Efruxifermin was associated with improvements in multiple non-invasive tests indicative of fibrosis regression in participants with compensated cirrhosis due to MASH (SYMMETRY)

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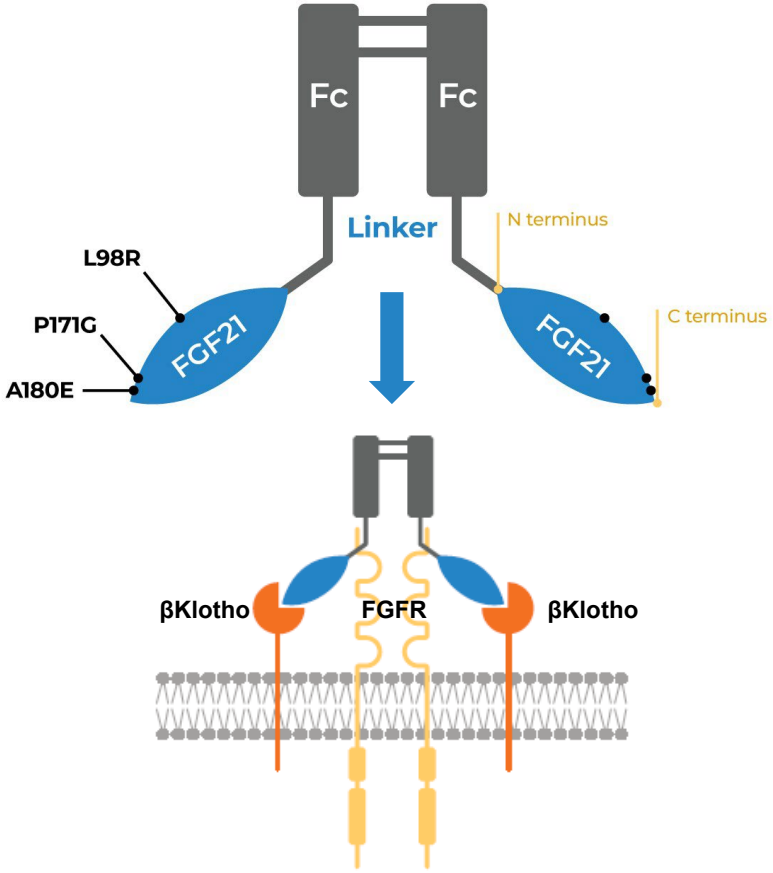
9 November 2025

AASLD The Liver Meeting®

Efruxifermin is an Engineered Bivalent FGF21 Analog

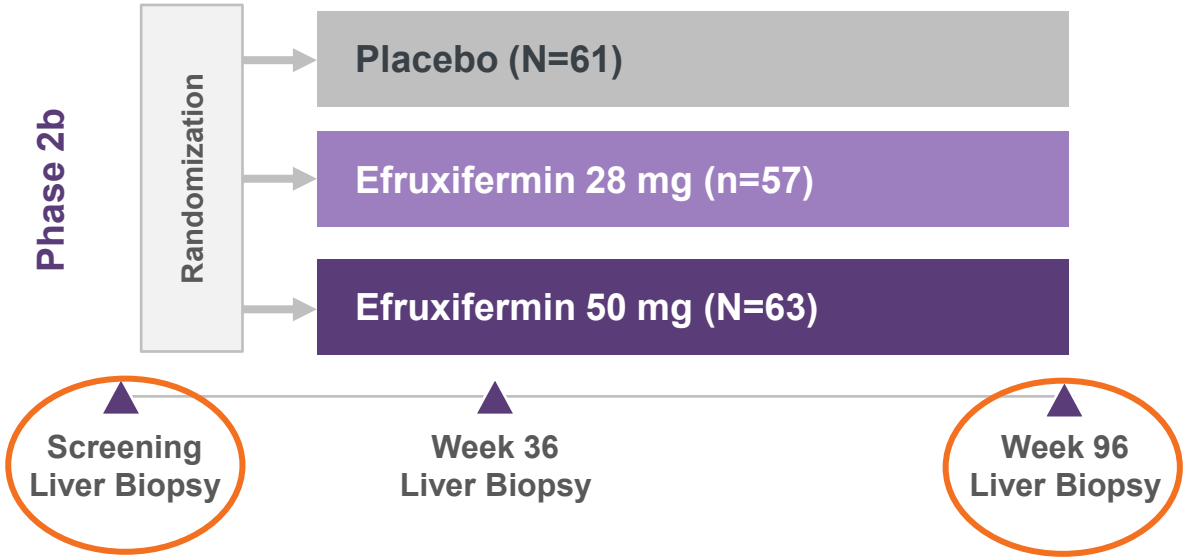


- Akero proprietary Fc-FGF21, Point mutations
- Increases half-life from < **2 hours** to **~3 days**
- **High affinity** for β-Klotho
- Better translation to **human** pharmacology
- **Balanced potency** at FGFR1c, 2c, 3c
- **Inactive** at FGFR4

