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Pharmaceuticals



A Phase 2 dose ranging, randomized, double-blind and placebo-controlled study of EDP-305 in subjects with primary biliary cholangitis (PBC) with or without an inadequate response to ursodeoxycholic acid (UDCA)

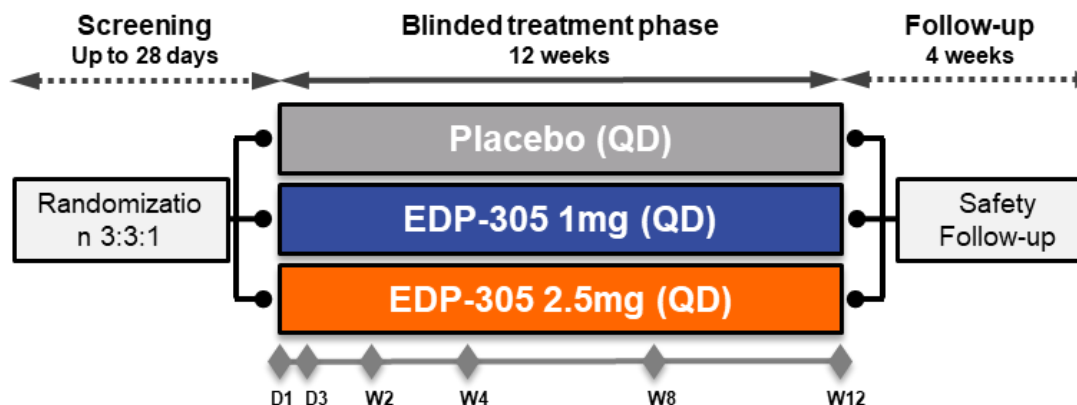
Topline Results

06MAY2020

Forward Looking Statements Disclaimer

This presentation contains forward-looking statements concerning 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. Please refer to these and other risk factors described or referred to in “Risk Factors” in Enanta’s most recent Form 10-Q, and other periodic reports filed with the Securities and Exchange Commission. Enanta cautions investors not to place undue reliance on the forward-looking statements contained in this presentation. These statements speak only as of the date of this presentation, and Enanta undertakes no obligation to update or revise these statements, except as may be required by law.

INTREPID Study Design



- The primary objective of the study was:
 - To evaluate the effect of EDP-305 on ALP levels
- Key secondary objectives included:
 - To evaluate the safety and tolerability of EDP-305
 - To evaluate the effects of EDP-305 on other markers of liver function
 - To evaluate the effects of EDP-305 on lipids
 - To evaluate the effects of EDP-305 on pruritus
 - To evaluate the pharmacodynamics of EDP-305
- The primary endpoint of the study was:
 - Proportion of subjects with at least 20% reduction in ALP from pre-treatment value OR normalization of ALP at Week 12

Key Eligibility Criteria

Key Inclusion

- At least two of the following criteria:
 - History of ALP above ULN for at least six months
 - Positive Anti-Mitochondrial Antibodies (AMA) titers ($>1/40$ on immunofluorescence or M2 positive by enzyme linked immunosorbent assay (ELISA) or positive PBC-specific antinuclear antibodies)
 - Documented liver biopsy result consistent with PBC (with no cirrhosis)
- Must be on a stable dose of UDCA 12-20 mg/kg/day for at least 6 months prior to Screening or intolerant of UDCA in the opinion of the Investigator (no UDCA for at least 12 weeks prior to Screening)
- Alkaline Phosphatase (ALP) $\geq 1.67 \times$ ULN and/or total bilirubin $>ULN$ but $< 2 \times$ ULN
- Subjects on a stable dose of statins for least 3 months prior to screening are allowed

Key Exclusion Criteria

- Evidence of other chronic disease
- Any histology or clinical evidence of cirrhosis
- Prior use of OCA
- Current use of fibrates, including fenofibrates. *Note: Subjects who discontinued fibrates for at least 3 months before screening can participate*
- Patients with a history of severe pruritus requiring current or prior systemic treatment (e.g., with BAS or rifampicin)

OCA: obeticholic acid; BAS: bile acid sequestrants

Demographics

| Characteristic | Placebo (N=9) | EDP-305 1 mg (N=31) | EDP-305 2.5 mg (N=28) | P-value 1mg v Pbo | P-value 2.5mg v Pbo |
|--------------------------------------------|------------------|------------------------|--------------------------|----------------------|------------------------|
| Female, n (%) | 9 (100 %) | 31 (100 %) | 27 (96.4%) | Not Computable | 0.565 |
| White, n (%) ¹ | 9 (100 %) | 29 (93.5%) | 27 (96.4%) | 0.434 | 0.565 |
| Not Hispanic or Latino | 9 (100 %) | 27 (87.1%) | 25 (89.3%) | 0.525 | 0.592 |
| Age (years) Mean (sd) | 56.9 (8.49) | 57.4 (8.61) | 54.9 (10.92) | 0.586 | 0.579 |
| BMI (kg/m ²) Mean (sd) | 29.43 (6.321) | 25.98 (6.087) | 28.64 (4.741) | 0.146 | 0.688 |
| Prior or Concomitant Use of UDCA, n (%) | 9 (100.0%) | 28 (90.3%) | 27 (96.4%) | 0.332 | 0.565 |

