ENANTA Pharmaceuticals

ARGON-1

A Phase 2 dose ranging, randomized, double-blind and placebo-controlled study of EDP-305 in subjects with non-alcoholic steatohepatitis (NASH)

Topline Results

September 25, 2019

Forward Looking Statements Disclaimer

This presentation contains forward-looking statements concerning our NASH program, as well as our plans, objectives and expectations for EDP-305 and its development for NASH. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would," and other similar expressions that are predictions of or indicate future events and future trends, as well as other comparable terminology. All are forward-looking statements based on our management's current expectations, estimates, forecasts and projections about our business and the industry in which we operate and our management's beliefs and assumptions. These forward-looking statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. These risks and uncertainties include, among others: the development risks of early stage development efforts in the disease areas in Enanta's research and development pipeline, such as NASH; the impact of development, regulatory and marketing efforts of others with respect to competitive treatments for NASH; and Enanta's limited clinical development experience. As a result, any or all of our forward-looking statements in this presentation may turn out to be inaccurate.

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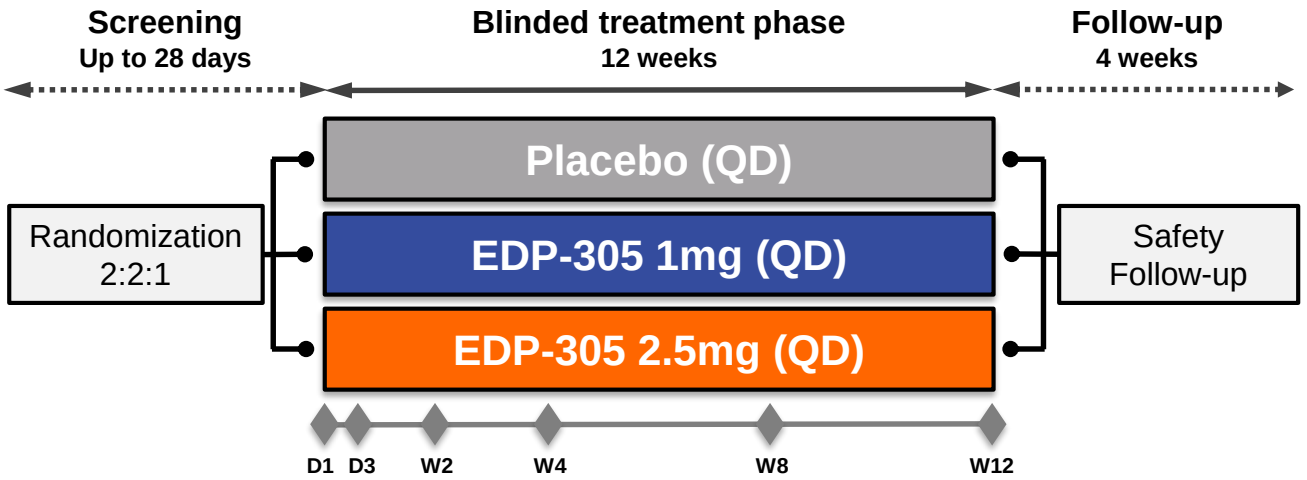
EDP-305
A Novel, Potent FXR Agonist

- NASH is considered the fastest-growing cause of cirrhosis, hepatocellular carcinoma and indication for liver transplantation
- EDP-305 is a potent, non-bile acid FXR receptor agonist [1-4]
  - Improvement in hepatocyte ballooning and overall NAFLD Activity Score (NAS) in the STAM™ and dietary-induced NASH (DIN) mouse models
  - Reduced liver fibrosis in multiple rodent models of fibrosis
    - *Mdr2*$^{-/-}$ mice, methionine- and choline-deficient diet, thioacetamide, and bile duct ligation
- In a 2-week Phase 1 study, EDP-305 was generally safe over a broad range of single and multiple doses with PK suitable for once daily oral dosing [5]
  - Doses were identified with significant target engagement of the FXR receptor that neither elicited adverse effects on lipids nor resulted in pruritus
  - >400 subjects exposed to EDP-305 across the entire program
- Fast Track Designation granted by FDA

ARGON-1 Study Design



- The primary objectives of the study were as follows:
  - To evaluate change in ALT levels at Week 12
  - To evaluate the safety and tolerability of EDP-305
- Key secondary objectives included:
  - Change in liver fat by MRI-PDFF
  - Change in lipids
  - Pharmacokinetics
  - Pharmacodynamic parameters: C4 and FGF19

Key Eligibility Criteria

Key Inclusion Criteria

- Histologic evidence on a historical liver biopsy within 24 months of screening consistent with NASH with fibrosis (no cirrhosis), and elevated ALT at screening

OR

- Phenotypic diagnosis of NASH based on elevated ALT (≥ 50 IU/L and ≤ 200 IU/L) and diagnosis of type 2 diabetes mellitus (T2DM)

