Topline Results From a New Analysis of the REGENERATE Trial of Obeticholic Acid for the Treatment of Nonalcoholic Steatohepatitis

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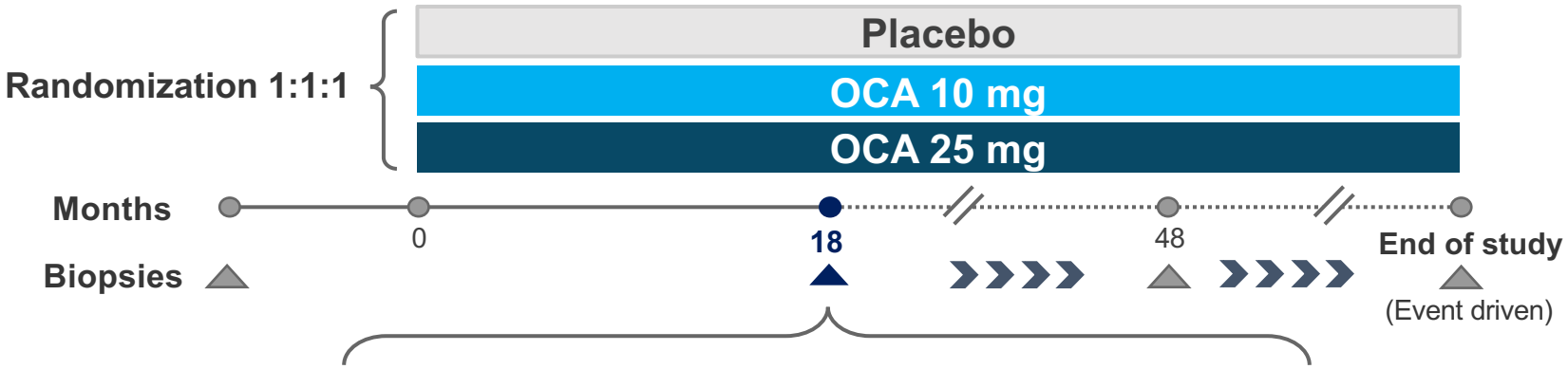
Current Status

- NDA resubmission for OCA for NASH was submitted on 22DEC2022
- NDA filing was accepted by FDA in January 2023
- Advisory Committee Meeting on 19MAY2023
- PDUFA action date is 22JUN2023

REGENERATE: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 3 Study (N=2477)

ITT=F2/F3 (n=2187); exploratory F1 cohort n=290



Planned month 18 interim analysis primary endpoints

Fibrosis improvement by ≥1 stage and no worsening of NASH

OR

NASH resolution and no worsening of fibrosis

Success at 18 months = achievement of at least 1 of these 2 primary endpoints

Intercept Pharmaceuticals [Protocol v11].
Abbreviations: ITT, intent-to-treat; NASH, nonalcoholic steatohepatitis; OCA, obeticholic acid.

REGENERATE/Study 303 Subject Retention

- Maintaining study integrity and ensuring the successful completion of REGENERATE is a top company priority
  - Study 303 has been ongoing for 6½ years
    - Last patient first visit was in September 2019
  - Patient retention stable at **~ 70%** for the past year
- Based on current modeling, the total number of clinical outcomes could be accrued as early as 2026

Research Article

JOURNAL OF HEPATOLOGY

Fibrosis stage but not NASH predicts mortality and time to development of severe liver disease in biopsy-proven NAFLD

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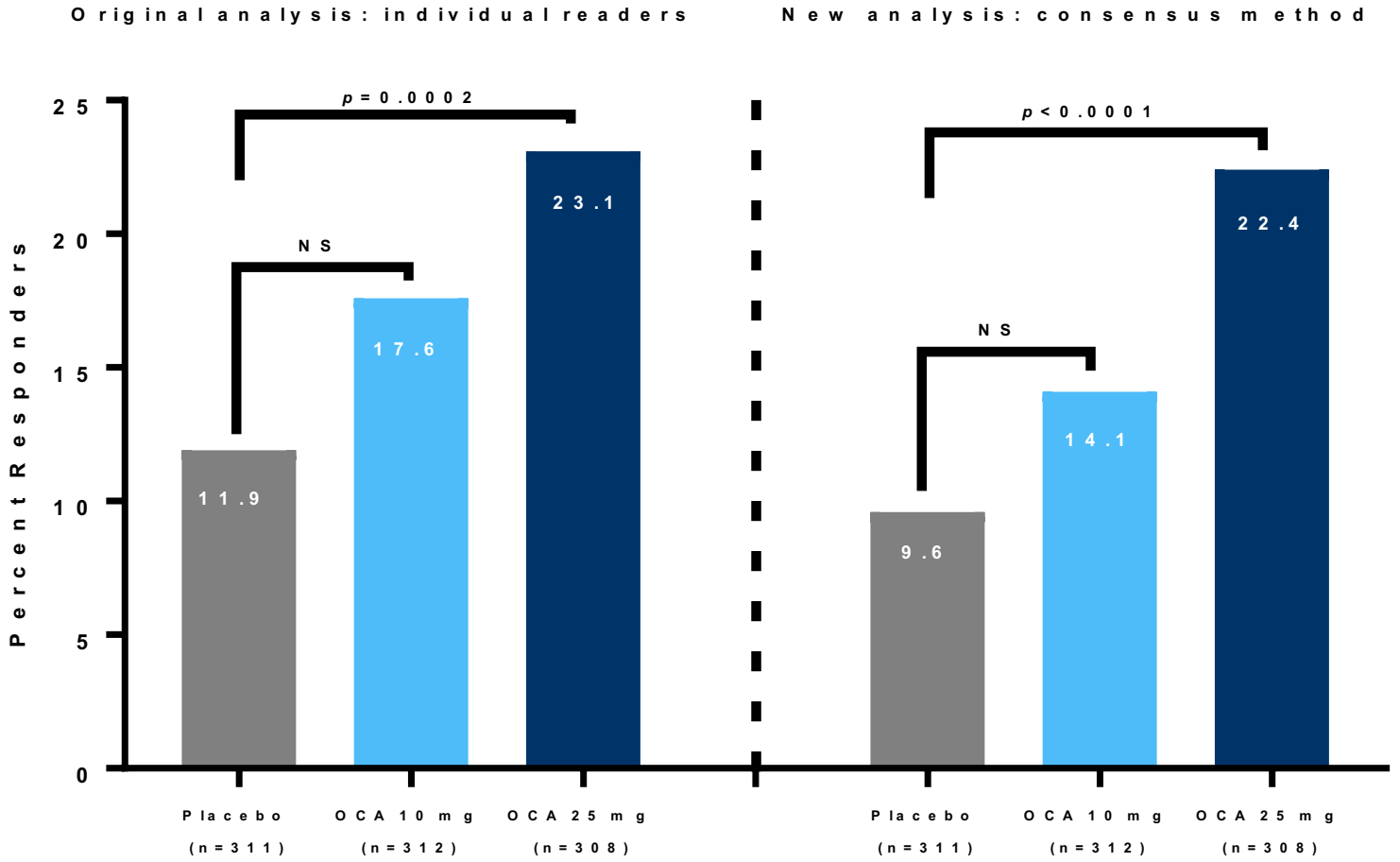
Consistent Dose-Dependent Improvement in Fibrosis Across Two Independent Methodologies (ITT Population, n=931)