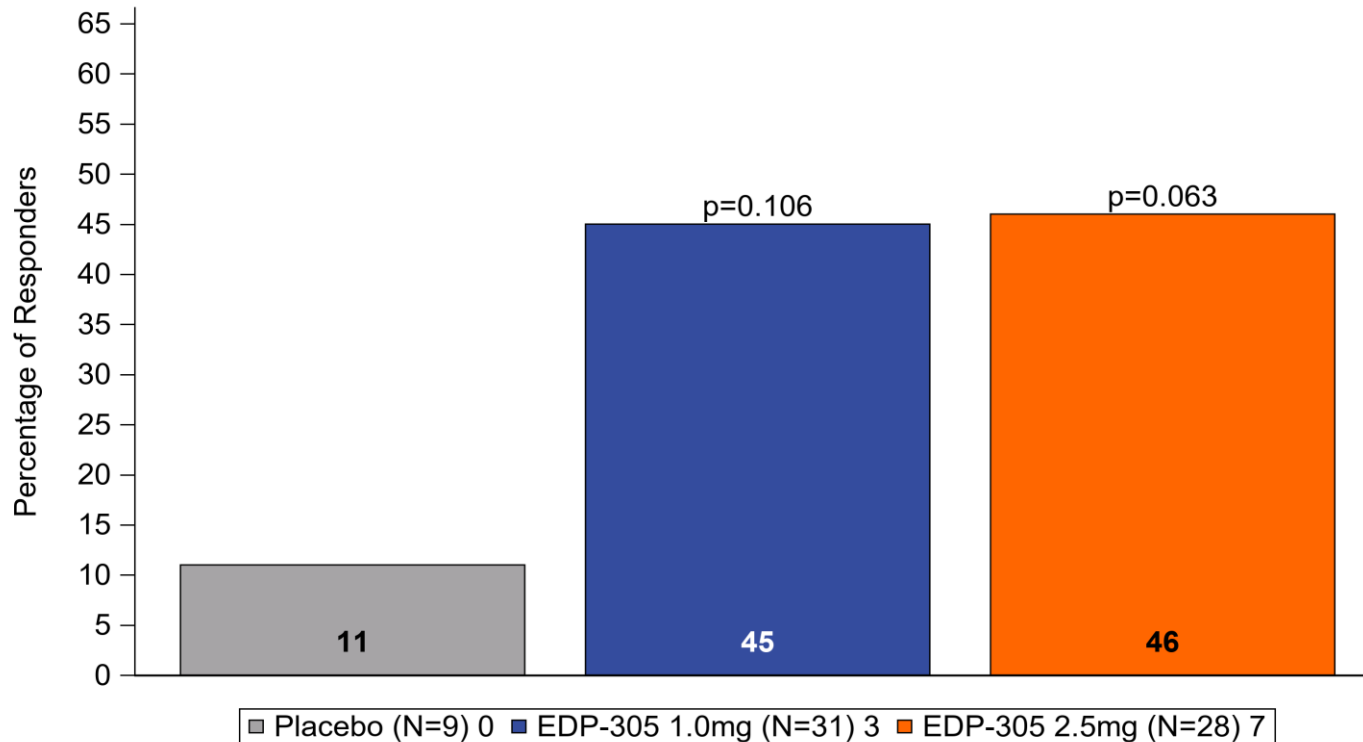
¹ "Multiple" category counted only as White in analysis

Baseline Characteristics

| Characteristic | Placebo (N=9) | EDP-305 1 mg (N=31) | EDP-305 2.5 mg (N=28) | P-value 1mg v Pbo | P-value 2.5mg v Pbo |
|------------------------------------------------|--------------------|---------------------------|-----------------------------|-------------------------|------------------------|
| Alkaline Phosphatase (U/L), Mean (sd) | 320.17 (136.70) | 342.48 (147.90) | 259.59 (62.79) | 0.688 | 0.073 |
| Alanine Aminotransferase (U/L), Mean (sd) | 76.4 (49.78) | 66.0 (45.10) | 45.1 (19.17) | 0.555 | 0.008 |
| Gamma Glutamyl Transferase (U/L), Mean (sd) | 330.6 (381.30) | 237.6 (245.67) | 170.9 (143.38) | 0.386 | 0.068 |
| Total Bilirubin (U/L), Mean (sd) | 12.6 (7.21) | 10.0 (5.41) | 8.3 (2.71) | 0.249 | 0.012 |

Primary Endpoint:

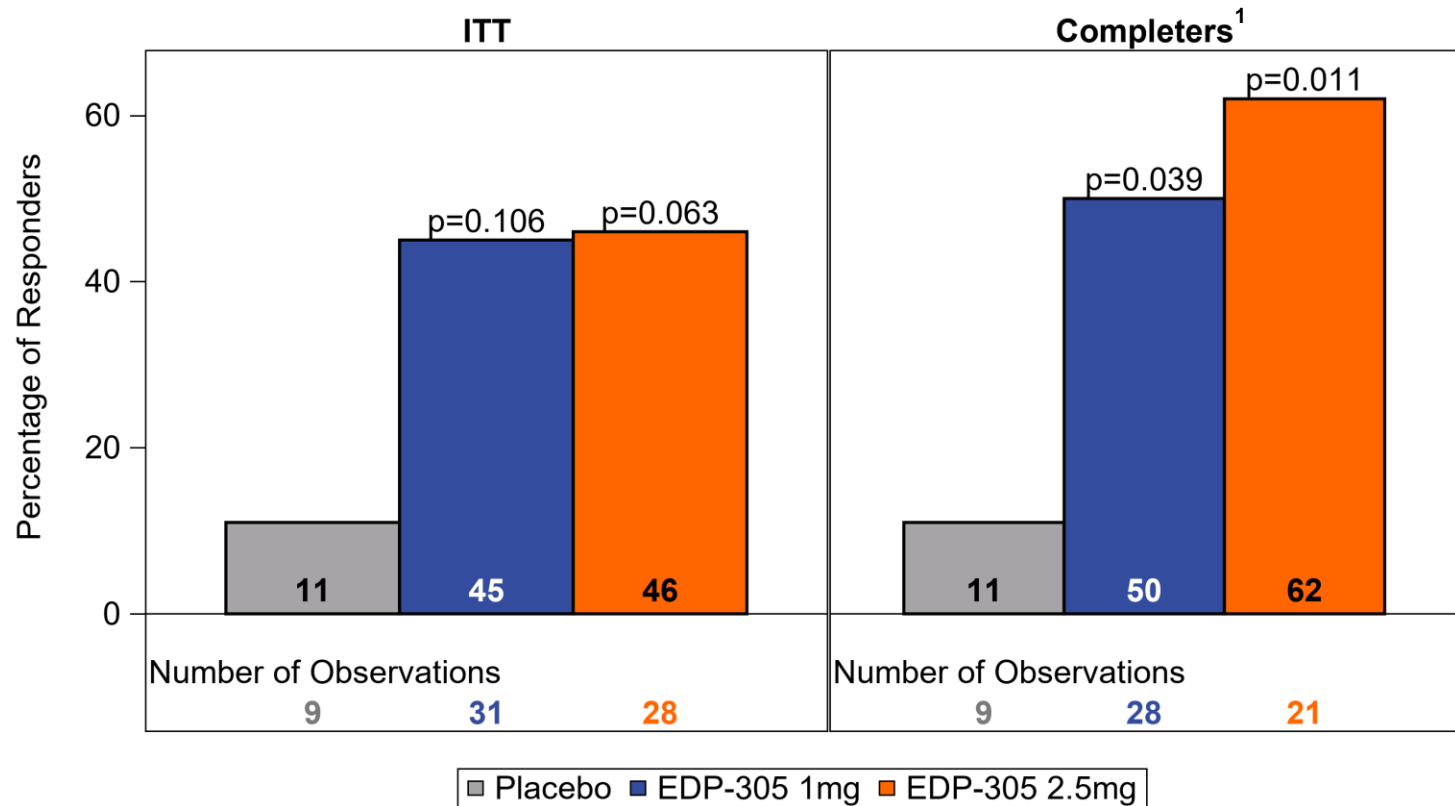
Proportion of Subjects With at least 20% Reduction in ALP From Pre-Treatment Value OR Normalization of ALP at Week 12