AND

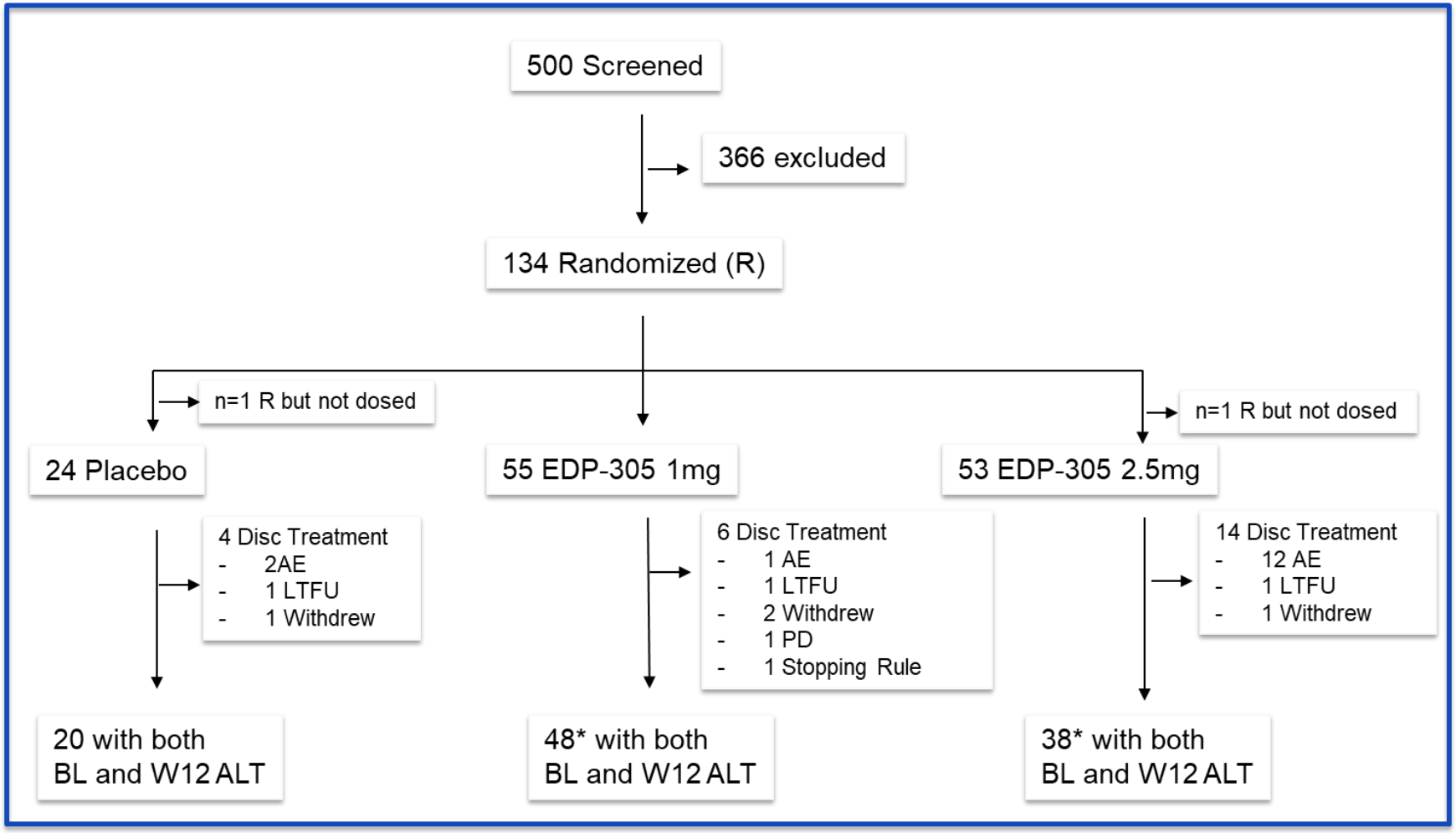
- Screening MRI-PDFF with >8 % steatosis

Key Exclusion Criteria

- Evidence of other chronic disease
- Any histology or clinical evidence of cirrhosis
- HbA1c ≥ 9%
- Prior use of OCA
- Use of a new statin regimen
- Use of a new antidiabetic regimen
- Significant alcohol consumption

NASH: non-alcoholic steatohepatitis ; ALT: alanine aminotransferase; MRI-PDFF: magnetic resonance imaging-proton density fat fraction; HbA1c: hemoglobin A1c; OCA: obeticholic acid

ARGON-1: Subject Disposition Efficacy Population, N=132



* n=1 in each arm with value assessed outside of visit window

R: randomized; Disc: discontinued; AE: adverse event; LTFU: lost to follow-up; BL: baseline; ALT: alanine aminotransferase

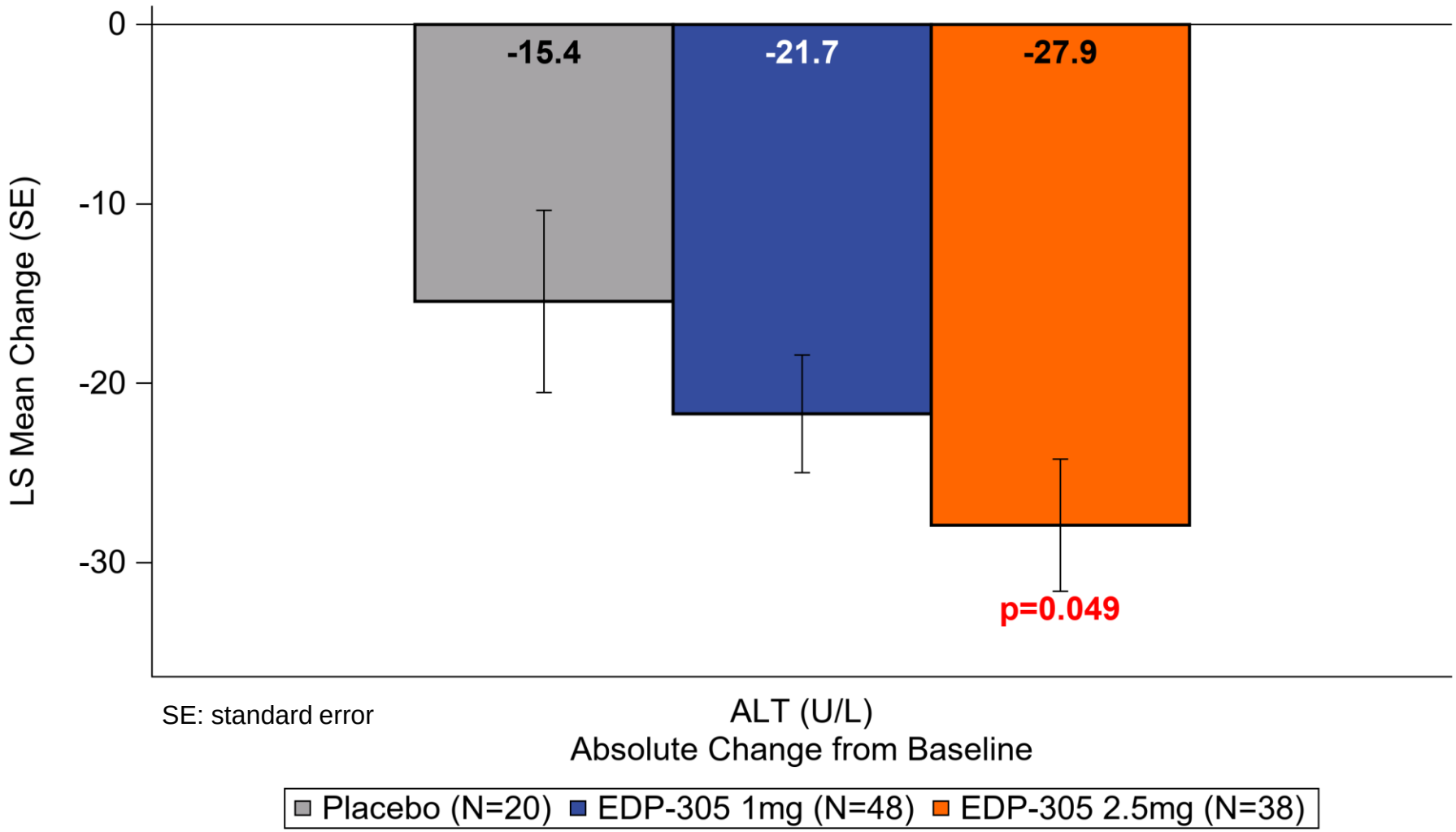
Demographic and Baseline Characteristics Efficacy Population