Stanislaus (2017) *Endocrinology;* Lee (2018) *Nature*; Kharitonenkov (2007) *Endocrinology.*

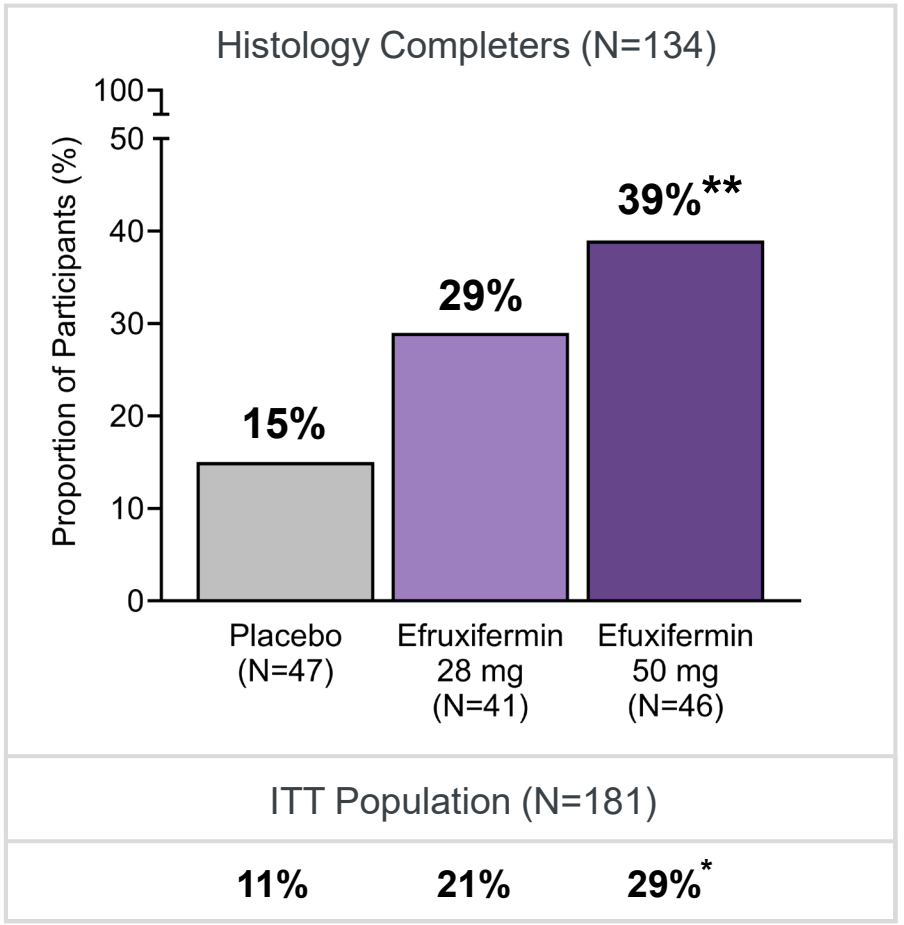
Efruxifermin-Induced Fibrosis Reversal in Participants with MASH Cirrhosis: SYMMETRY Trial

Population	181 randomized and dosed 134 with Week 96 liver biopsy
Primary End Point	≥1-stage fibrosis improvement without MASH worsening
Participants	Age 61 years, 67% female 80% T2D, GLP-1 RA 35%, BMI 36 kg/m^2



Noureddin (2025) *N Engl J Med.*

Fibrosis improvement ≥1 stage without MASH Worsening at Week 96



*p<0.05,**p<0.01 vs placebo. Missing biopsy imputed as non-response for analysis of the ITT population.