- Only 1 subject had ALP normalization in 2.5mg arm

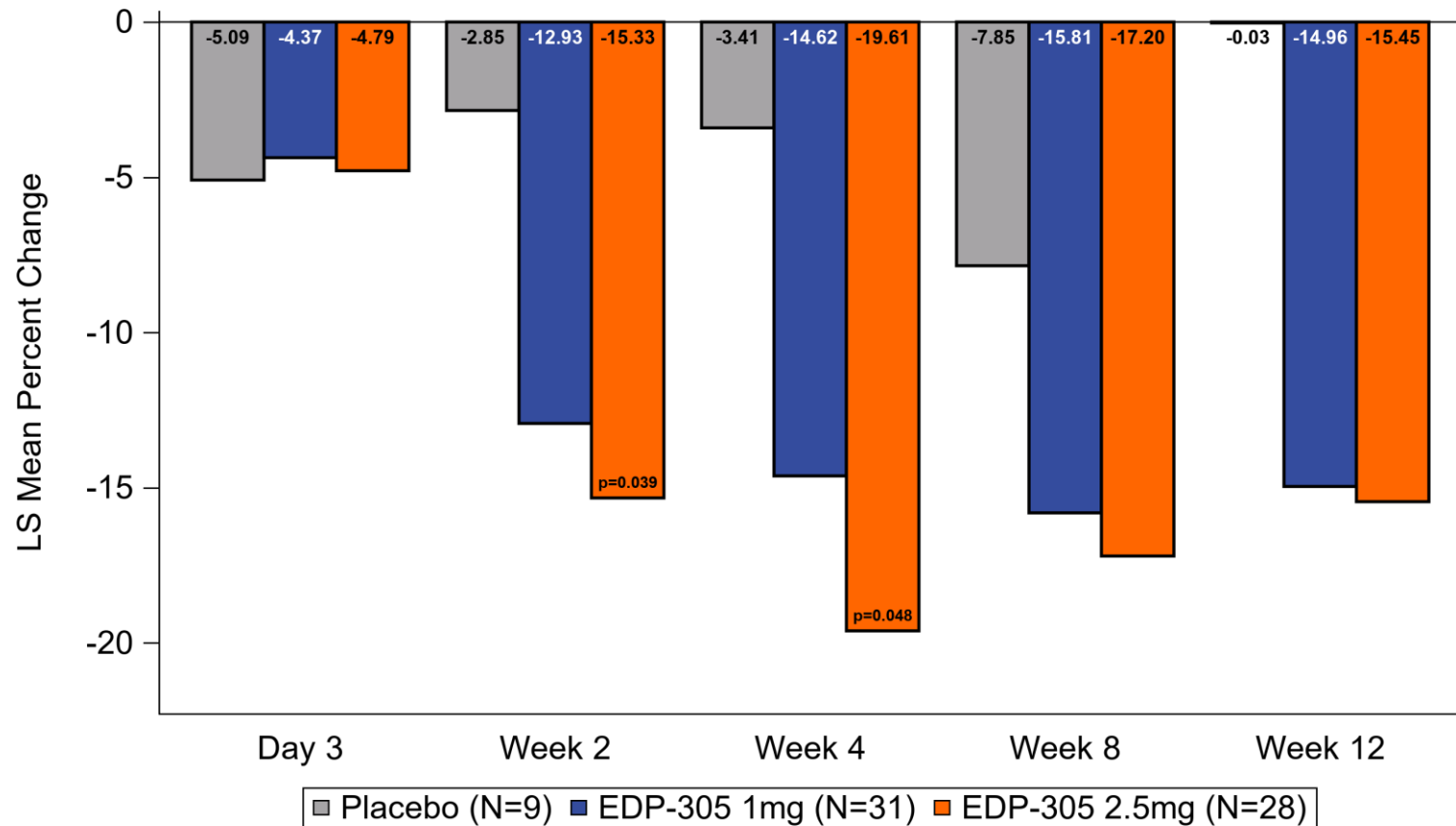
Proportion of Responders at Week 12

ITT (Missing=Failure) and Completers Analysis

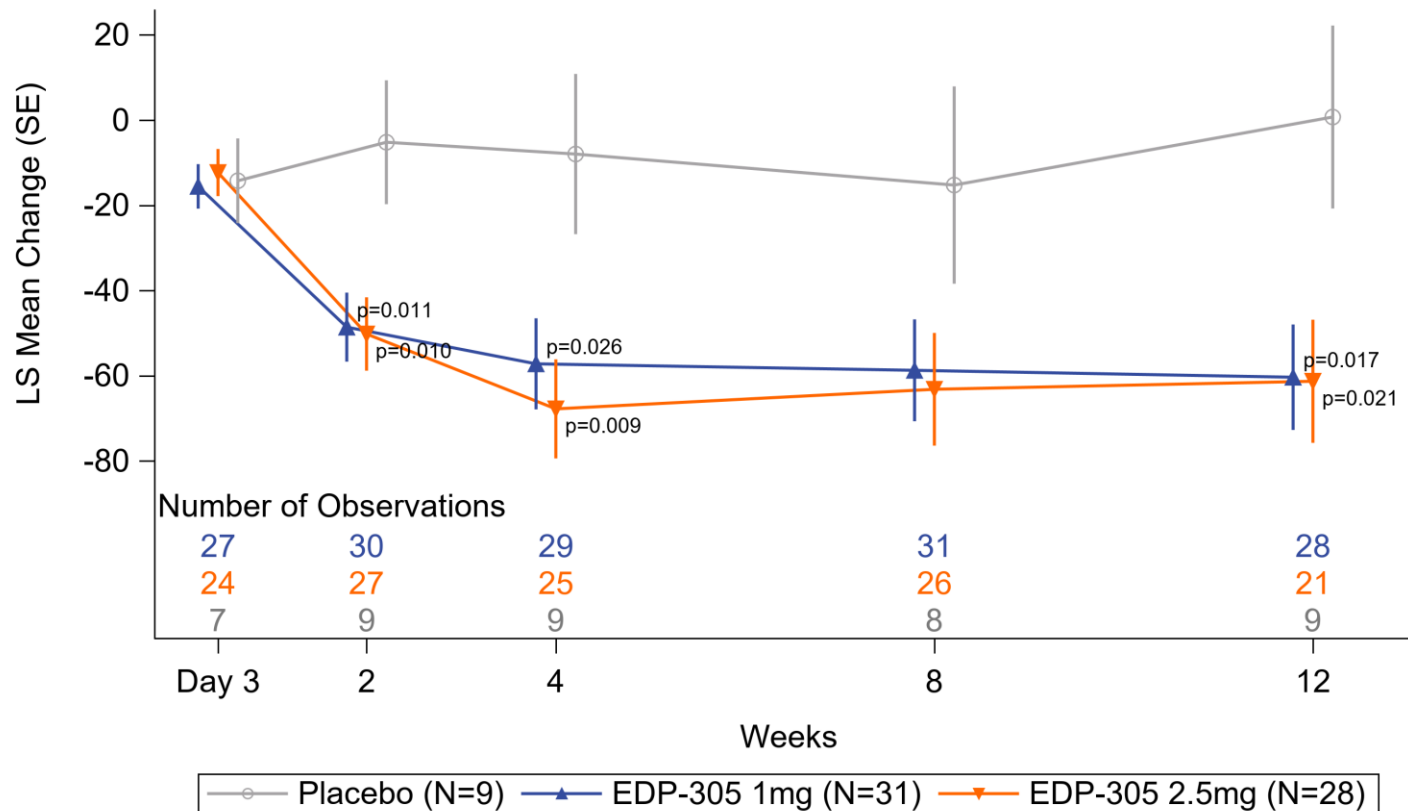


¹ Completers = The analysis only uses subjects who completed study drug treatment with non-missing observations at week 12