The Regulatory Primary Endpoint:

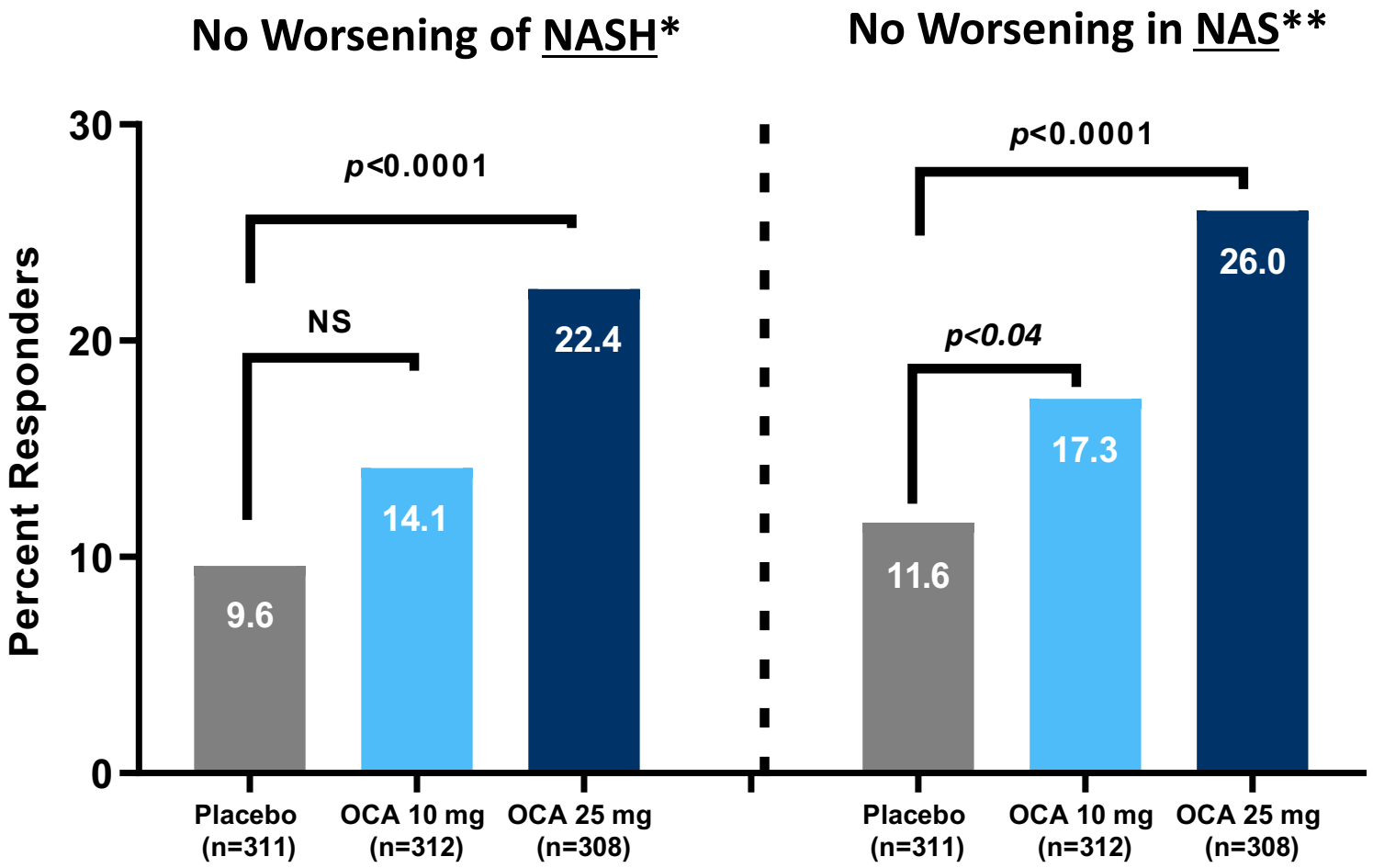
- Improved fibrosis stage

  +

- No worsening on ANY of 3 NAS components

Abbreviations: ITT, intent-to-treat; NAS, NAFLD Activity Score; OCA, obeticholic acid.