Characteristics	Placebo N=24	EDP-305 1 mg N=55	EDP-305 2.5 mg N=53
Age (years), mean (SD)	50.8 (10.5)	51.5 (12.0)	52.3 (11.8)
Female, n (%)	11 (45.8%)	29 (52.7%)	29 (54.7%)
White, n (%)	17 (70.8%)	42 (76.4%)	47 (88.7%)
Hispanic/Latino, n (%)	11 (45.8%)	22 (40.0%)	26 (49.1%)
BMI (kg/m^2), mean (SD)	36.1 (5.5)	34.5 (4.9)	33.8 (5.3)
ALT (U/L), mean (SD)	78.5 (22.2)	91.9 (35.5)	79.5 (25.8)
AST (U/L), mean (SD)	55.3 (29.2)	53.3 (24.9)	54.9 (29.2)
MRI-PDFF (%), mean (SD)	20.3 (8.7)	22.1 (7.6)	19.0 (7.9)
Concomitant medication use			
Antidiabetic	19 (79.2%)	39 (70.9%)	32 (60.4%)
Metformin	17 (70.8%)	35 (63.6%)	30 (56.6%)
Pioglitazone	1 (4.2%)	0	3 (5.7%)
Vitamin E	0	6 (10.9%)	4 (7.5%)
Antilipidemic	9 (37.5%)	25 (45.5%)	17 (32.1%)

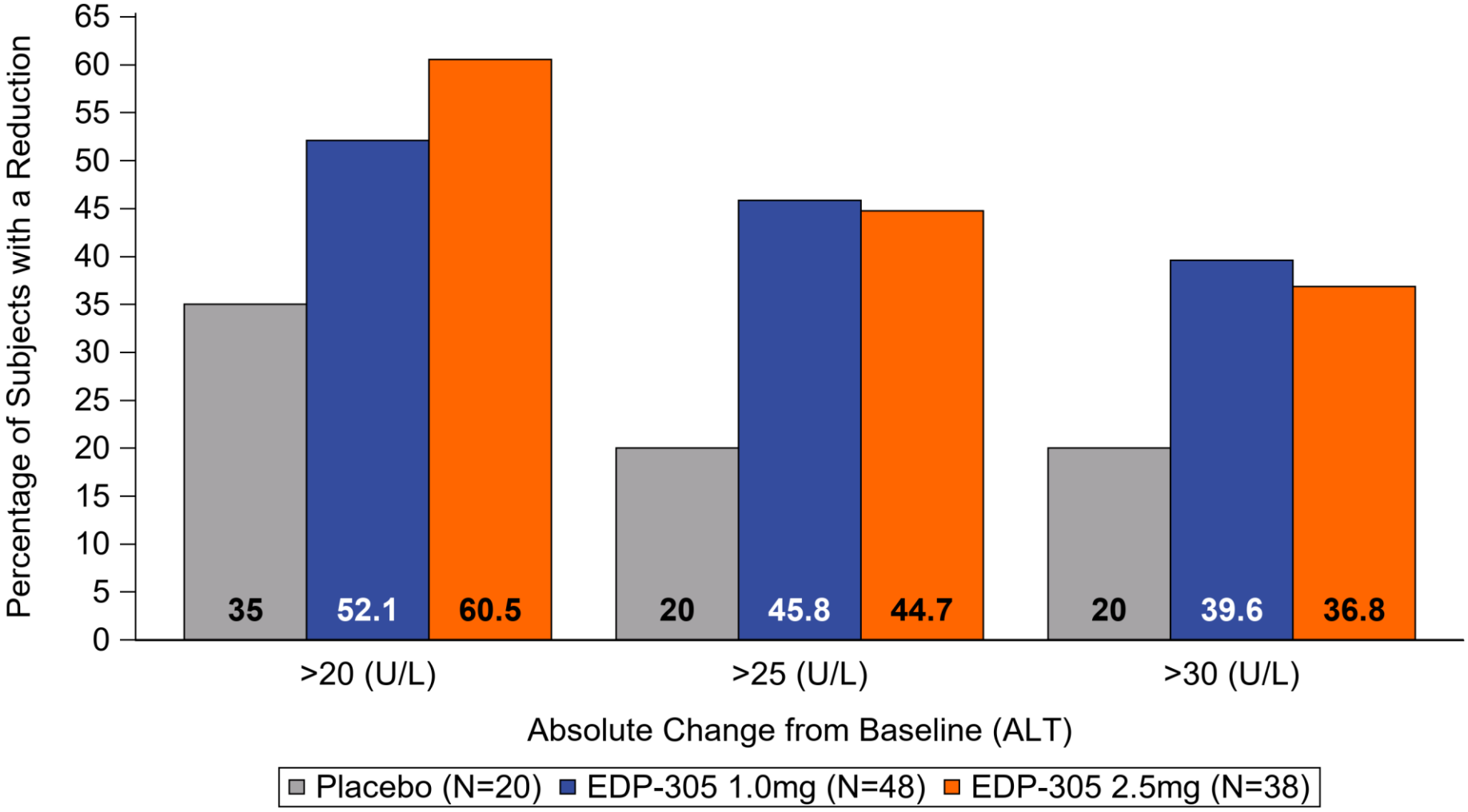
SD: standard deviation

ALT (U/L) Change at Week 12 - Efficacy Population

- **Primary Endpoint Was Met in the 2.5mg Arm**
- **Numerically Higher Reduction with 1mg Compared to Placebo**