Aims

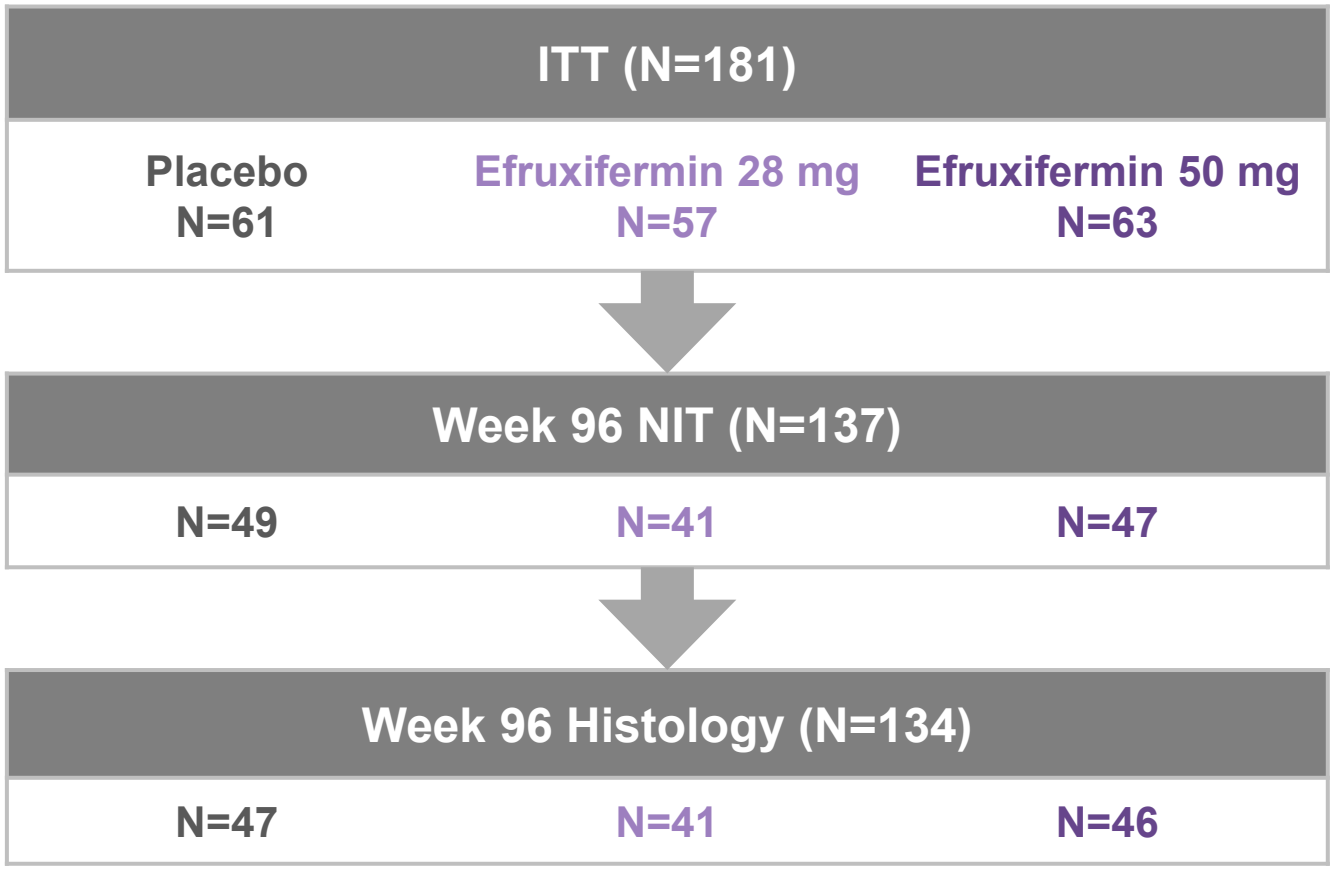
1. Corroborate the antifibrotic effect of efruxifermin, shown by liver biopsy (NASH CRN), using noninvasive tests of fibrosis.
    a) Determine if efruxifermin-induced changes in cirrhosis status are corroborated by a specifically designed noninvasive test (NIT) for cirrhosis diagnosis (i.e., Agile 4).
2. Evaluate if the magnitude of reduction of NITs is within the range shown to predict improvement in liver-related events.
3. Assess the overlap between response rates for different noninvasive tests.
4. Propose a definition of fibrosis response based on noninvasive tests.

