmaceuticals; EWR; Gilead Sciences, Inc.; GSK; Intercept Pharmaceuticals; Ipsen; Kowa; Mirum Pharma; Target RWE; and Zydus Pharmaceuticals. **KVK** reports receiving grants or contracts from 89Bio; Boston Pharmaceuticals; Corcept Therapeutics; CymaBay Therapeutics; Genfit; Gilead Sciences, Inc.; GSK; Hanmi Pharmaceuticals; Intercept Pharmaceuticals; Ipsen; Janssen; Madrigal Pharmaceuticals; Mirum Pharma; Novo Nordisk; NGM Bio; Pfizer; Pliant Therapeutics; Terns Pharmaceuticals; Viking Therapeutics; and Zydus Pharmaceuticals; royalties or licenses from UpToDate; consulting fees from 89Bio; CymaBay Therapeutics; Genfit; Gilead Sciences, Inc.; GSK; HighTide Biopharma; Inipharm; Intercept Pharmaceuticals; Ipsen; Madrigal Pharmaceuticals; Mirum Pharma; NGM Bio; and Zydus Pharmaceuticals; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from AbbVie; Gilead Sciences, Inc.; and Intercept Pharmaceuticals; participation on a data safety monitoring board or advisory board with CTI and Medpace; and stock or stock options with Inipharm. **HE** reports receiving grants or honoraria from AbbVie; CymaBay Therapeutics; Eisai; Fibronostics; Genfit; Gilead Sciences, Inc.; Intercept Pharmaceuticals; and Mallinckrodt Pharmaceuticals; and owns equity in AbbVie and Gilead Sciences, Inc. **JH** reports receiving grant support from Gilead Sciences, Inc., and Roche; receiving consultant fees from Roche; receiving lecture fees from AbbVie Korea; Gilead Sciences, Inc.; Oncolys BioPharma; Roche; and Yuhan Korea; and participation as a member on the steering committee for AstraZeneca. **KMK**, **JL**, **CB**, and **DBC** are employees of Gilead Sciences, Inc., and may own stock in Gilead Sciences, Inc. **MJM** reports receiving grants or contracts from CymaBay Therapeutics; Genfit; Gilead Sciences, Inc.; GSK; Ipsen; and Mirum Pharma; receiving consulting fees from CymaBay Therapeutics, GSK, Intra-Sana Laboratories, Ipsen, Ironwood, Mallinckrodt Pharmaceuticals, and Mirum Pharma; and support for attending meetings and/or travel from CymaBay Therapeutics, GSK, Ipsen, and Mallinckrodt Pharmaceuticals.

Primary Biliary Cholangitis

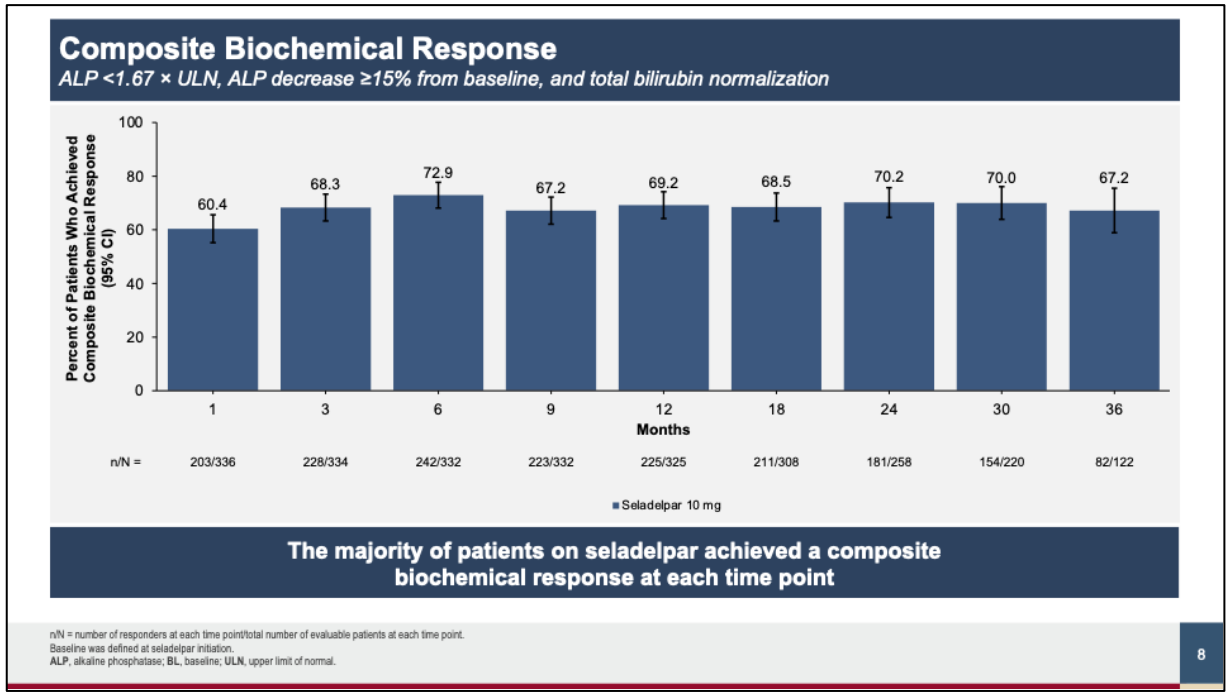
- PBC is a chronic, progressive, autoimmune, cholestatic liver disease that affects approximately 1 in 1000 women over 40 years of age[1]
- Cholestatic pruritus can occur in up to 80% of patients with PBC, is frequently debilitating, and can greatly reduce the QoL of patients[2,3]
- Treatment options for cholestatic pruritus, such as bile acid sequestrants and antihistamine, have limited efficacy, and off-label use of agents like rifampin have significant limitations[4]
- In the most severe cases of cholestatic pruritus, it can become an indication for liver transplantation even in the absence of liver failure[4,5]
- Seladelpar is the first-in-class selective PPARδ agonist that has been shown to significantly improve biochemical markers of disease and pruritus in the pivotal RESPONSE study[6]