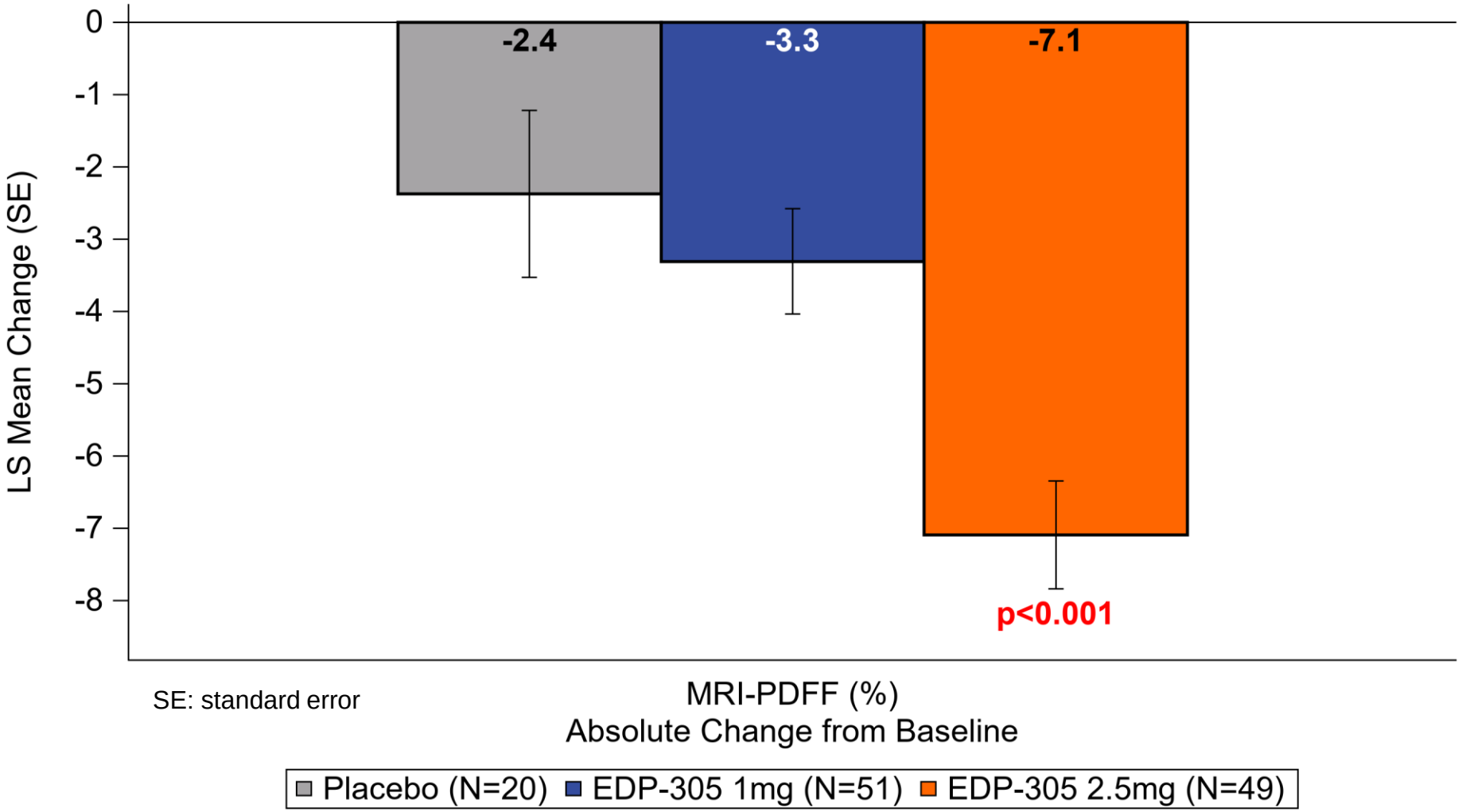


Proportion of Subjects with an Absolute Reduction in ALT (U/L) at Week 12
Efficacy Population



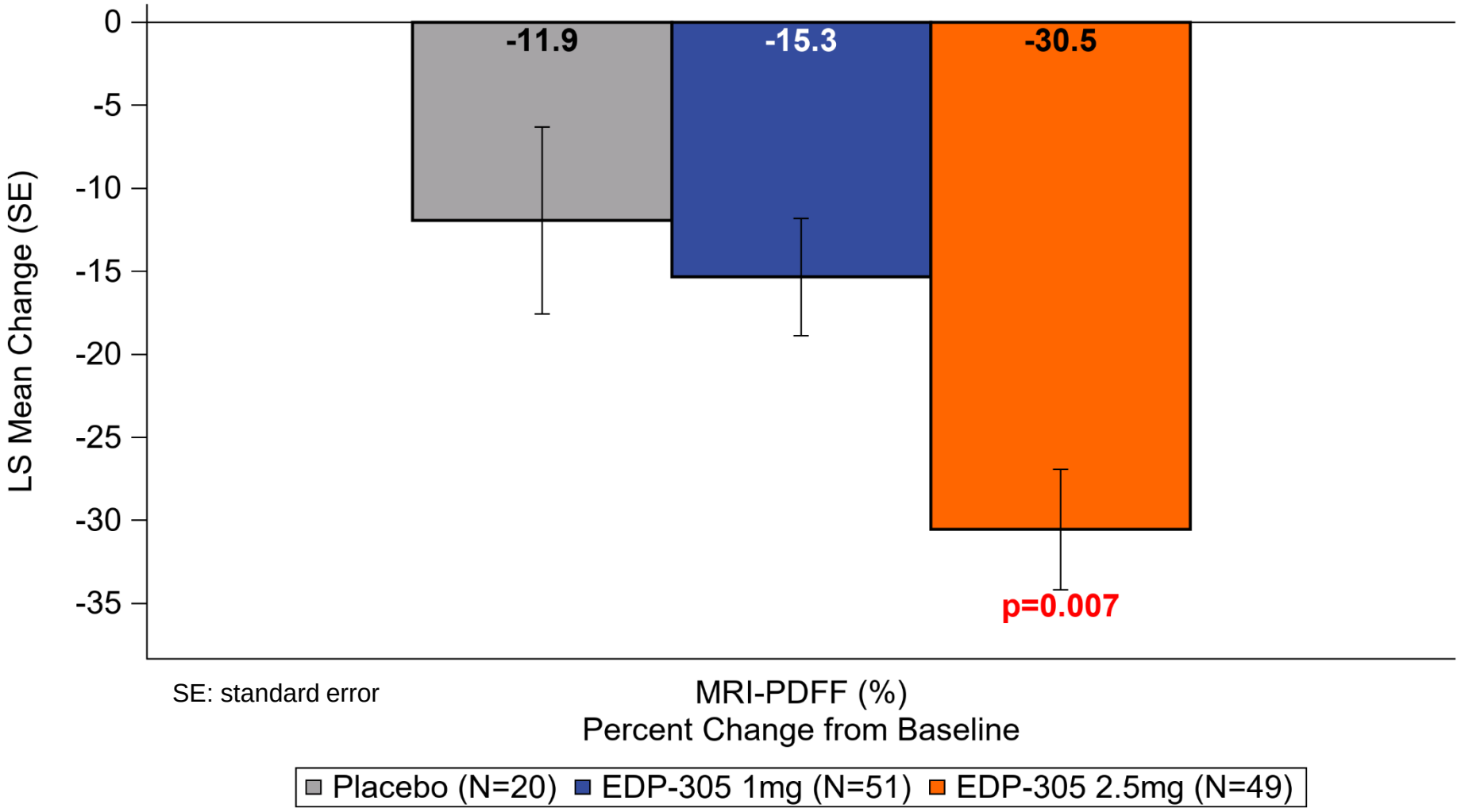
MRI-PDFF Absolute Change From Baseline at Week 12 Efficacy Population