Participants and Methods

- Post-hoc analysis of a subgroup of participants with Baseline and Week 96 data from SYMMETRY trial.
- ***Histological fibrosis staging*** was by the NASH CRN classification.
- ***Fibrosis NITs:***
  - LSM: Liver stiffness measurement by vibration controlled transient elastography (VCTE; Fibroscan, Echosens)
  - Circulating biomarkers: ELF test (Siemens)
- ***Cirrhosis NIT Agile 4:*** composite measure that includes clinical (type 2 diabetes, sex), laboratory measures (AST, ALT, platelets) and LSM. A value ≥0.565 is indicative of cirrhosis.
- ***Responder definitions*** based on change from baseline to Week 96:
  - Histology (Primary Endpoint): ≥1 stage fibrosis decrease without MASH worsening
  - LSM: ≥30% decrease in liver stiffness measurements
  - ELF: ≥0.5 decrease
- Magnitude of reduction in NITs associated with ***reduced risk of liver-related events***
  - (LSM: ≥30%; ELF: ≥0.5)
- ***Overlap*** between ELF and LSM defined as a concomitant response for both in a given participant.

Sanyal (2019) *Hepatology;* Lin (2024) *JAMA;* Gawrieh (2024) *J Hepatol*

Participant Flow



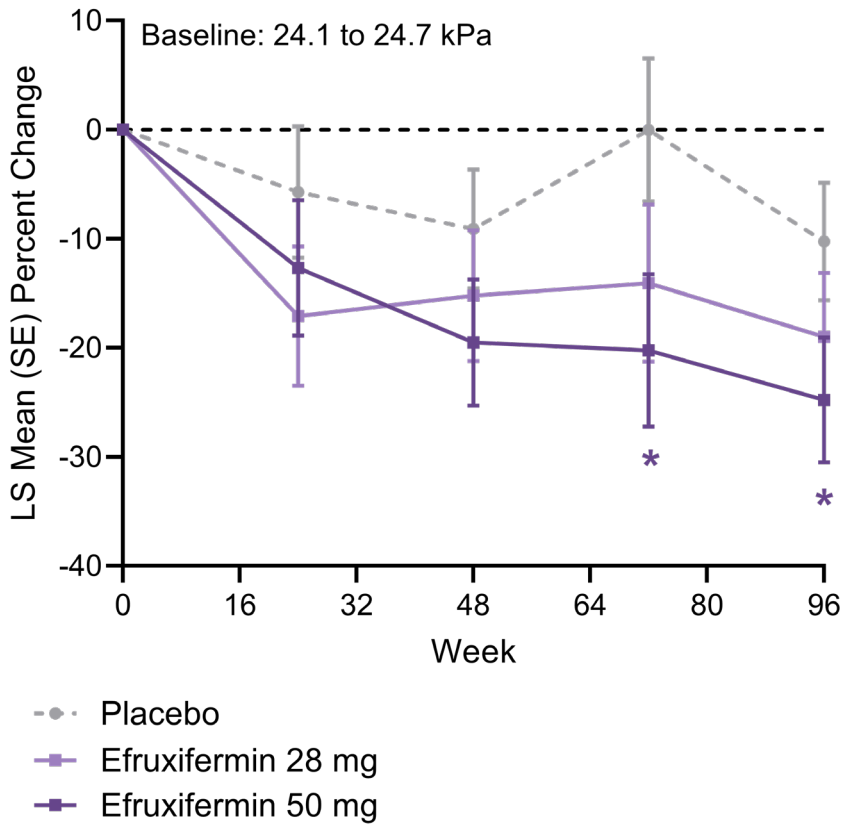
Randomized participants who received ≥1 dose of study drug

Participants with NIT results at Week 96.

Participants with both Week 96 liver biopsy and NIT results.