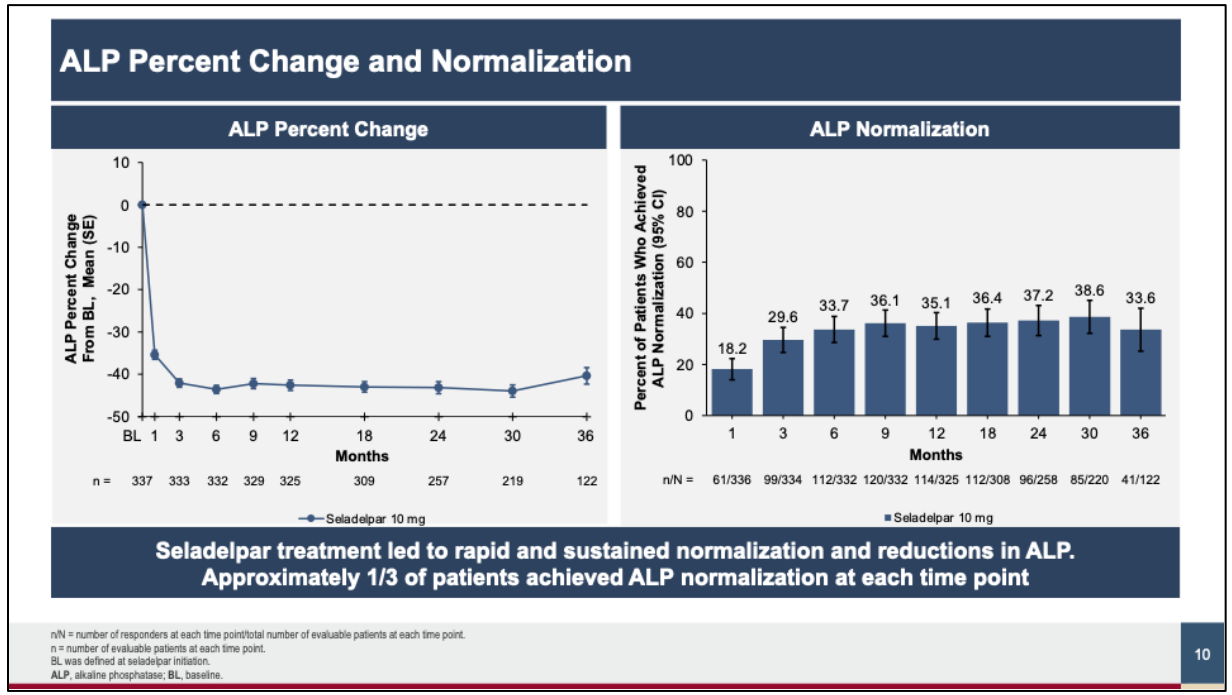
PBC, primary biliary cholangitis; **PPARδ**, peroxisome proliferator–activated receptor delta; **QoL**, quality of life.

1. European Association for the Study of the Liver. *J Hepatol.* 2017;67(1):145-72. **2.** Bowlus CL, et al. *J Hepatol.* 2022;77(2):353-64. **3.** Kremer AE, et al. *Dig Dis.* 2015;33(suppl 2):164-75. **4.** Düll MM, Kremer AE. *Curr Hepatol Rep.* 2020;19:86-95. **5.** Lindor KD, et al. *Hepatology.* 2018;0:0. **6.** Hirschfield GM, et al. *N Engl J Med.* 2024;390(9):783-94.

Seladelpar Long-Term Biochemical Efficacy and Safety From ASSURE
Presented at AASLD 2025

- Long-term seladelpar treatment (up to 36 months) led to **67%** of patients meeting the **composite biochemical response endpoint** and **34%** with **ALP normalization**[1]
- Seladelpar was overall **safe** and **well tolerated up to 48 months** [1]