Key Secondary Endpoint Was Met in the 2.5mg Arm

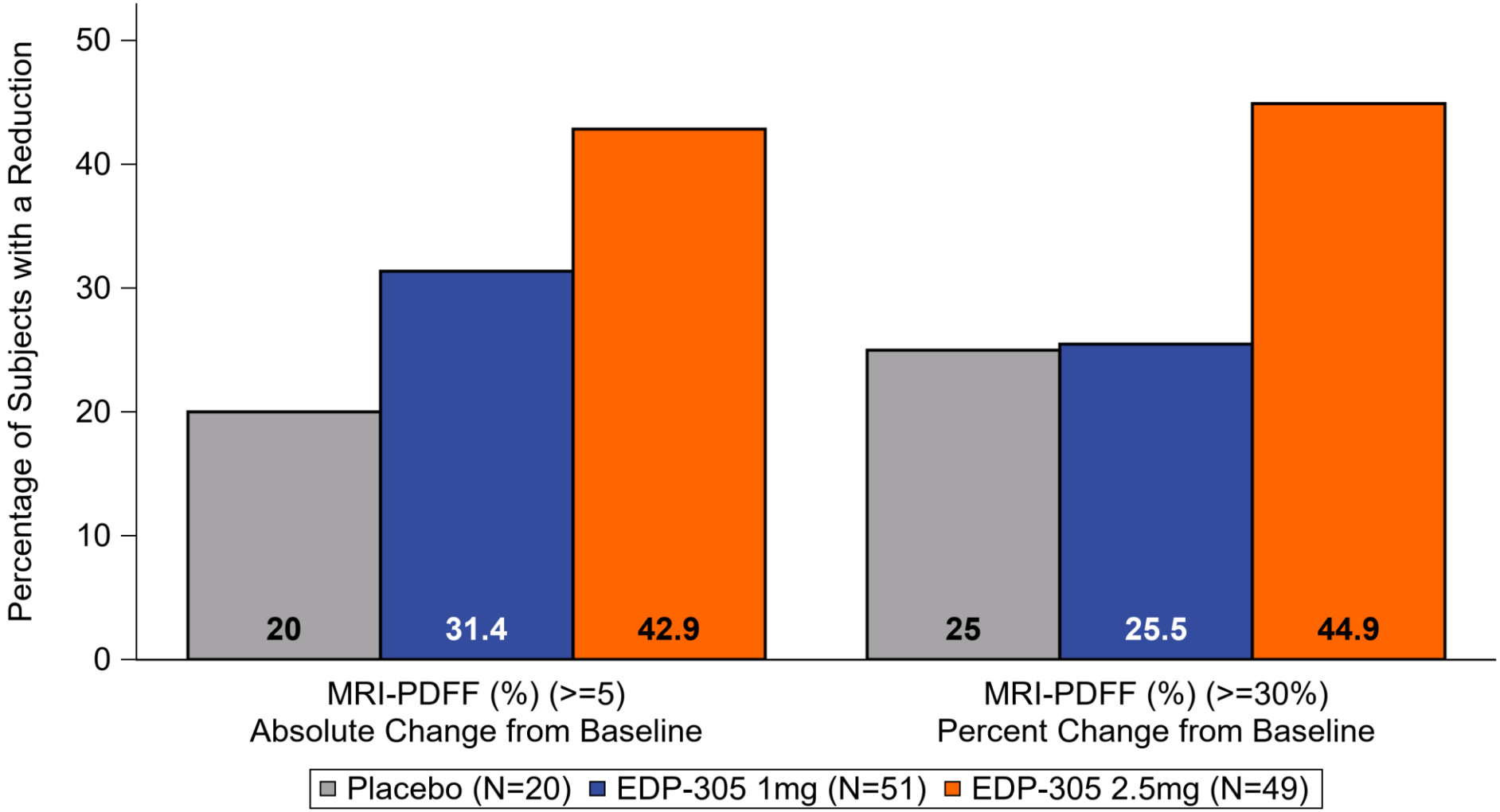


MRI-PDFF Percent Change From Baseline at Week 12 Efficacy Population

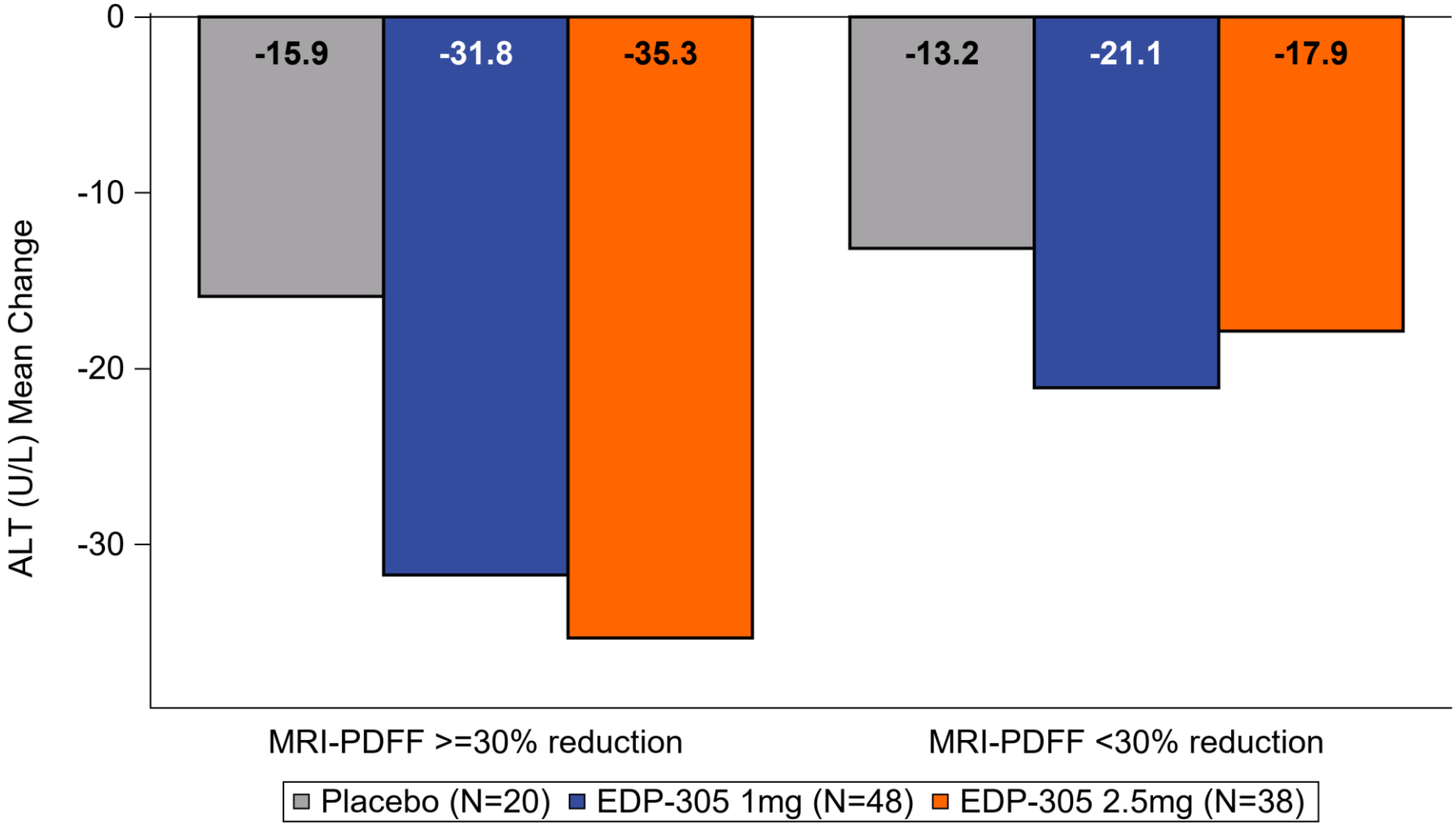