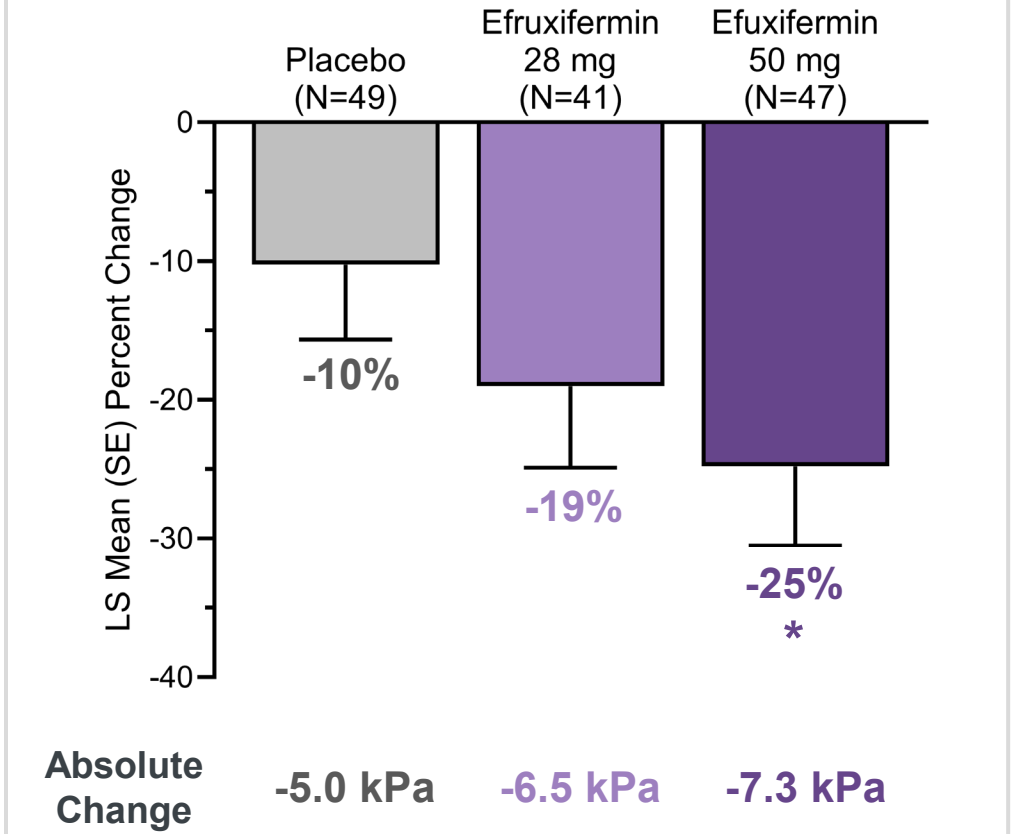
Aim 1: Statistically Significant Reduction in LSM with Efruxifermin at Week 96

Relative (%) Change in LSM by VCTE



*p<0.05 vs placebo. Figure shows observed data by visit for the ITT population. Week 96 data are for the NIT population.

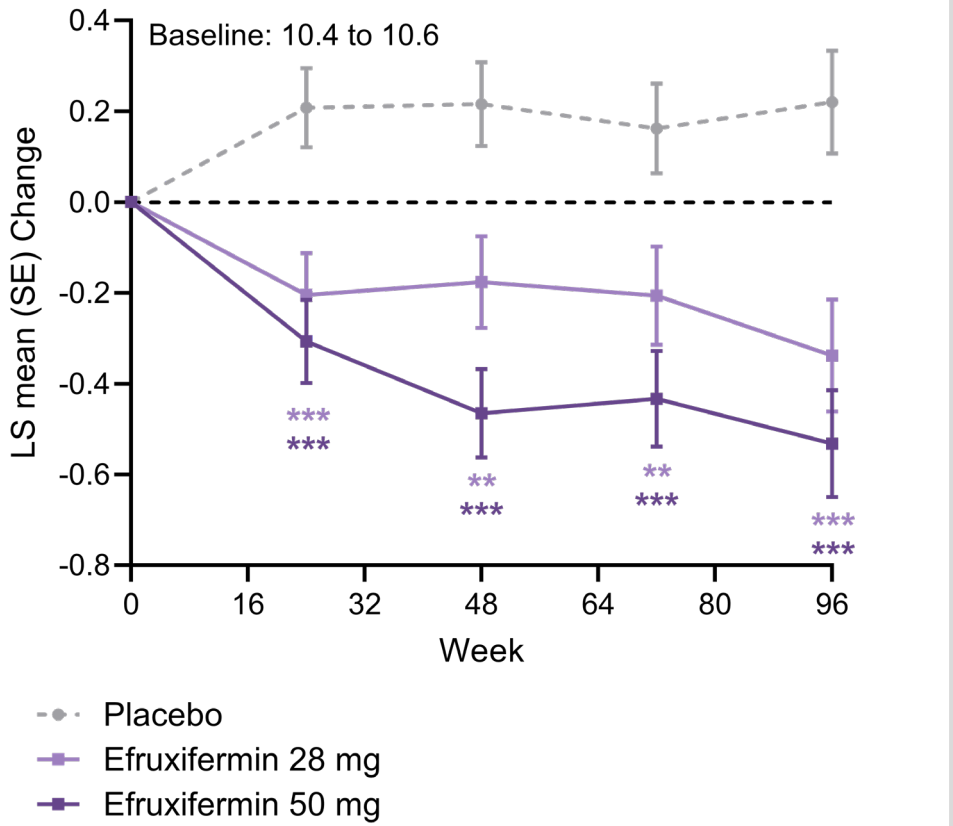
Relative Change in LSM by VCTE at Week 96



*p<0.05 vs placebo. Figure shows change from Baseline at Week 96 for the NIT population.