ALP % CFB (LS Mean) by Visits

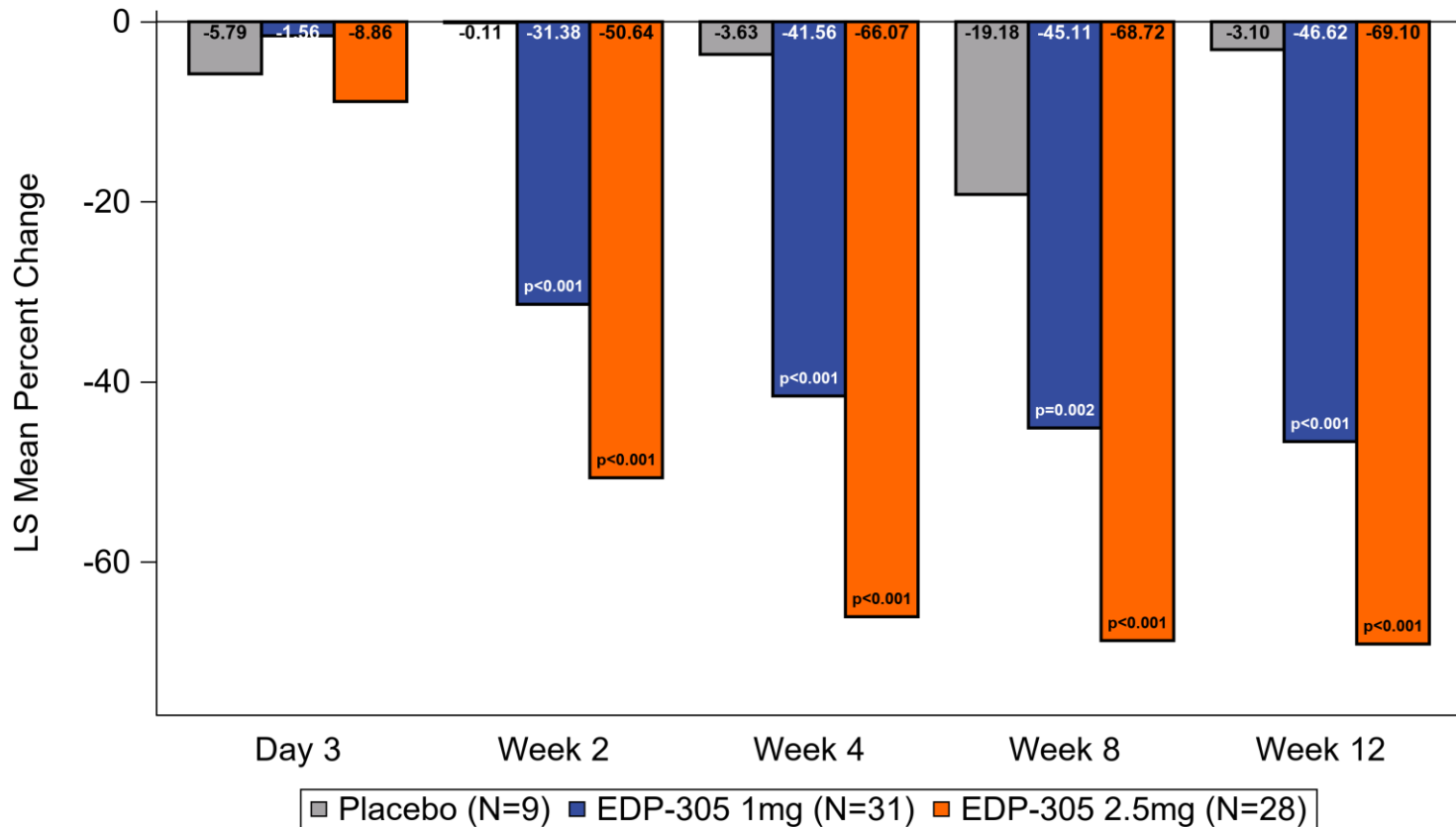


ALP CFB (LS Mean) by Visits



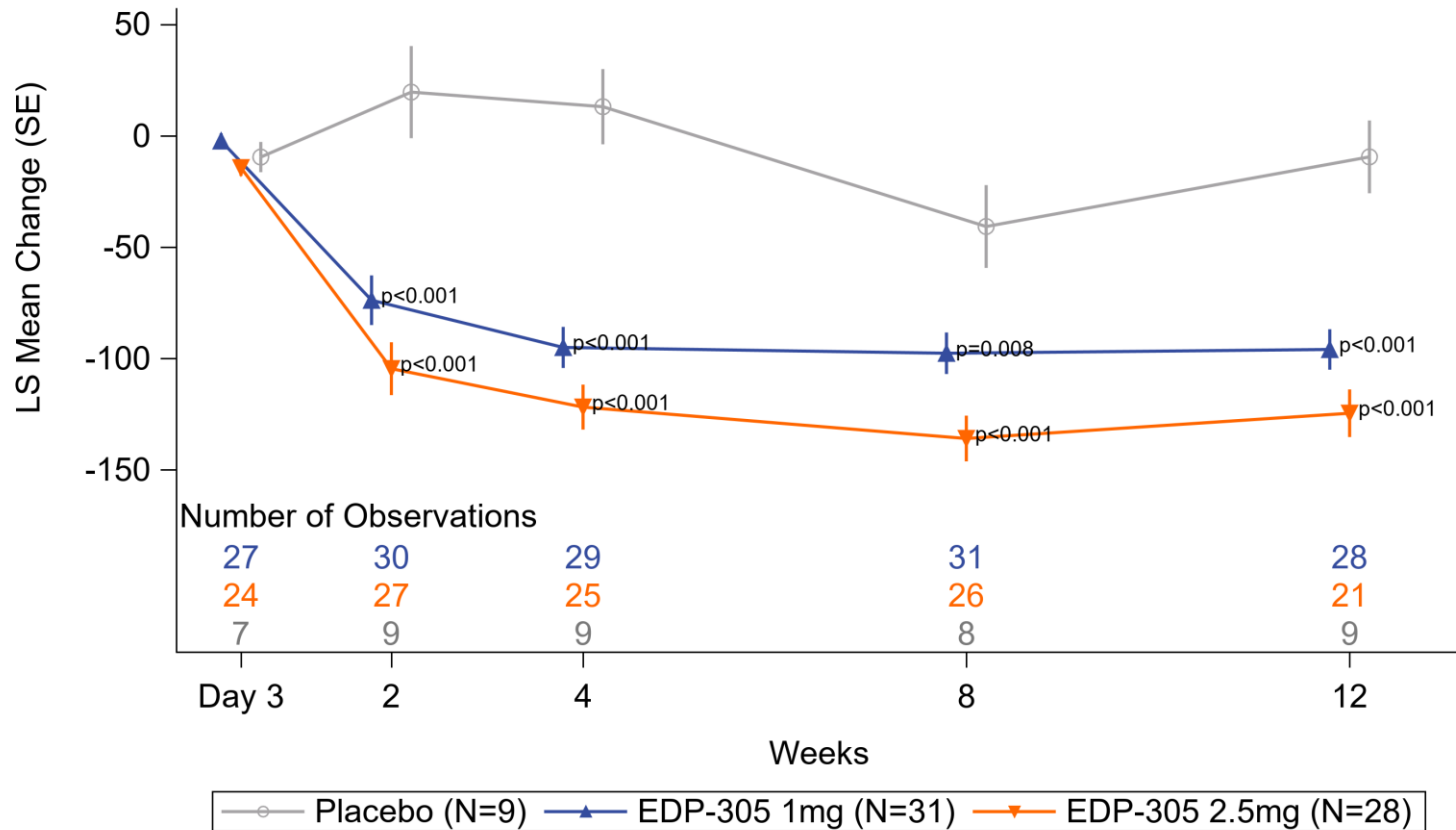
Key Secondary Endpoint

GGT % CFB (LS Mean) by Visits