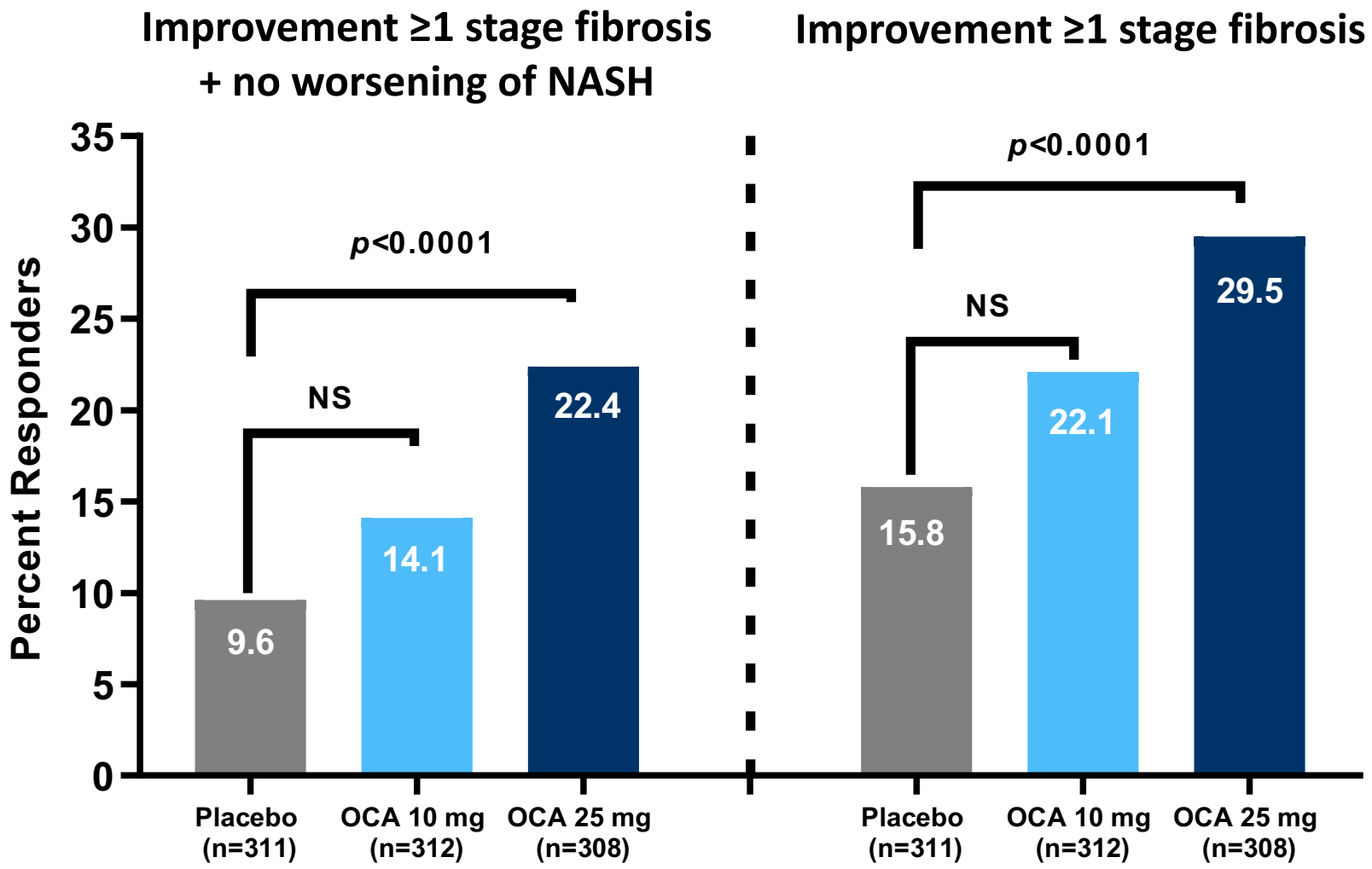
Higher Responder Rate for Anti-Fibrotic Primary Endpoint Using "No Worsening of NAS" compared to "No Worsening of NASH"



- *No worsening in any of the 3 NAS Components
- ** NAS = sum of ballooning, steatosis, and inflammation
- Missing or Not Evaluable Biopsies = Non-Responders
- Read by Consensus Method

Abbreviations: ITT, intent-to-treat; NAS, NAFLD Activity Score; OCA, obeticholic acid.

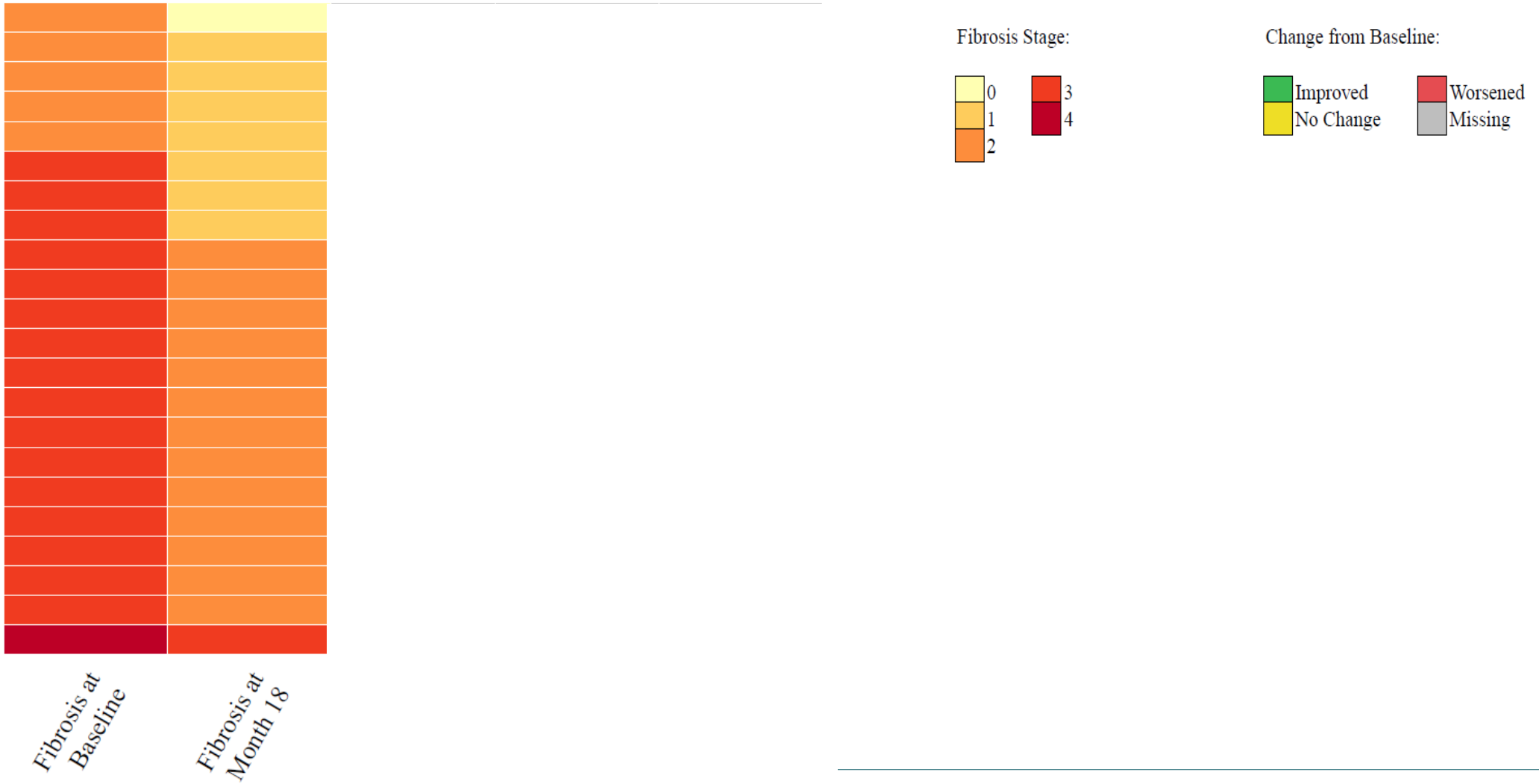
30% Responder Rate for Anti-Fibrotic Effect
Independent of NAS Parameters