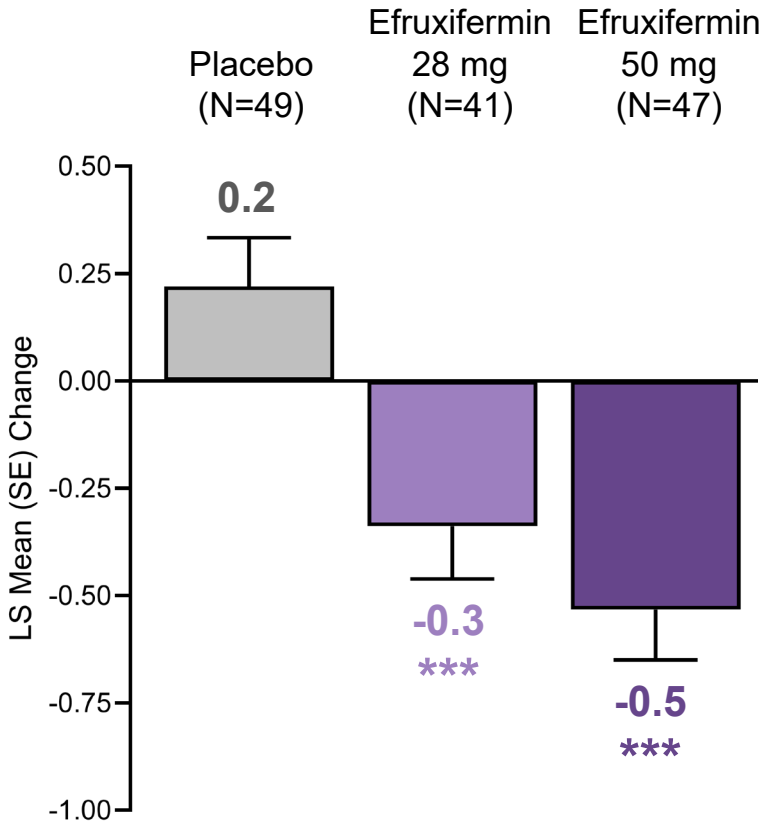
Aim 1: Early and Statistically Significant Reduction in ELF with Efruxifermin

Enhanced Liver Fibrosis (ELF) Test Score



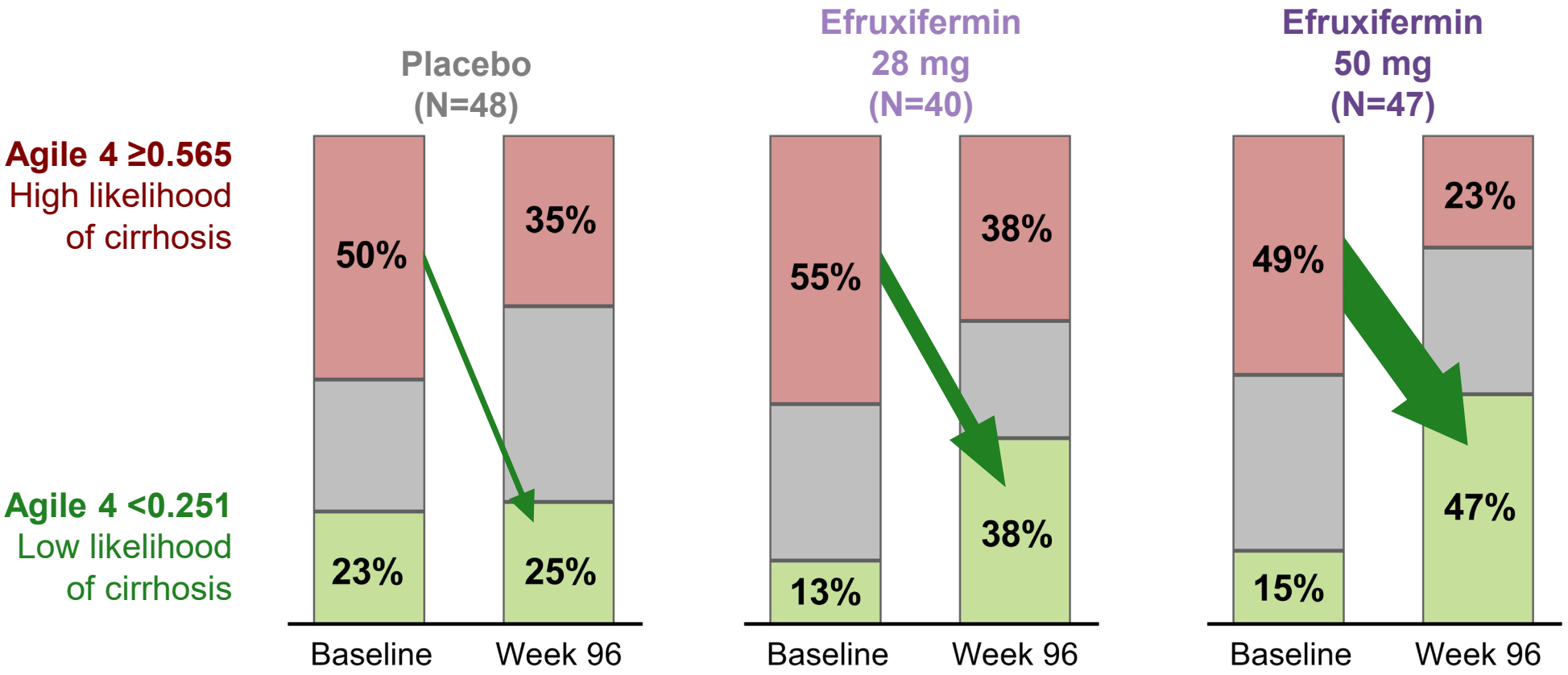
**p<0.01, ***p<0.001 vs placebo. Figure shows observed data by visit for the ITT population. Week 96 data are for the NIT population.