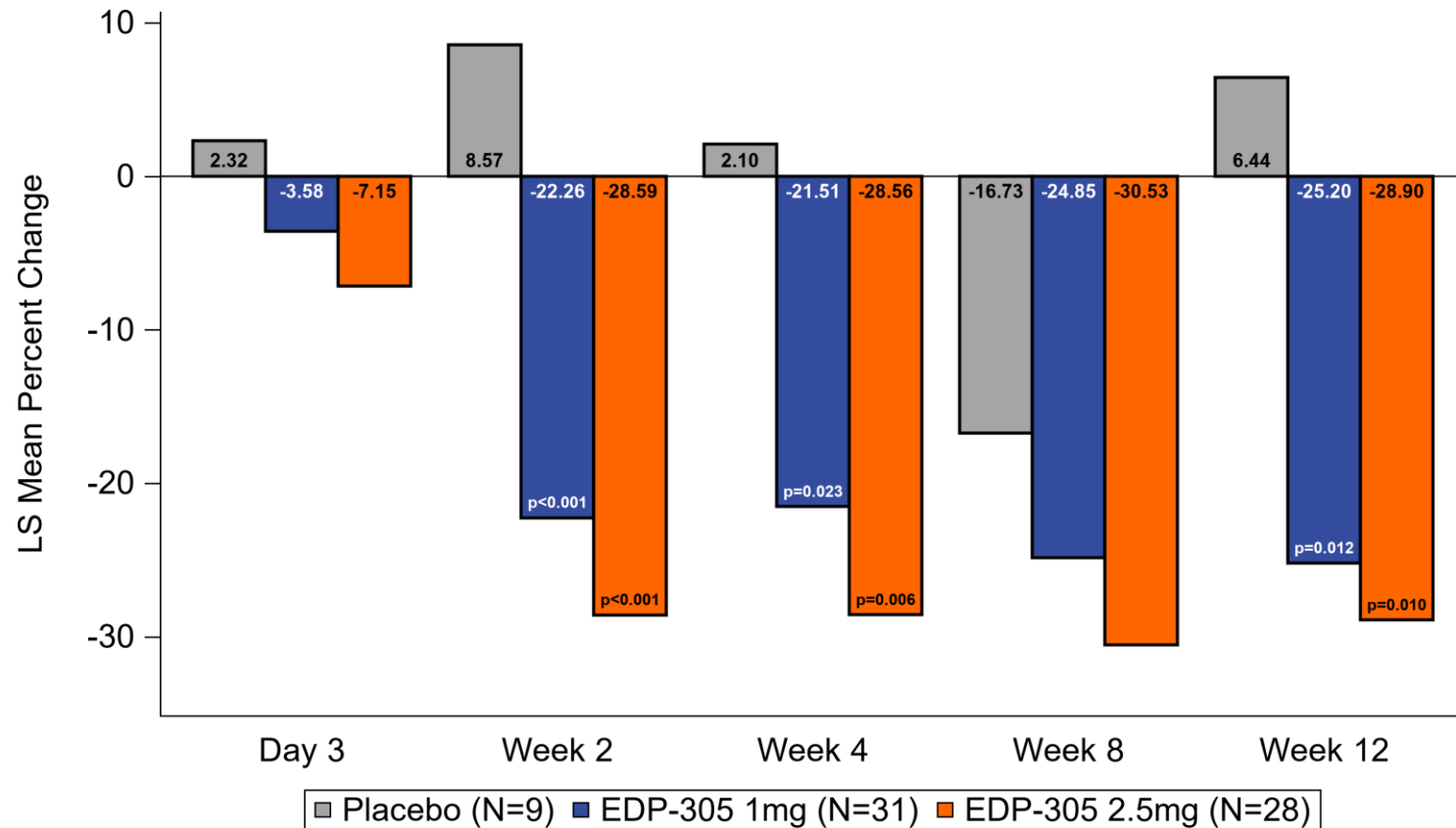
Key Secondary Endpoint

GGT CFB (LS Mean) by Visits



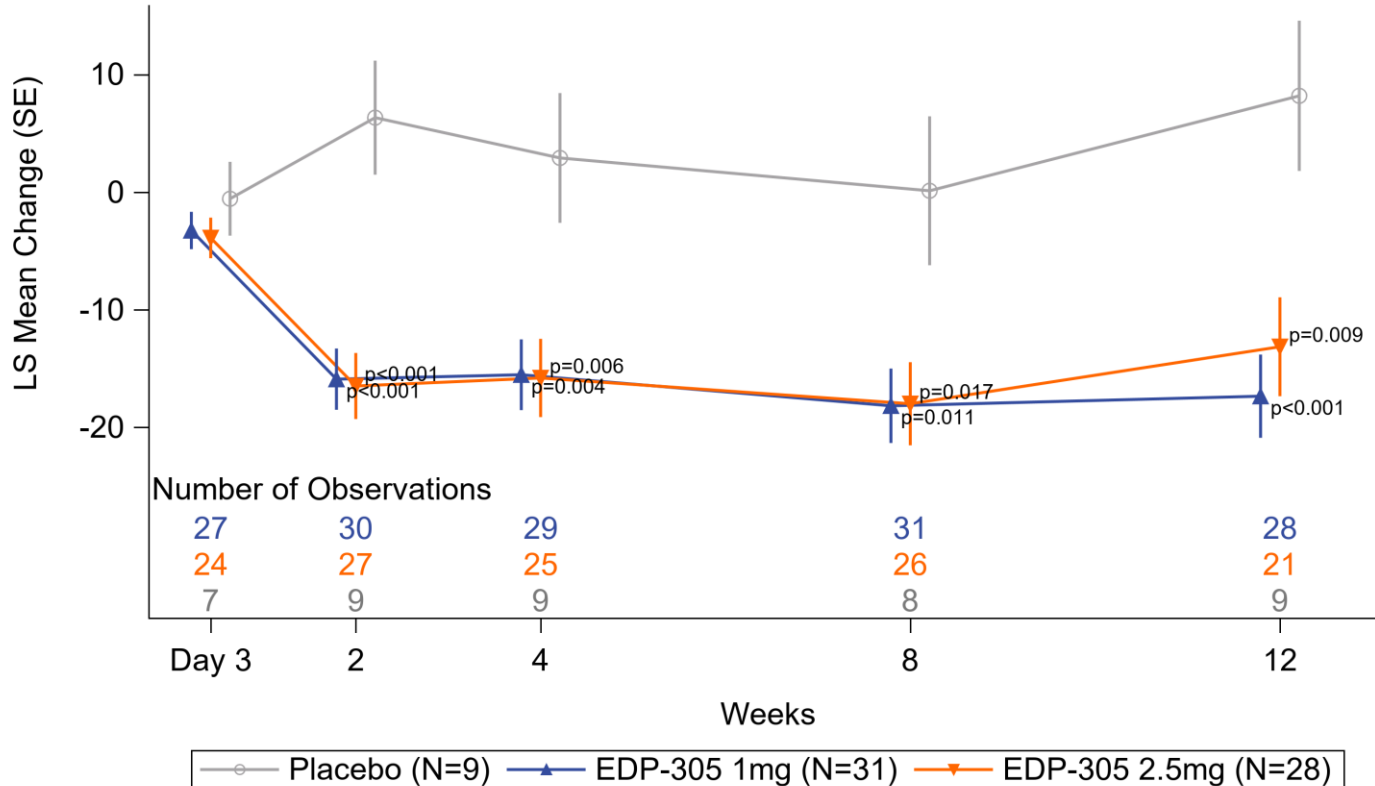
Key Secondary Endpoint

ALT % CFB (LS Mean) by Visits



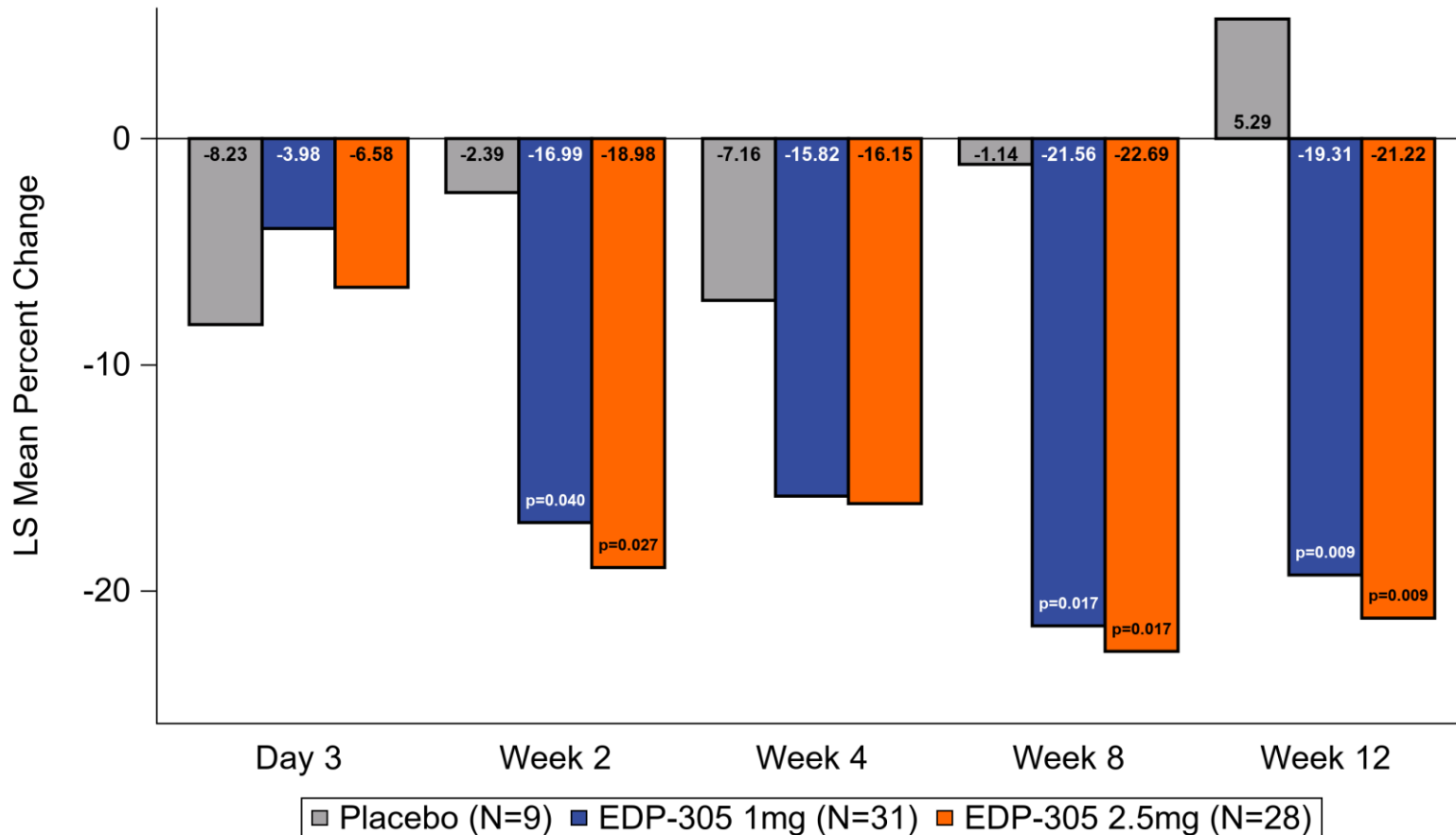