- Missing or Not Evaluable Biopsies = Non-Responders
- Read by Consensus Method

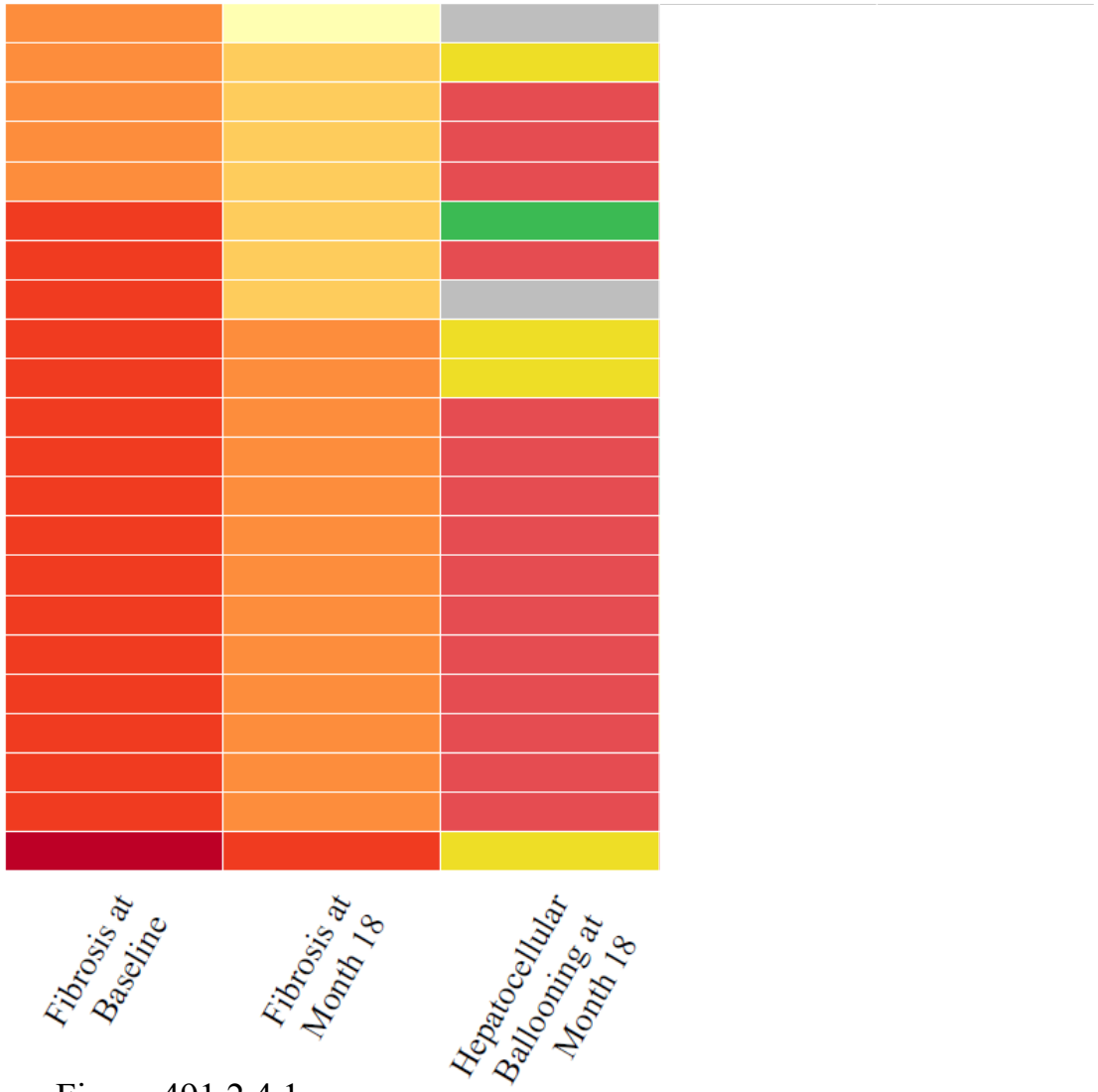
Abbreviations: ITT, intent-to-treat; OCA, obeticholic acid.

7% Subjects in OCA25 with ≥1 Fibrosis Stage Improvement Considered NON-Responders due to Worsening in NAS



Source Figure 491.2.4.1

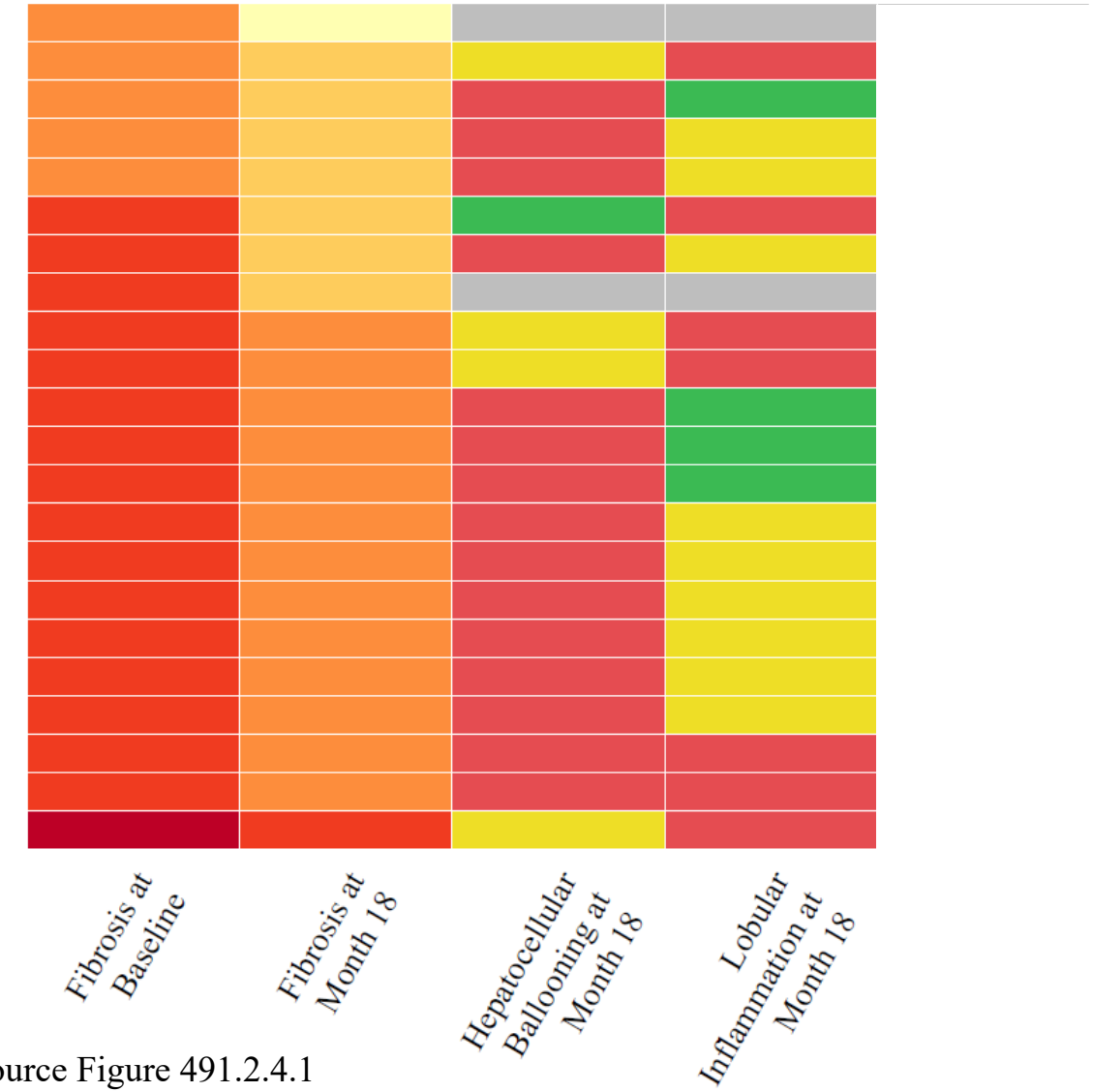
7% Subjects in OCA25 with ≥1 Fibrosis Stage Improvement Considered NON-Responders due to Worsening in NAS