Change in ELF Score at Week 96



***p<0.001 vs placebo. Figure shows change from Baseline at Week 96 for the NIT population.

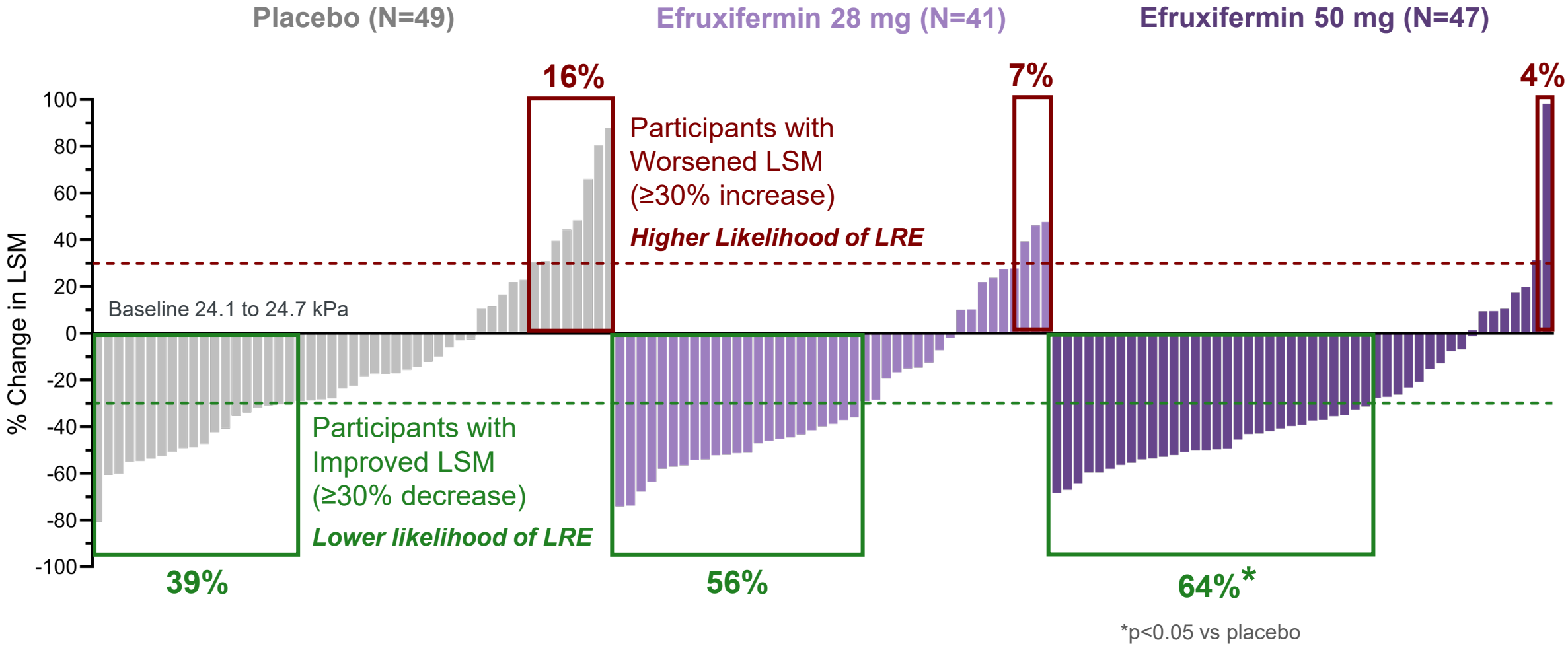
Aim 1a: Efruxifermin Reduced Likelihood of Cirrhosis as Assessed by Composite Measure: Agile 4