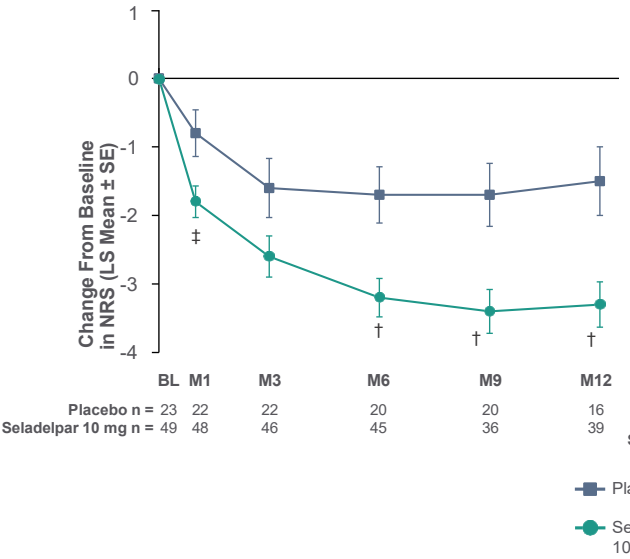
Composite biochemical response is defined as ALP <1.67 × ULN, ALP decrease ≥15% from baseline, and total bilirubin ≤ULN.
ALP, alkaline phosphatase; **BL**, baseline; **SEL**, seladelpar; **ULN**, upper limit of normal.

1. Pratt D, et al. Presented at: AASLD, The Liver Meeting; November 7–11, 2025. Oral 0213.

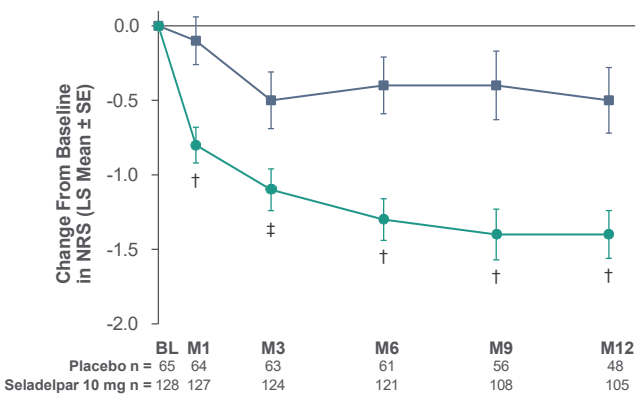
Seladelpar and Pruritus
Previously Published

RESPONSE: Changes in Pruritus NRS Over 12 Months[1]

A. Baseline Pruritus NRS ≥4 Population (MSPN)



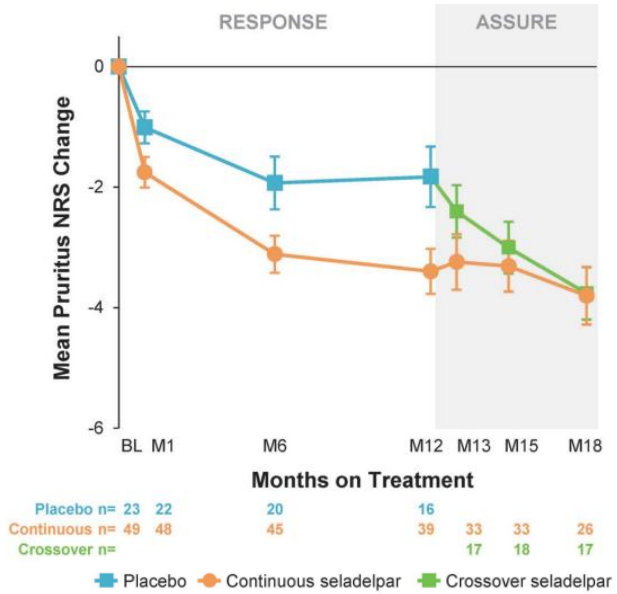
B. Overall Population



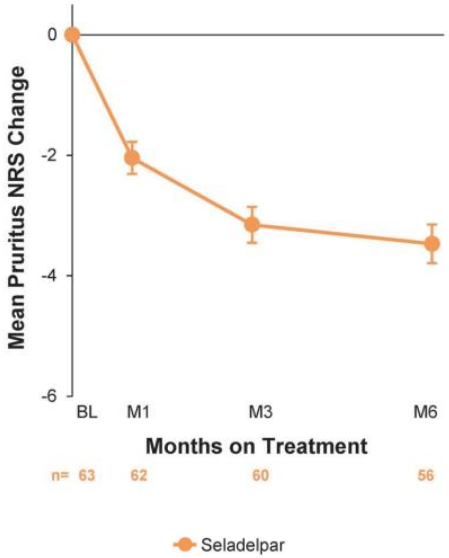
Seladelpar significantly improved itch at month 6 in patients with NRS ≥4 at baseline, with effect maintained through month 12

ASSURE: Changes in Pruritus NRS Over 6 Months (NRS ≥4 Population)[2]

C. RESPONSE Rollover Patients



D. Patients From Legacy Studies



The **NRS decrease** was **maintained after 6 additional months of treatment** in ASSURE and was similar in patients from legacy studies

†*P* < .005 vs placebo. ‡*P* < .05 vs placebo.
BL, baseline; **LS**, least-squares; **M**, month; **MSPN**, patients with moderate to severe pruritus defined as RESPONSE baseline NRS ≥4; **NRS**, numeric rating scale; **PBC**, primary biliary cholangitis.
1. Hirschfield GM, et al. *N Engl J Med.* 2024;390(9):783-94. **2.** Levy C, et al. *Am J Gastroenterol.* 2025;1-46.