Breakdown by Fib and NAS components – Consensus at M 18	Worsened	No Change	Improved	Missing
Hepatocellular Ballooning at M18	15	4	1	2

Source Figure 491.2.4.1

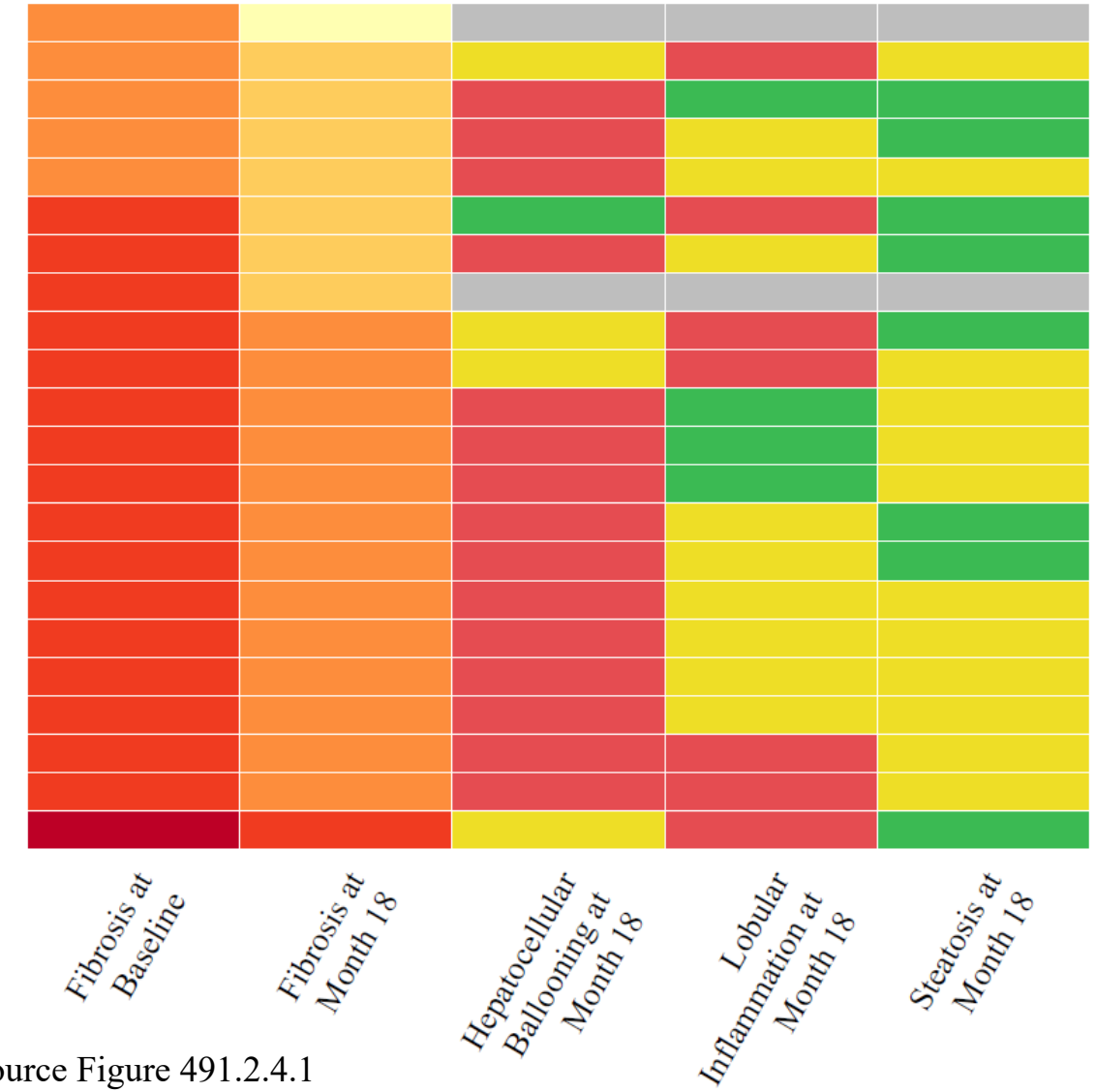
7% Subjects in OCA25 with ≥1 Fibrosis Stage Improvement Considered NON-Responders due to Worsening in NAS



Breakdown by Fib and NAS components – Consensus at M 18	Worsened	No Change	Improved	Missing
Hepatocellular Ballooning at M18	15	4	1	2
Lobular Inflammation at M18	7	9	3	2