Key Secondary Endpoint Was Met in the 2.5mg Arm



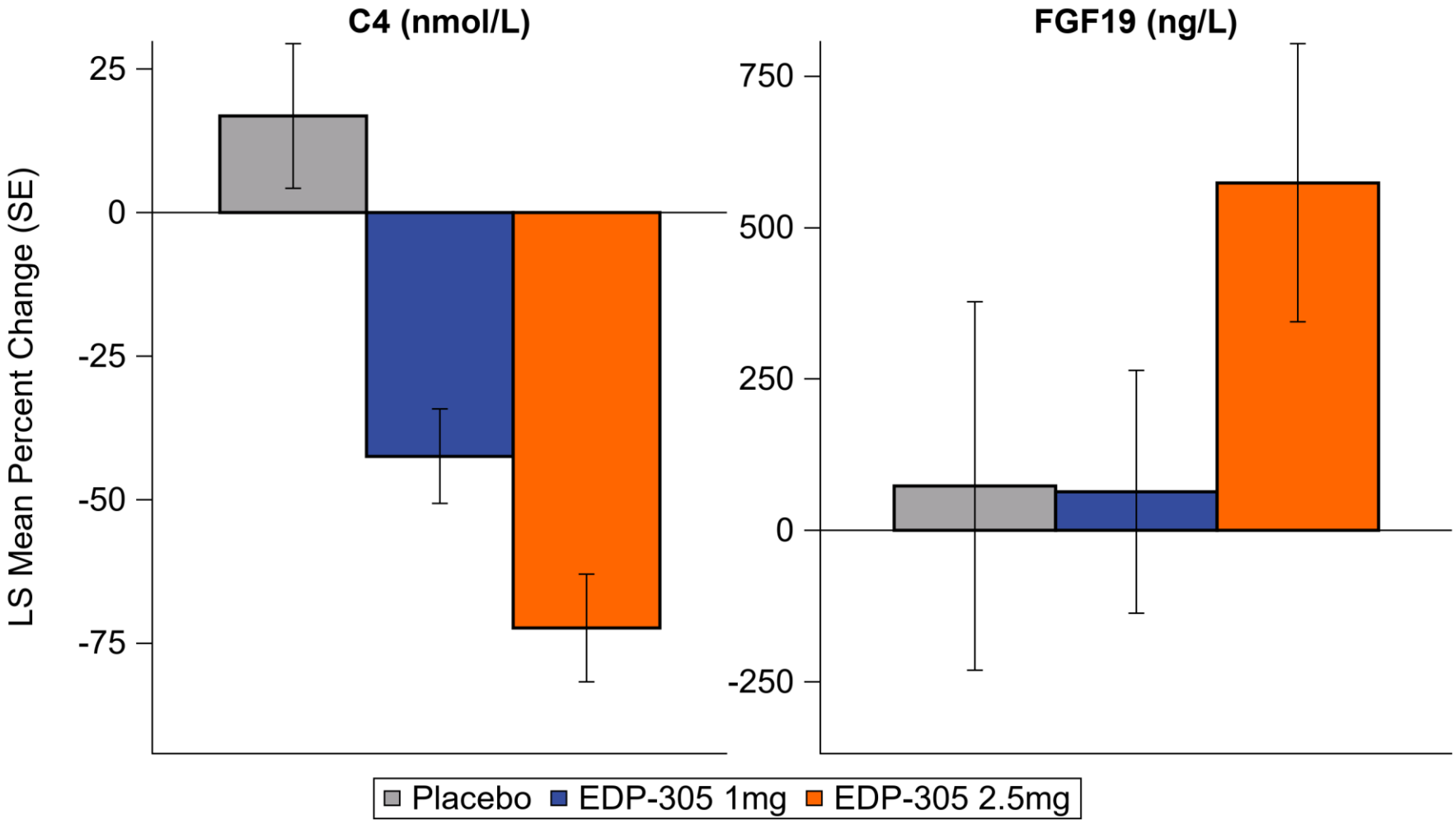
Proportion of Subjects with Relative Change From Baseline (Absolute and Percent) in Liver Fat Reduction (%) at Week 12 Efficacy Population