Objectives

- To present the **latest interim long-term pruritus results** from the **ASSURE** (NCT03301506) study, as of 31 Jan 2025, in patients who rolled over from the RESPONSE study

- To assess **comparability of a single-visit pruritus NRS** vs weekly-averaged NRS in **ASSURE**

NRS, numeric rating scale.

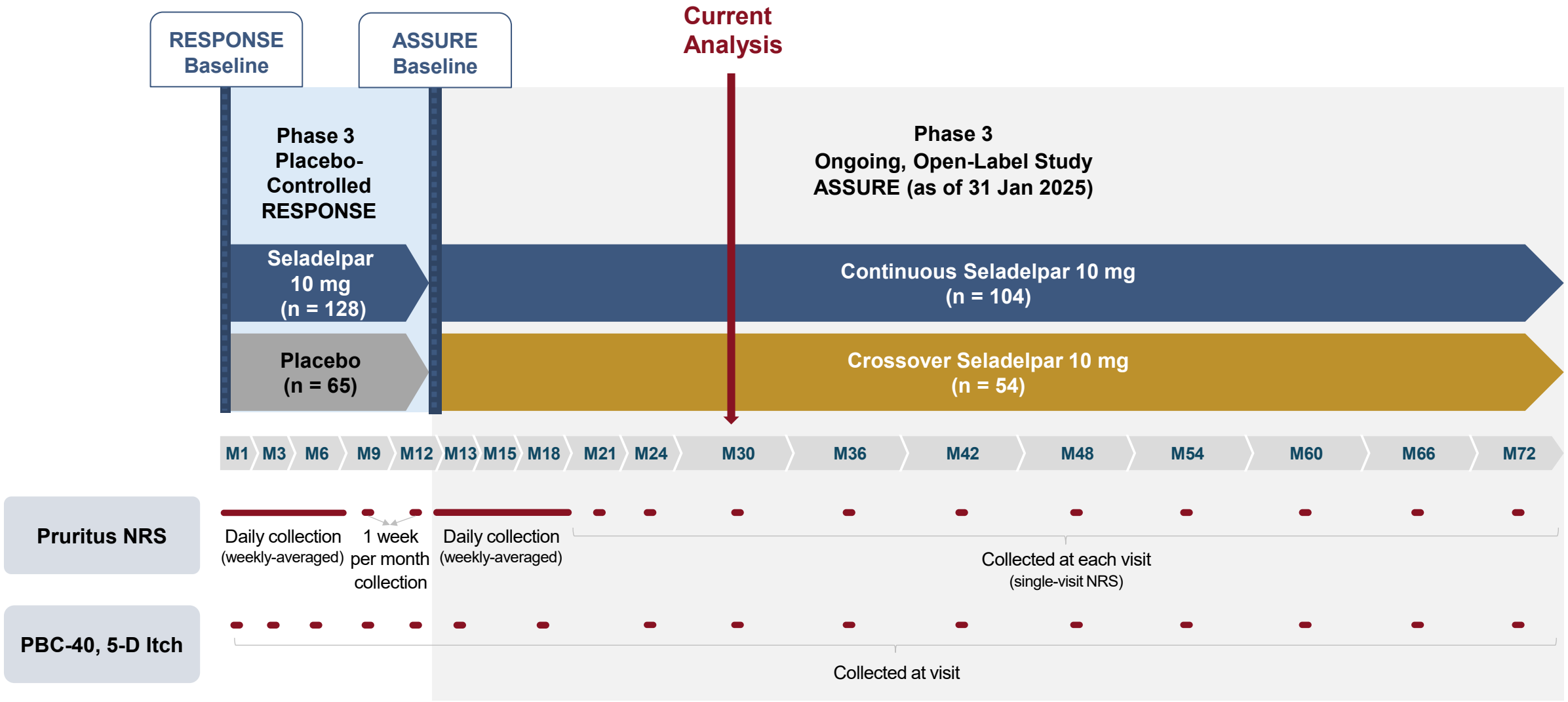
Tools to Assess Pruritus in RESPONSE and ASSURE

	Pruritus NRS Scale	5-D Itch	PBC-40 Itch
Description	**Validated scale evaluating the intensity of pruritus**[1]	**Multidimensional assessment of pruritus**[2]	**Disease-specific, quality-of-life measure** of itch and other symptoms[3]
Time Period	Past **24 hours recall**	Past **2-week recall** method	Past **4-week recall** period
Itch Assessment	Rate 0–10: 0 no itch – 10 worst imaginable itch	Scores ranging between 1 to 5 (most severe) for each domain	Itch domain score ranges from 0 to 15

NRS, numeric rating scale; **PBC**, primary biliary cholangitis.

1. Kremer AE, et al. Poster presented at: EASL 2025; May 7–10, 2025. Poster THU-277. **2.** Elman S, et al. *Br J Dermatol.* 2010;162(3):587-93. **3.** Jacoby A, et al. *Gut.* 2005; 54(11):1622-9.