Source Figure 491.2.4.1

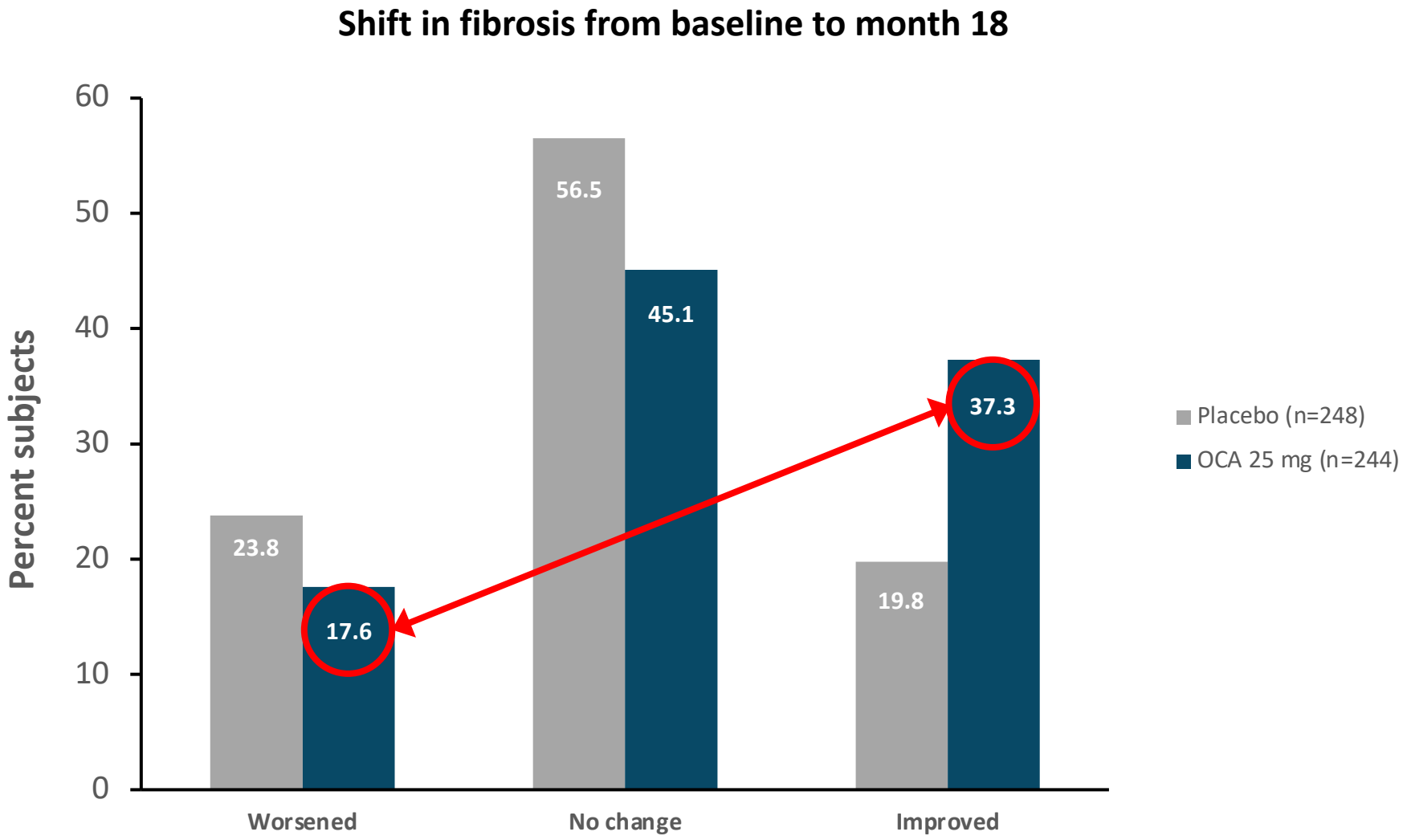
7% Subjects in OCA25 with ≥1 Fibrosis Stage Improvement Considered NON-Responders due to Worsening in NAS



Breakdown by Fib and NAS components – Consensus at M 18	Worsened	No Change	Improved	Missing
Hepatocellular Ballooning at M18	15	4	1	2
Lobular Inflammation at M18	7	9	3	2
Steatosis at M18	0	12	8	2

Source Figure 491.2.4.1

Shift in Fibrosis Stage at Month 18 in Subjects With Available Baseline and Month 18 Liver Biopsy