Key Secondary Endpoint

ALT CFB (LS Mean) by Visits



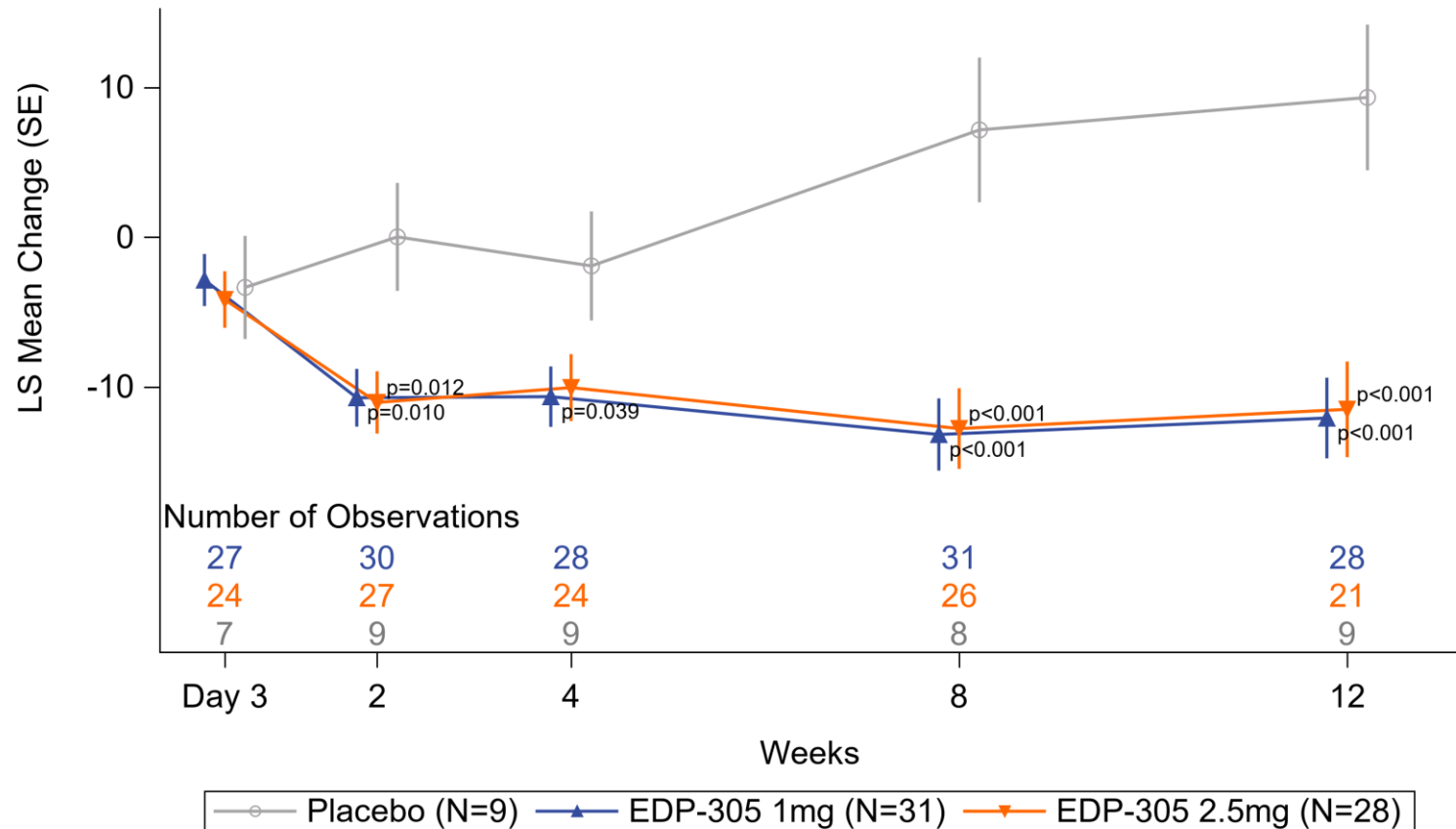
Key Secondary Endpoint

AST % CFB (LS Mean) by Visits



Key Secondary Endpoint

AST CFB (LS Mean) by Visits