Study Design



Phase 3 placebo-controlled RESPONSE study (NCT04620733) enrolled patients with inadequate response or intolerance to first-line UDCA. Study details have been published (Hirschfield GM, et al. *N Engl J Med.* 2024;390(9):783-94). Patients completing RESPONSE could roll over into ASSURE.
In ASSURE, clinic visits occurred at months 1, 3, and 6, then every 6 months; pruritus NRS was self-assessed daily from day 1 through month 6, and at each clinic visit thereafter; PBC-40, 5-D Itch, and PGI-S were assessed at screening, day 1, and every 6 months after initiation of treatment until end of treatment or early termination.
Data cutoff: January 31, 2025. In ASSURE, 2 patients initiated seladelpar at 5 mg and were excluded from the analysis.
M, month; **NRS**, numeric rating scale; **PBC**, primary biliary cholangitis; **PGI-S**, Patient Global Impression of Severity; **UDCA**, ursodeoxycholic acid.

Methods

Study Population

- Participants in the **RESPONSE** study with **baseline pruritus NRS ≥4**, including all available follow-up time in the ongoing **ASSURE** study as of 31 Jan 2025

Analyses

- **Change in pruritus** assessed by **pruritus NRS, 5-D Itch,** and **PBC-40 itch domain** from baseline up to **30 months** of treatment
- Percentage of patients with a **clinically meaningful improvement in the NRS** (≥3-point change) through **30 months** of treatment
- Comparing **single-visit NRS** and weekly-averaged NRS in **ASSURE**

A ≥3-point improvement in the pruritus NRS score shown as clinically meaningful in RESPONSE (Kremer AE, et al. Poster presented at EASL 2025; May 7–10, 2025. Poster THU-277).
NRS, numeric rating scale; **PBC**, primary biliary cholangitis.

RESPONSE Baseline Characteristics of Pruritus NRS ≥4 Population

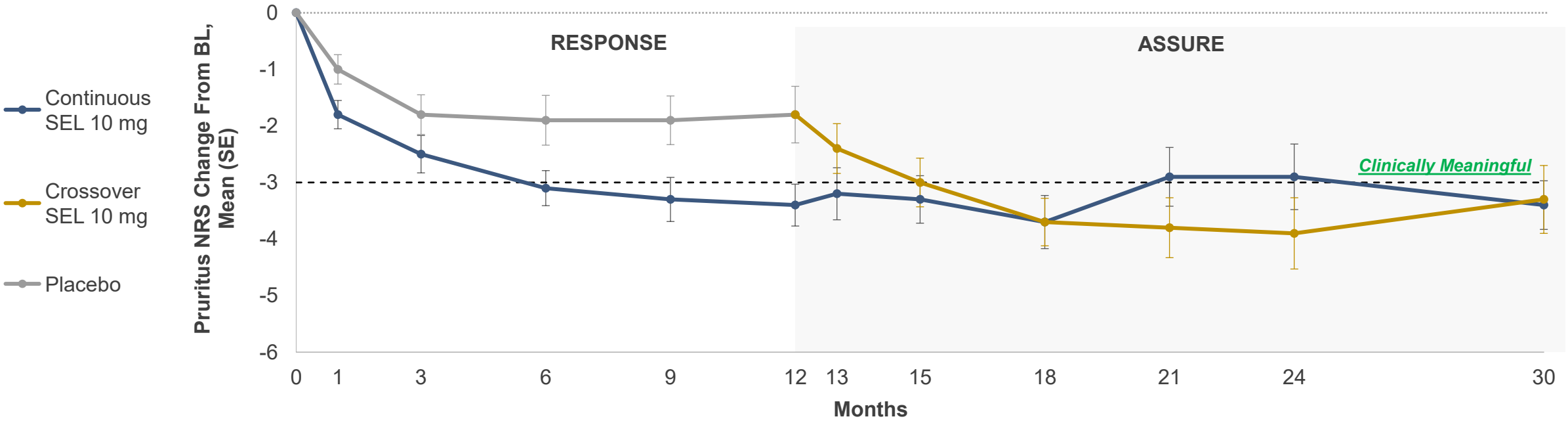
	Seladelpar 10 mg (n = 49)	Placebo (n = 23)
Age, years, mean (SD)	53.4 (10.7)	54.6 (10.3)
Female sex, n (%)	48 (98)	22 (96)
Race, n (%)		
American Indian or Alaska Native	2 (4)	2 (9)
Asian	1 (2)	1 (4)
Black or African American	1 (2)	0
White	44 (90)	20 (87)
Other	1 (2)	0
Pruritus NRS score, mean (SD)	6.1 (1.4)	6.6 (1.4)
5-D Itch total score, mean (SD)	16.2 (3.6)	16.4 (2.8)
PBC-40 itch domain score, mean (SD)	8.7 (2.7)	9.6 (2.6)

Baseline characteristics were well balanced between the seladelpar and placebo arms in patients with moderate to severe pruritus

Moderate to severe pruritus was defined as baseline pruritus NRS ≥4 at RESPONSE baseline. Among the patients with moderate to severe pruritus randomized into RESPONSE, 34 (seladelpar) and 18 (placebo) continued in ASSURE.
PBC, primary biliary cholangitis; **NRS**, numeric rating scale.