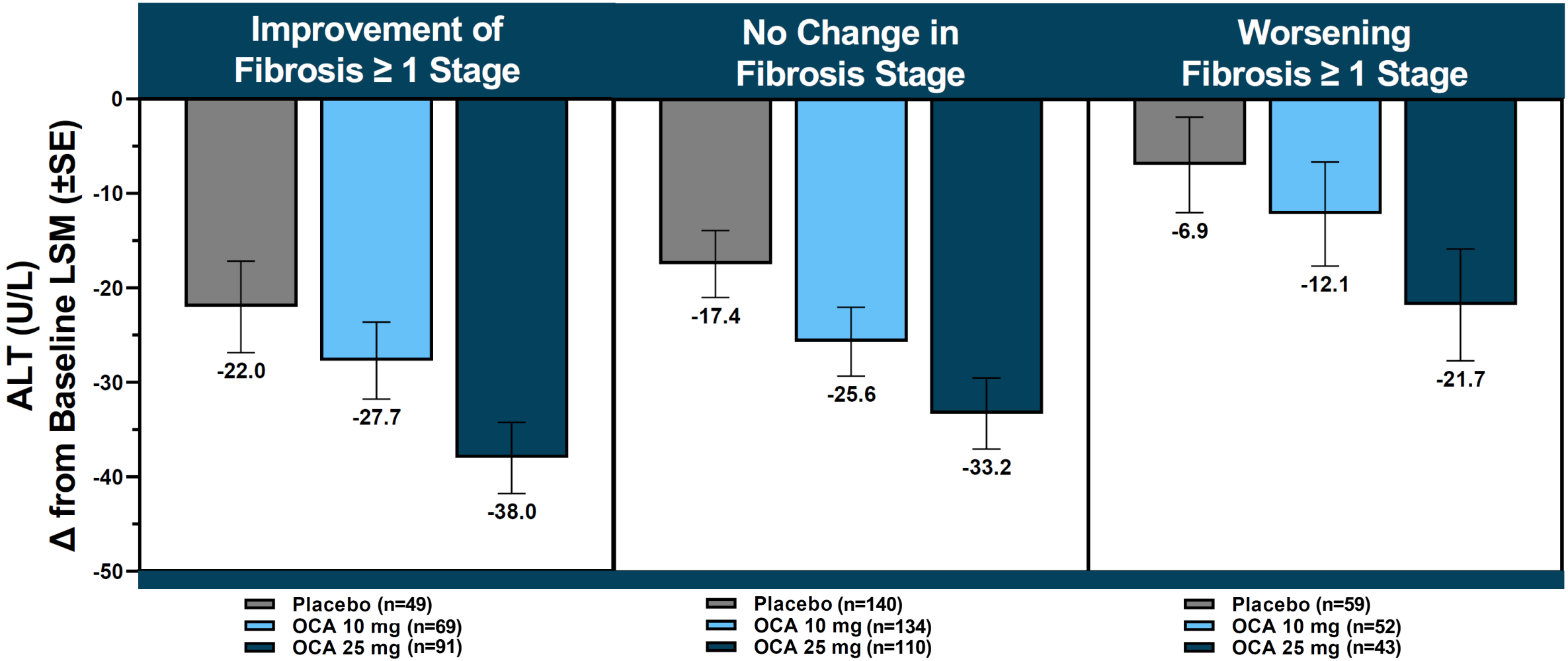


Abbreviation: OCA, obeticholic acid.

Intercept

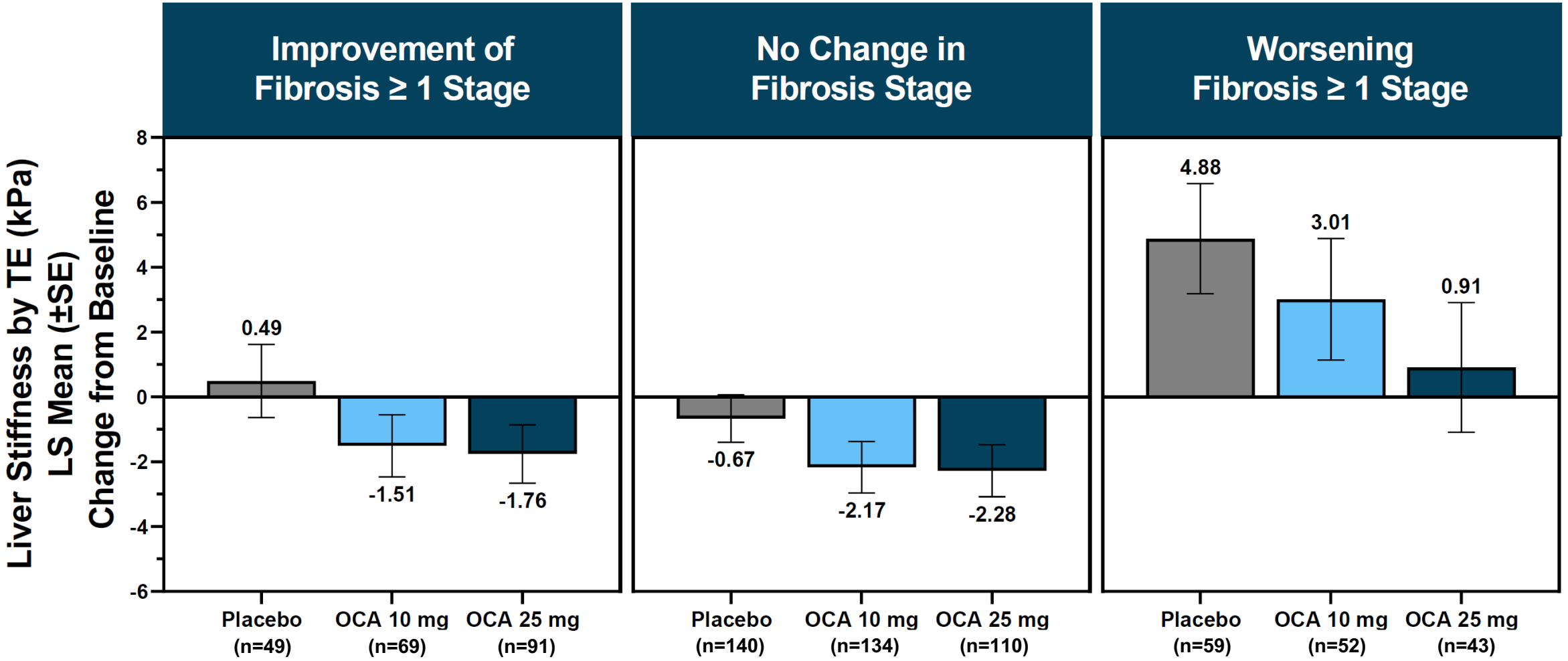
Thank you!

Dose-Dependent Reduction in ALT at Month 18 Regardless of Histologic Fibrosis Response (ITT Population, n=931)



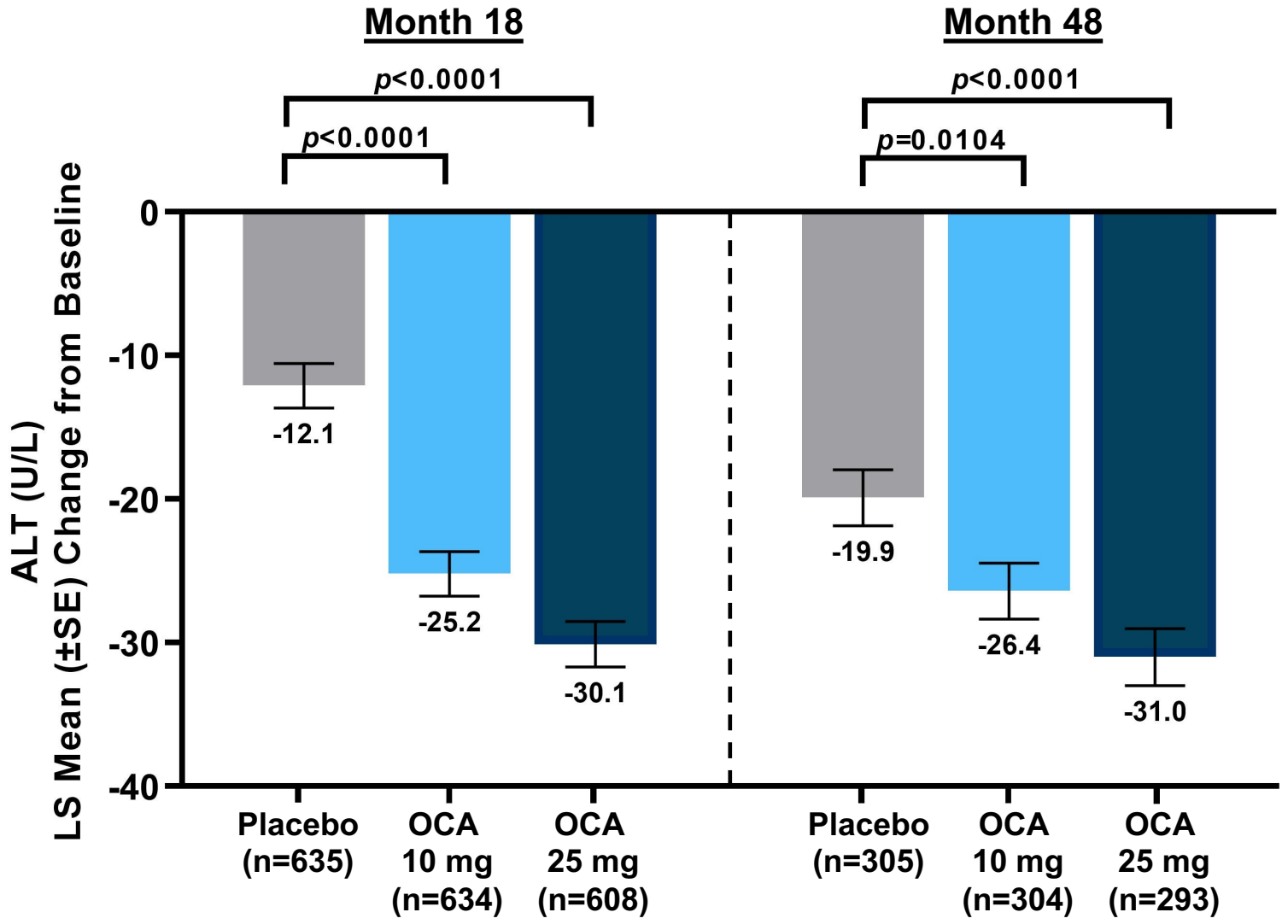
Abbreviations: ALT, alanine aminotransferase; ITT, intent-to-treat; LSM, least squares mean; OCA, obeticholic acid.