Mean Change in ALT by MRI-PDFF Response at Week 12 Efficacy Population

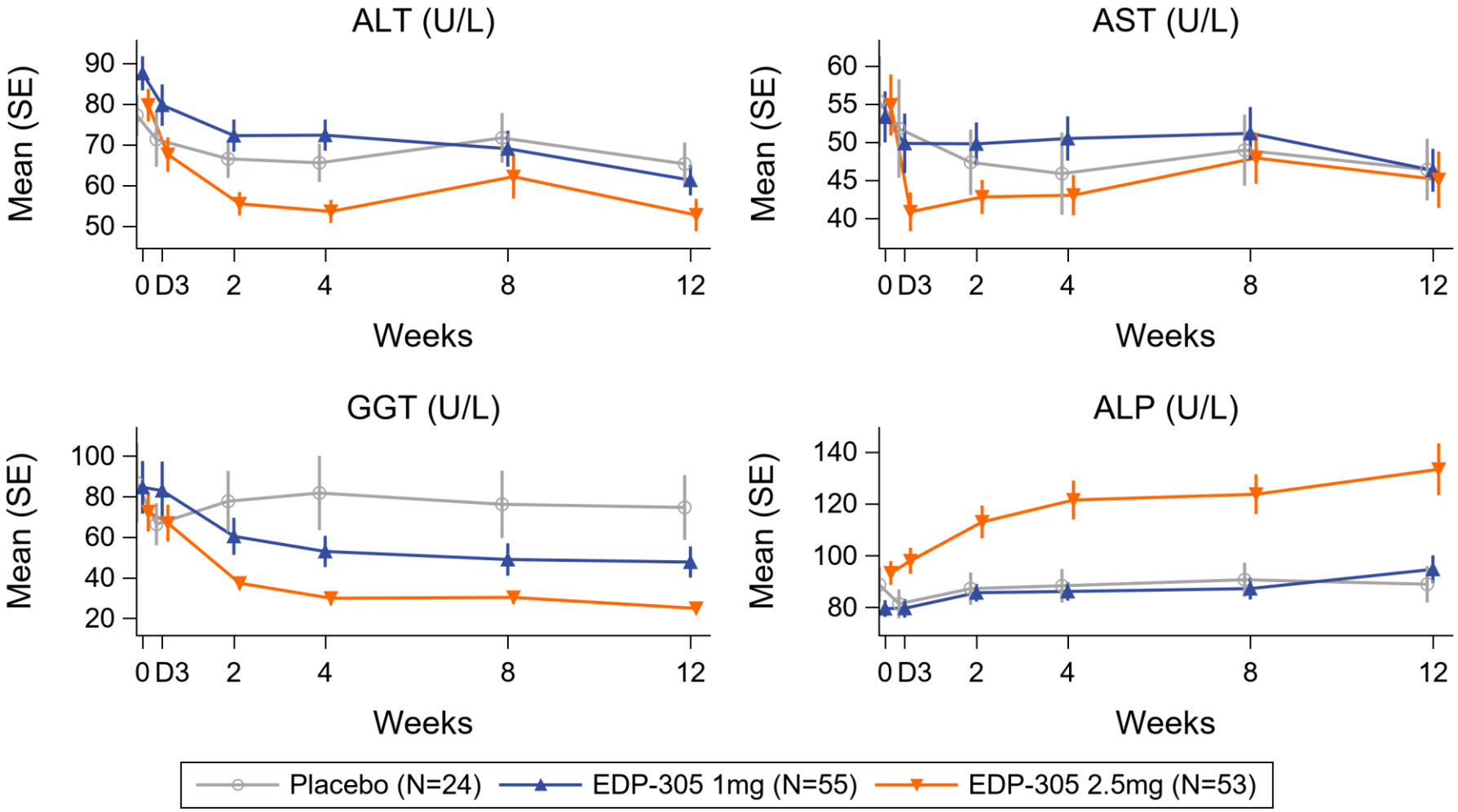


Percentage Change in C4 and FGF19 (Pre-dose) at Week 12 - Efficacy Population



SE: standard error

Response in Markers of Liver Injury and Target Engagement (ALP)
Efficacy Population



SE: standard error

Summary of Treatment-Emergent Adverse Events Safety Population

Subjects, n (%)	Placebo N=24	EDP-305 1mg N=55	EDP-305 2.5mg N=53
Number of Subjects with any TEAE	12 (50.0%)	32 (58.2%)	39 (73.6%)
• Subjects with any Severe TEAE	3 (12.5%)	2 (3.6%)	2 (3.8%)
• Subjects with any Serious TEAE	1 (4.2%)	1 (1.8%)	0
• Subjects with any TEAE Leading to Study Drug Discontinuation	2 (8.3%)	1 (1.8%)	12 (22.6%)
– Pruritus generalized	0	1 (1.8%)	11 (20.8%)
– Rash	0	0	1 (1.9%)
– Vomiting	1 (4.2%)	0	0
– Cerebrovascular accident	1 (4.2%)	0	0

- TEAEs were mostly mild to moderate in severity
- Severe TEAEs were more frequent in placebo arm
- No SAEs occurred in EDP-305 2.5mg arm
- Majority of discontinuations occurred in EDP-305 2.5mg arm
  - All were due to moderate pruritus (=11) or moderate rash (n=1)