Pruritus NRS Scores With Seladelpar

Mean Change in NRS Score in Patients With Baseline Pruritus NRS ≥4



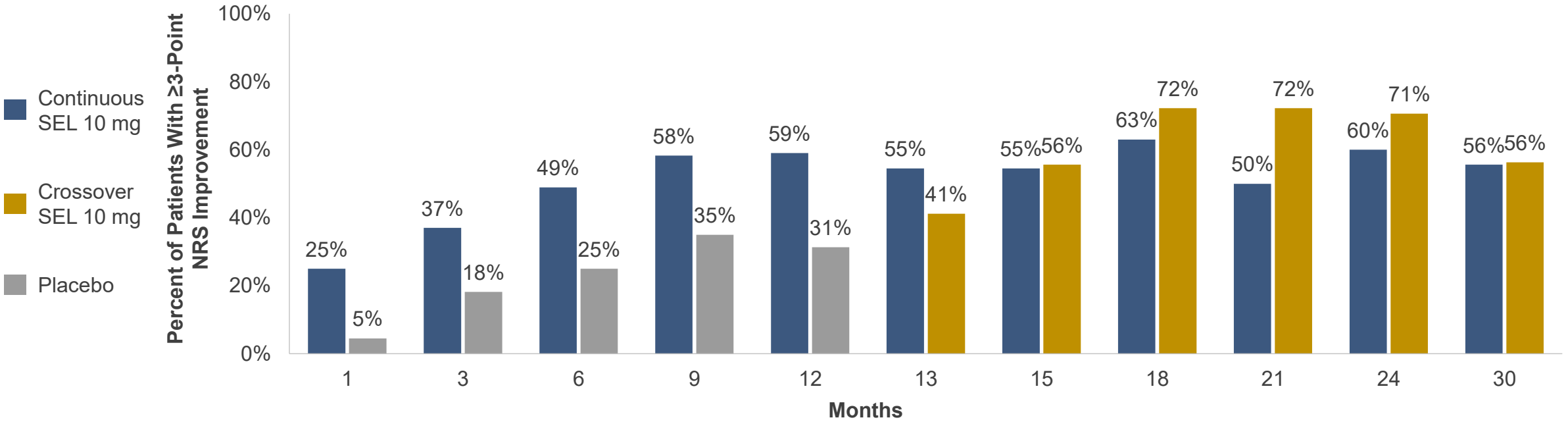
Continuous SEL 10 mg, n =	49	48	46	45	36	39	33	33	27	32	30	27
Crossover SEL 10 mg, n =							17	18	18	18	17	16
Placebo, n =	23	22	22	20	20	16						

The reduction in pruritus with seladelpar was persistent in patients with moderate to severe pruritus

n = number of evaluable patients at each time point. Moderate to severe pruritus was defined as baseline pruritus NRS ≥4 at RESPONSE baseline.
Pruritus NRS scores ranged from 0 to 10, with higher scores indicating worse itch. A ≥3-point improvement in the pruritus NRS score, shown by the dashed line, was previously shown as clinically meaningful in RESPONSE (Kremer AE, et al. Poster presented at: EASL 2025; May 7–10, 2025. Poster THU-277).
BL, baseline; **NRS**, numeric rating scale; **SEL,** seladelpar.

Clinically Meaningful Improvement in Pruritus With Seladelpar

NRS Improvement of ≥3 Points[a] in Patients With Baseline Pruritus NRS ≥4



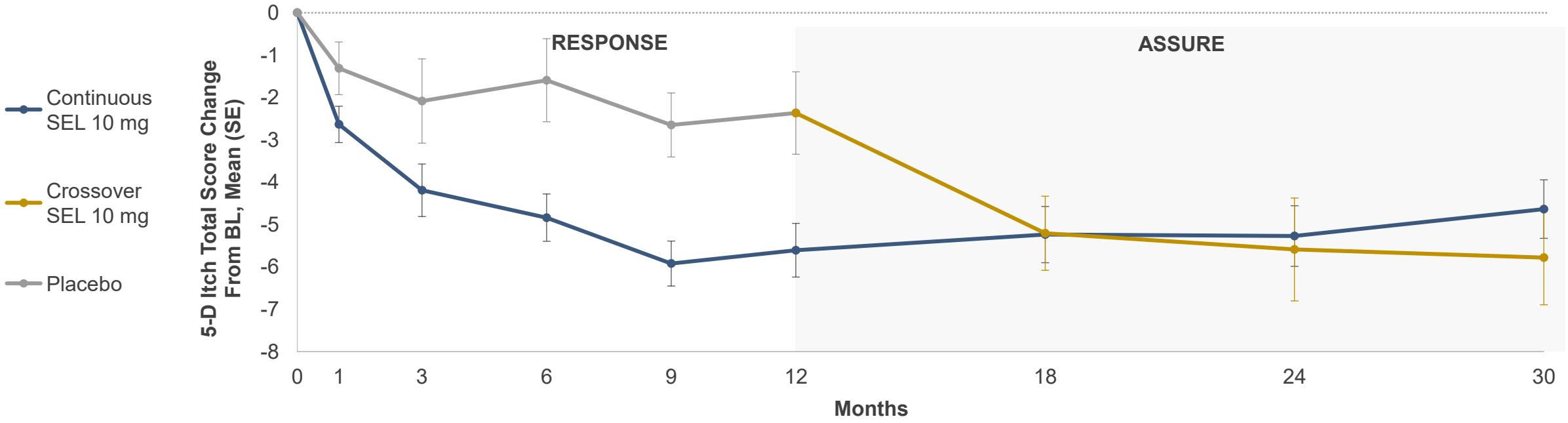
Continuous SEL 10 mg, n/N =	12/48	17/46	22/45	21/36	23/39	18/33	18/33	17/27	16/32	18/30	15/27
Crossover SEL 10 mg, n/N =						7/17	10/18	13/18	13/18	12/17	9/16
Placebo, n/N =	1/22	4/22	5/20	7/20	5/16						