Most Frequent Treatment-Emergent Adverse Events

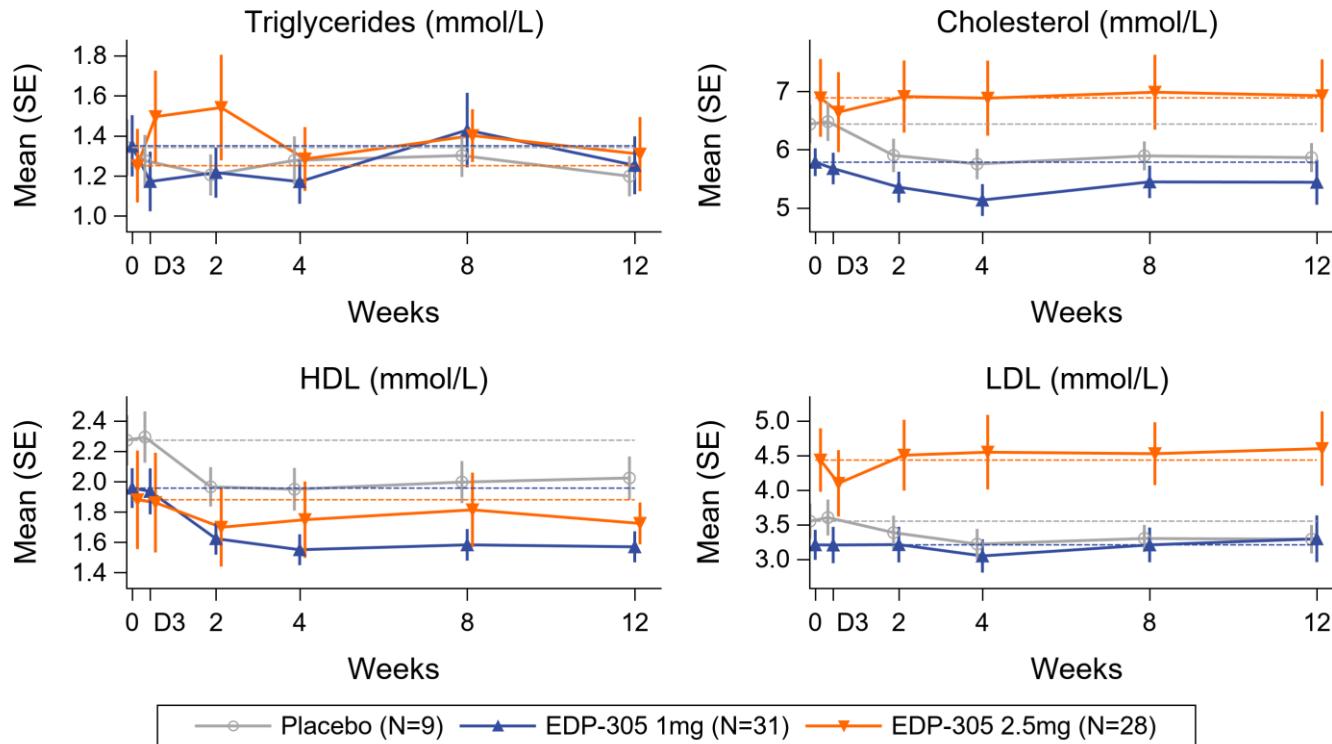
Events Occurring in $\geq 10\%$ of Subjects and/or > 1 Subject in Any Treatment Arm - Safety Population