Improvements in Liver Stiffness at Month 18 in Subjects With Improvement of Fibrosis and No Change in Fibrosis (ITT Population, n=931)



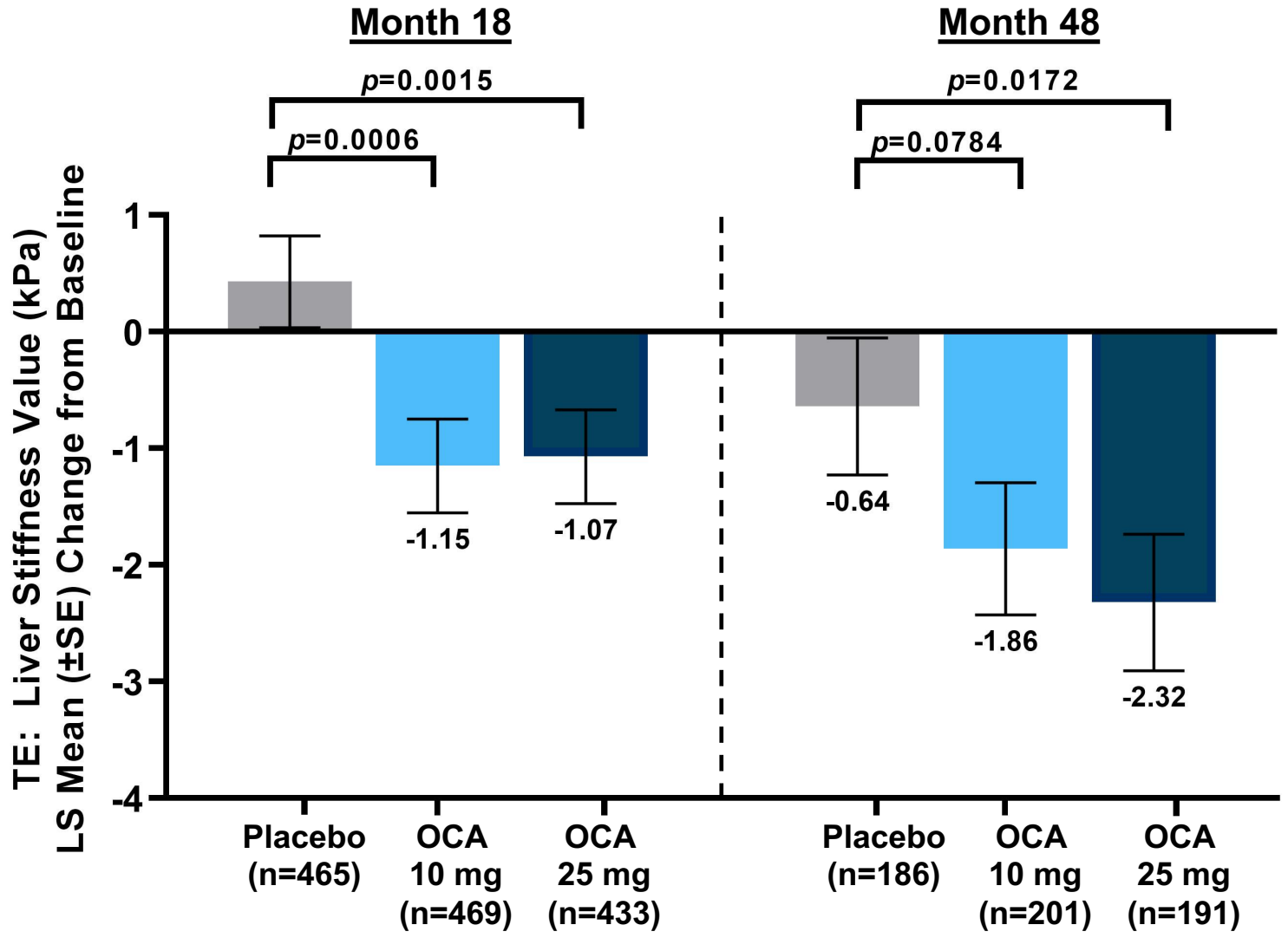
Abbreviations: ITT, intent-to-treat; LS, least squares; TE, transient elastography; OCA, obeticholic acid.

Dose-Dependent Reduction in ALT at Month 48 (ITT_all Population, n=2187)



Abbreviations: ALT, alanine aminotransferase; ITT, intent-to-treat; LS, least squares; OCA, obeticholic acid.

Dose-Dependent Reduction in Liver Stiffness at Month 48 (ITT_all Population, n=2187)



Abbreviations: ITT, intent-to-treat; LS, least squares; OCA, obeticholic acid; TE, transient elastography.