Among patients with moderate to severe pruritus,
≥50% of patients achieved clinically meaningful improvement in pruritus up to 30 months

n/N = number of patients with ≥3-point NRS improvement / number of evaluable patients at each time point. Moderate to severe pruritus was defined as baseline pruritus NRS ≥4 at RESPONSE baseline.
[a]A ≥3-point improvement in the pruritus NRS score was previously shown as clinically meaningful in RESPONSE (Kremer AE, et al. Poster presented at: EASL 2025; May 7–10, 2025. Poster THU-277).
NRS, numeric rating scale; **SEL**, seladelpar.

5-D Itch Score With Seladelpar

Mean Change in 5-D Itch Total Score in Patients With Baseline Pruritus NRS ≥4



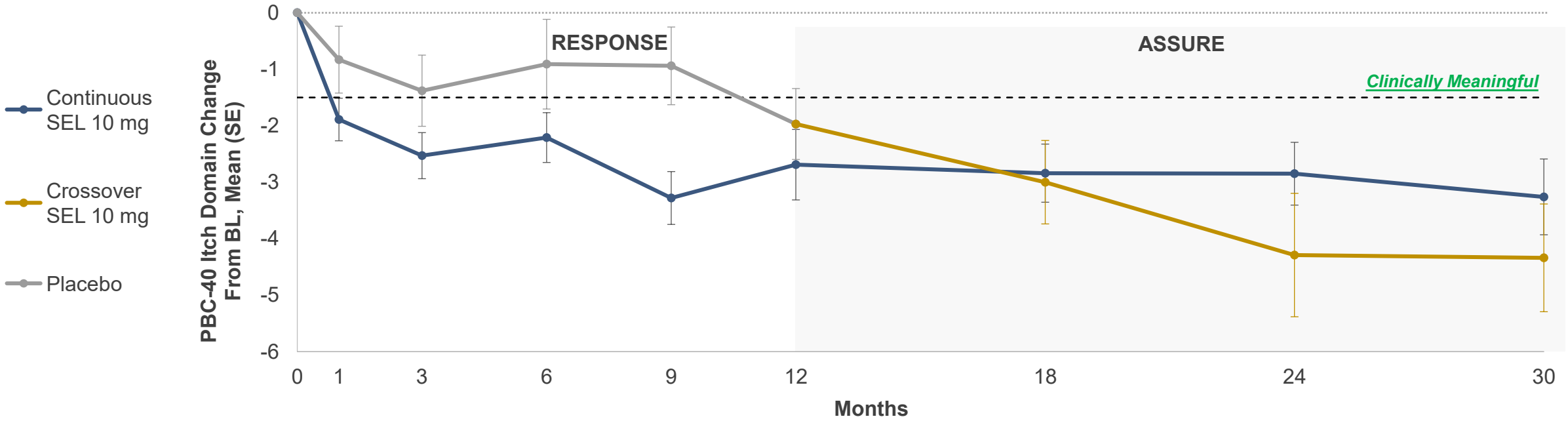
Continuous SEL 10 mg, n =	49	49	48	45	40	33	31	30	26
Crossover SEL 10 mg, n =							17	17	16
Placebo, n =	23	22	22	20	19	15			

5-D Itch total score was improved and persistent over time in patients with moderate to severe pruritus

n = number of evaluable patients at each time point. Moderate to severe pruritus was defined as baseline pruritus NRS ≥4 at RESPONSE baseline.
Each of the 5-D Itch domains was scored from 1 to 5, and the total score ranged from 5 to 25, with higher scores indicating increased itch severity.
BL, baseline; **NRS**, numeric rating scale; **SEL**, seladelpar.

PBC-40 Itch Domain Score With Seladelpar

Mean Change in PBC-40 Itch Score in Patients With Baseline Pruritus NRS ≥4



Continuous SEL 10 mg, n =	49	42	45	42	40	36	31	30	27
Crossover SEL 10 mg, n =							17	17	16
Placebo, n =	23	21	20	17	16	16			

PBC-40 itch score was improved and sustained in patients with moderate to severe pruritus up to 30 months

n = number of evaluable patients at each time point. Moderate to severe pruritus was defined as baseline pruritus NRS ≥4 at RESPONSE baseline.
PBC-40 itch domain scores ranged from 0 to 15, with higher scores indicating poorer quality of life. A meaningful response in a PBC-40 domain score was defined as a 0.5-point change from baseline per item. For the PBC-40 itch domain, which has 3 items, a meaningful response is shown by the dashed line (Jones D, et al. *Hepatol Commun.* 2023;7(3):e0057).
BL, baseline; **NRS**, numeric rating scale; **PBC**, primary biliary cholangitis; **SEL**, seladelpar.