| N (%) | Placebo N=9 | EDP-305 1mg N=31 | EDP-305 2.5mg N=28 |
|----------------------|----------------|---------------------|-----------------------|
| Pruritus generalized | 0 | 5 (16.1%) | 9 (32.1%) |
| Pruritus | 3 (33.3%) | 11 (35.5%) | 16 (57.1%) |
| Abdominal pain upper | 0 | 4 (12.9%) | 1 (3.6%) |
| Diarrhea | 0 | 1 (3.2%) | 3 (10.7%) |
| Gastroesoph. reflux | 0 | 1 (3.2%) | 3 (10.7%) |
| Dry mouth | 2 (22.2%) | 0 | 1 (3.6%) |
| Headache | 3 (33.3%) | 3 (9.7%) | 6 (21.4%) |
| Back pain | 2 (22.2%) | 0 | 0 |
| Insomnia | 0 | 0 | 3 (10.7%) |

- 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

Lipid Values (mmol/L) Over Time

Minimal Effect on Lipids



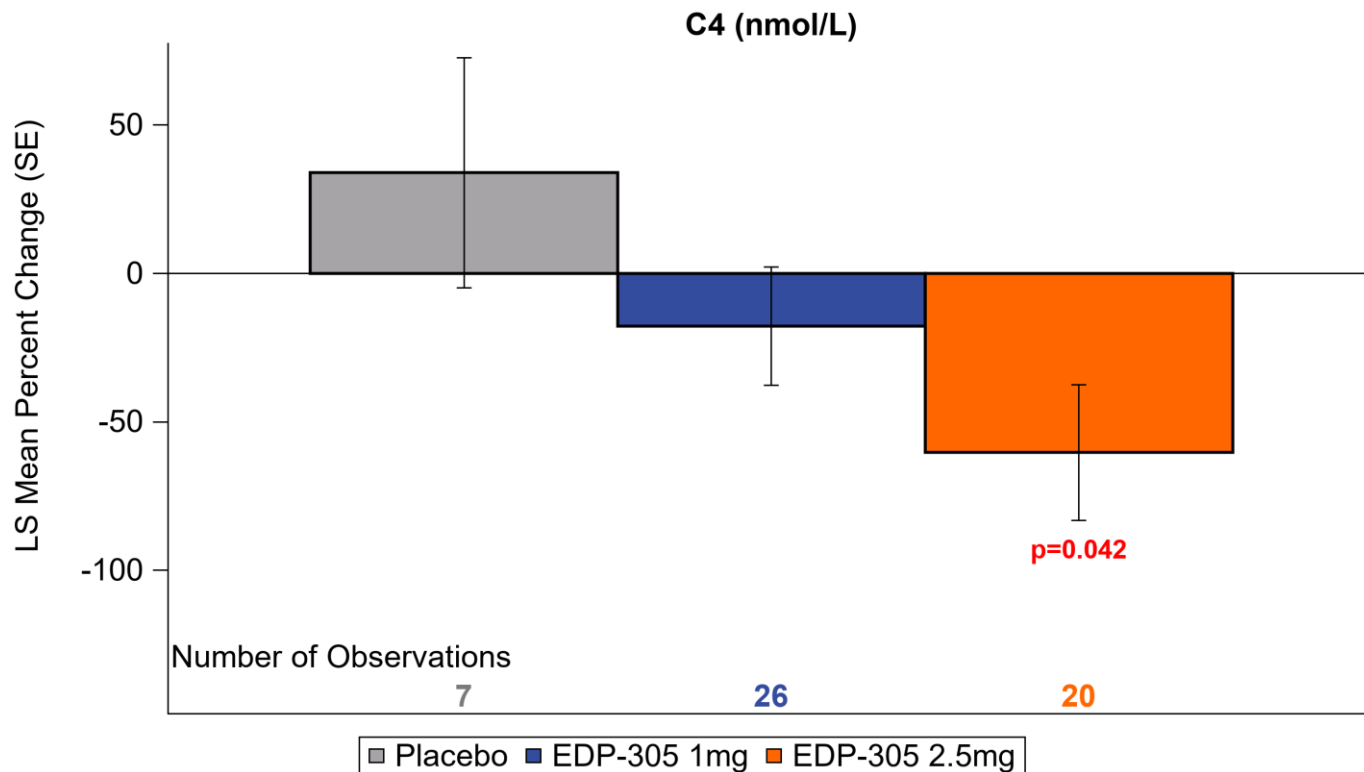
Summary of INTREPID Analysis

Safety and Tolerability

- EDP-305 regimens were generally safe in patients with PBC for up to 12 weeks with the majority of TEAEs being mild to moderate
- The most common ($\geq 10\%$ or >1 subject/arm) TEAEs included pruritus, GI related symptoms, headache and insomnia
 - Consistent safety profile observed in >400 subjects exposed to EDP-305 up to 12 weeks
 - Incidence of treatment discontinuation due to pruritus was approx. 3% for 1mg, 18% for 2.5mg and 0% for placebo
- Treatment with EDP-305 was accompanied by small numeric absolute changes in lipids at week 12 relative to baseline

Biomarker of Target Engagement

%CFB (LS Mean) at Week 12



Conclusion

- INTREPID did not meet the primary endpoint in subjects with PBC, as defined by at least a 20% reduction in ALP in the ITT set analysis, there were numerically higher response rates with 1mg and 2.5mg compared to placebo
 - In the completers, those subjects who finished treatment had a significant ALP response
- Good signs of target engagement with acceptable safety and dose-response tolerability observed at 1mg and 2.5mg, similarly to what was observed in ARGON-1 NASH study
- Data from Intrepid provides support to doses being currently tested in ARGON-2:
 - Doses of 1.5 and 2mg may help further optimize target engagement and balance between efficacy and safety/tolerability

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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