TEAE: treatment-emergent adverse event

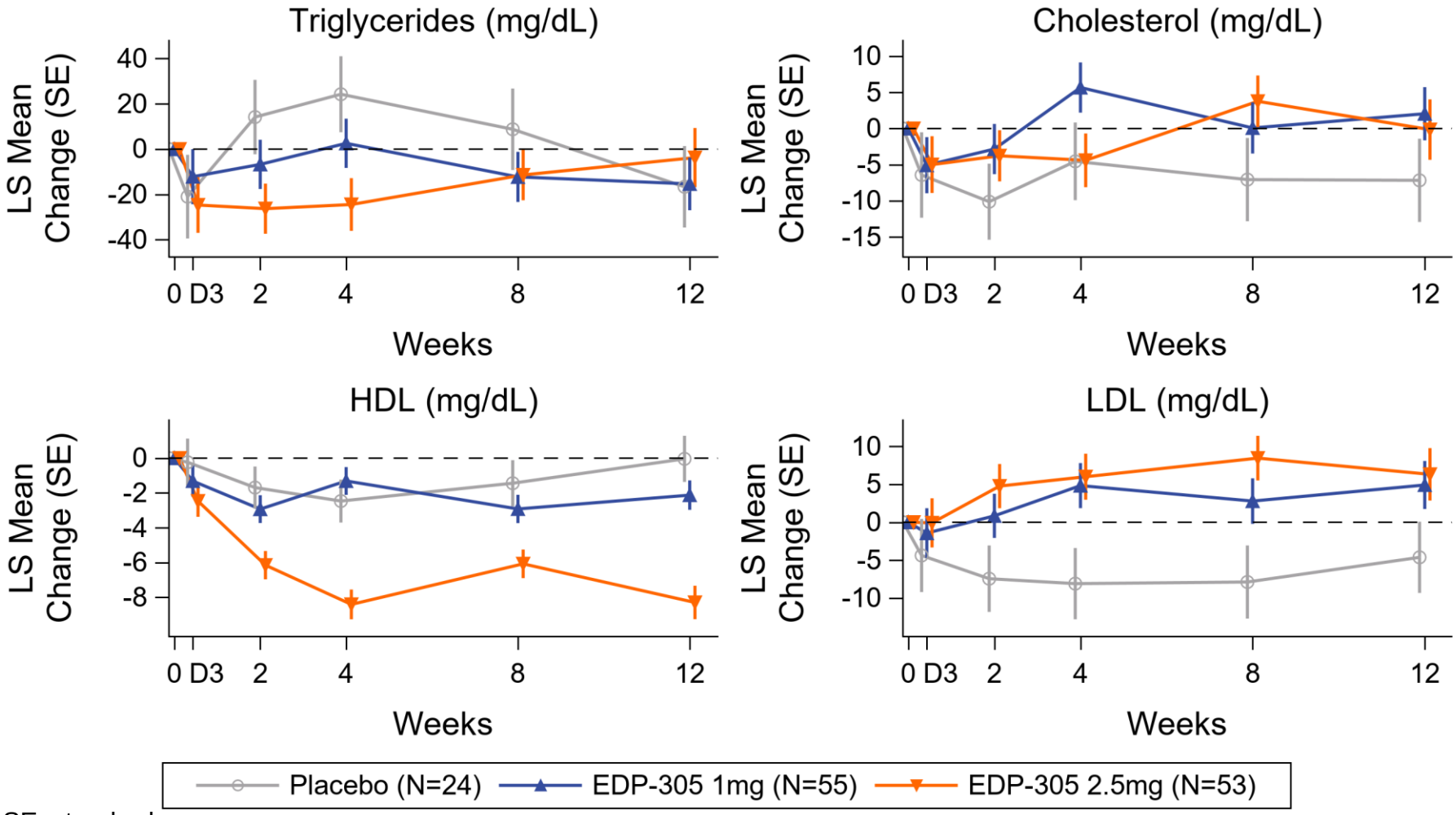
Most Frequent Treatment-Emergent Adverse Events
Events Occurring in ≥ 5% of Subjects in Any Treatment Arm
Safety Population

N (%)	Placebo N=24	EDP-305 1mg N=55	EDP-305 2.5mg N=53
Pruritus generalized	1 (4.2%)	5 (9.1%)	25 (47.2%)
Rash	0	1 (1.8%)	4[a] (7.5%)
Pruritus [c]	1 (4.2%)	0	3[b] (5.7%)
Nausea	1 (4.2%)	3 (5.5%)	2 (3.8%)
Diarrhea	0	2 (3.6%)	3 (5.7%)
Vomiting	2 (8.3%)	1 (1.8%)	1 (1.9%)
Urinary tract infection	0	3 (5.5%)	1 (1.9%)
Headache	2 (8.3%)	2 (3.6%)	2 (3.8%)
Dizziness	1 (4.2%)	3 (5.5%)	1 (1.9%)
Decreased appetite	0	3 (5.5%)	1 (1.9%)
Cough	0	1 (1.8%)	3 (5.7%)
Fatigue	2 (8.3%)	2 (3.6%)	2 (3.8%)

- Most frequent TEAEs were mild to moderate in severity
- TEAEs are consistent with the observed safety profile of EDP-305 in >400 subjects exposed to the drug to date

[a] *Three of the 4 subjects are also counted in pruritus generalized*
[b] *Two of the 3 subjects reported intermittent local and generalized pruritus and are also counted in pruritus generalized*
[c] *Localized*

Lipid Values (mg/dL) Over Time
Efficacy Population



SE: standard error

Summary of ARGON-1 Study Efficacy

Primary (ALT change) and key secondary (MRI-PDFF) endpoints were met at week 12

- EDP-305 2.5mg achieved statistically significant ALT change
  - Mean reduction of ~28 U/L *vs.* 15 U/L in pbo group ($p<0.05$)
  - Numerically higher reduction with 1mg (~22 U/L) *vs.* pbo
- A statistically significant reduction in liver fat by MRI-PDFF with EDP-305 2.5mg ($p<0.001$)
  - 45% of subjects were MRI-PDFF responders (i.e. ≥30% fat reduction)
- EDP-305 exhibited strong target engagement as shown by reductions in C4, and increases in FGF-19 and ALP
  - Robust reduction in marker of liver injury, GGT

Summary of ARGON-1 Study Safety and Tolerability

- EDP-305 regimens were generally safe in patients with NASH for up to 12 weeks with the majority of TEAEs being mild to moderate
  - The most common (≥5%) TEAEs included pruritus, GI related symptoms (nausea, vomiting, diarrhea), headache and dizziness
  - Consistent safety profile observed in >400 subjects exposed to EDP-305 up to 12 weeks
  - Incidence of treatment discontinuation due to pruritus was 1.8% for 1mg and 20.8% for 2.5mg
- Treatment with EDP-305 was associated with a small numeric absolute changes in lipids at week 12 relative to baseline

Next Steps

- Progress EDP-305 into a Ph2b NASH study called ARGON-2
  - Randomized, placebo-controlled in liver biopsy-proven NASH patients
  - 72-week treatment duration

Currently planning two doses versus placebo:

- Dose 1 (TBD) is designed to push for maximal efficacy in terms of histologic improvement
  - Based on ARGON-1, we expect to see some pruritus at this dose, but we also expect it to be manageable in the majority of these patients
- Dose 2 (TBD) is designed to offer a balanced profile in terms of efficacy and tolerability
  - Potential dose to explore in combinations for NASH while ARGON-2 is on-going

Acknowledgments

- We extend our thanks to the subjects who participated in this study, the Investigators and the site personnel for their conduct of the study

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