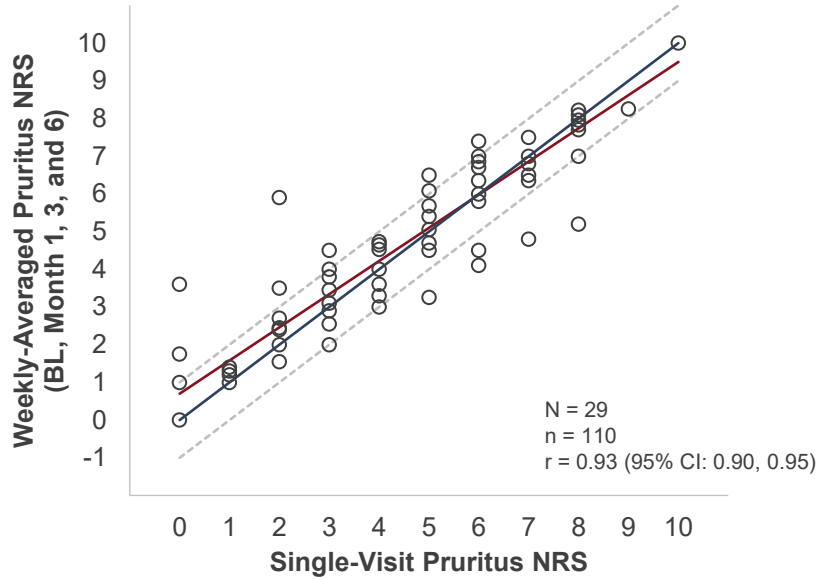
Comparing Single-Visit NRS and Weekly-Averaged NRS

- Patients with moderate to severe pruritus (baseline NRS ≥4) upon initiation of ASSURE were evaluated from baseline to month 6 in ASSURE
- Regression analysis between single-visit pruritus NRS and weekly-averaged NRS scores and plots over time were generated

NRS, numeric rating scale.

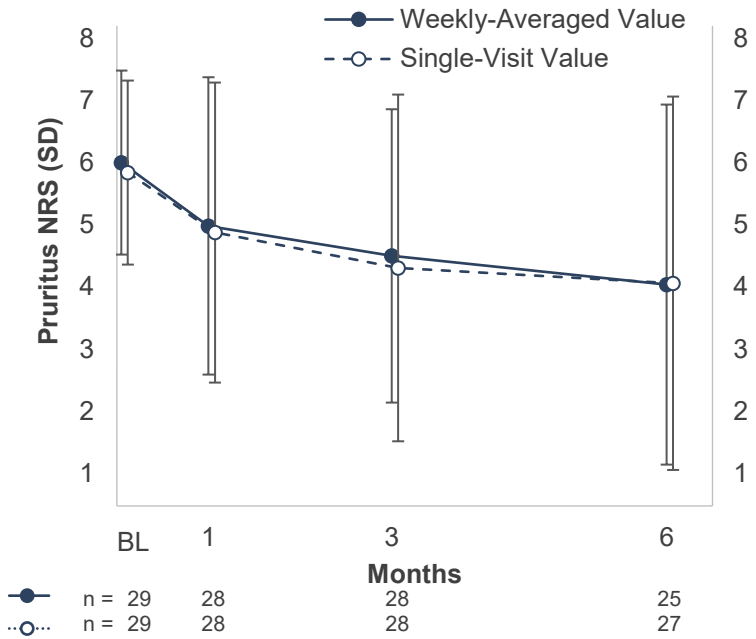
Comparability Between Single-Visit NRS and Weekly-Averaged NRS[a]

Regression Analysis Between Single-Visit and Weekly-Averaged Pruritus NRS Scores[b]



Single-visit and **weekly-averaged NRS scores** were **strongly correlated**[c]

Plot of Mean NRS Over Time Between Single-Visit and Weekly-Averaged NRS Scores



Single-visit and **weekly-averaged NRS scores** showed **strong agreement**

Single-visit NRS was comparable to weekly-averaged NRS in ASSURE

[a]Data included ASSURE baseline to month 6 among patients who had pruritus NRS ≥4 at ASSURE baseline. [b] Blue line: y=x; dotted lines: y=x±1; N = number of patients included in the analysis; n = number of data points; Spearman correlation (r) = 0.93 (95% CI: 0.90, 0.95). [C] Spearman correlations. A correlation coefficient between 0.10 and 0.30 implies a weak association, 0.31 to 0.50 indicates moderate convergent validity, and coefficients greater than 0.5 indicate strong convergent validity.
BL, baseline; **NRS**, numeric rating scale.

Conclusions

- **Seladelpar led to sustained, clinically meaningful improvement in pruritus** in ASSURE with up to 30 months of treatment
- **The improvement in pruritus was consistent** across pruritus NRS, 5-D Itch, and PBC-40 itch domain scores
- More than half of the patients with moderate to severe itch had **meaningful improvement in pruritus**
- A **single-visit NRS was comparable to weekly-averaged NRS** assessments in the ASSURE study

NRS, numeric rating scale; **PBC**, primary biliary cholangitis.

Acknowledgments

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