	Placebo (N=48)	Efruxifermin 28 mg (N=40)	Efruxifermin 50 mg (N=47)
Proportion of participants with high likelihood of cirrhosis at baseline that shift to low likelihood at Week 96	4%	9%	30%*

*p<0.05 vs placebo. Data are for participants in the NIT population.

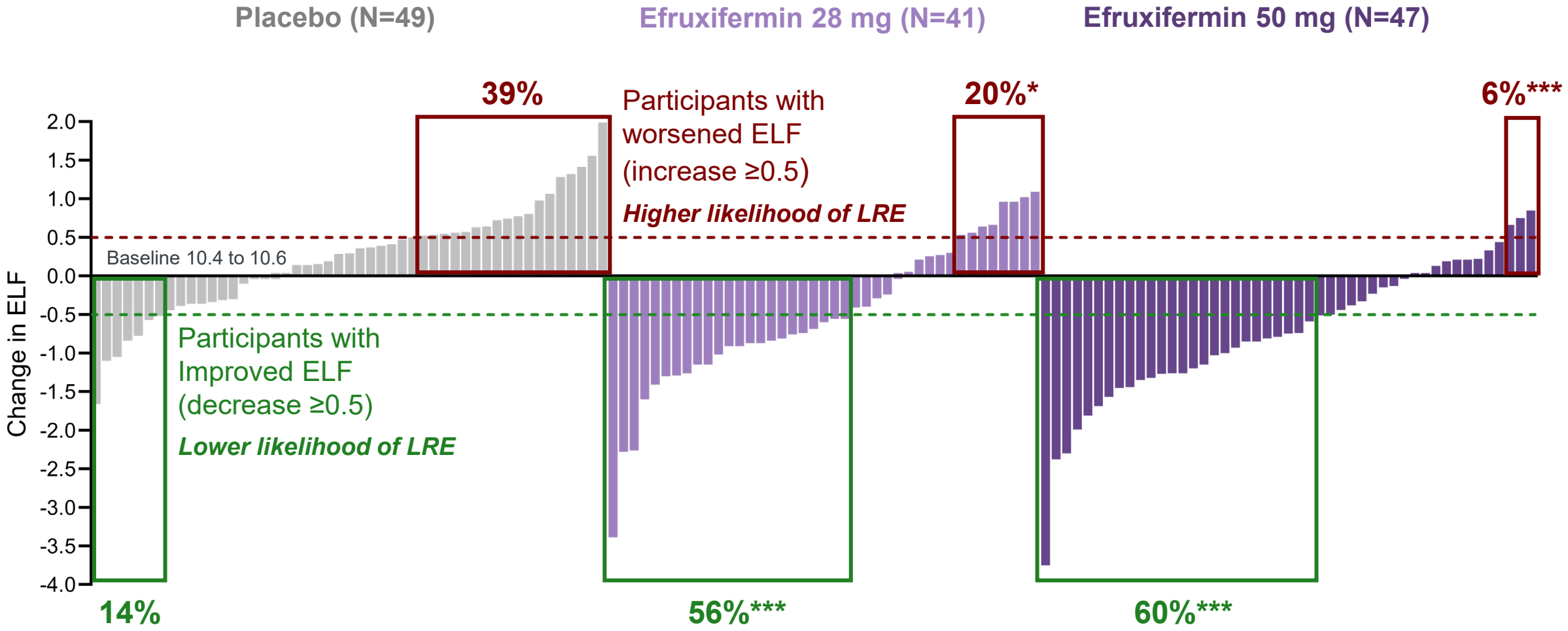
Aim 2: Changes in LSM at Week 96 Among Efruxifermin Participants Predict a Lower Risk of Liver-Related Events (LRE)



Lin (2024) *JAMA*

Figure shows percent change from Baseline to Week 96 in LSM by VCTE (FibroScan) for the NIT population.

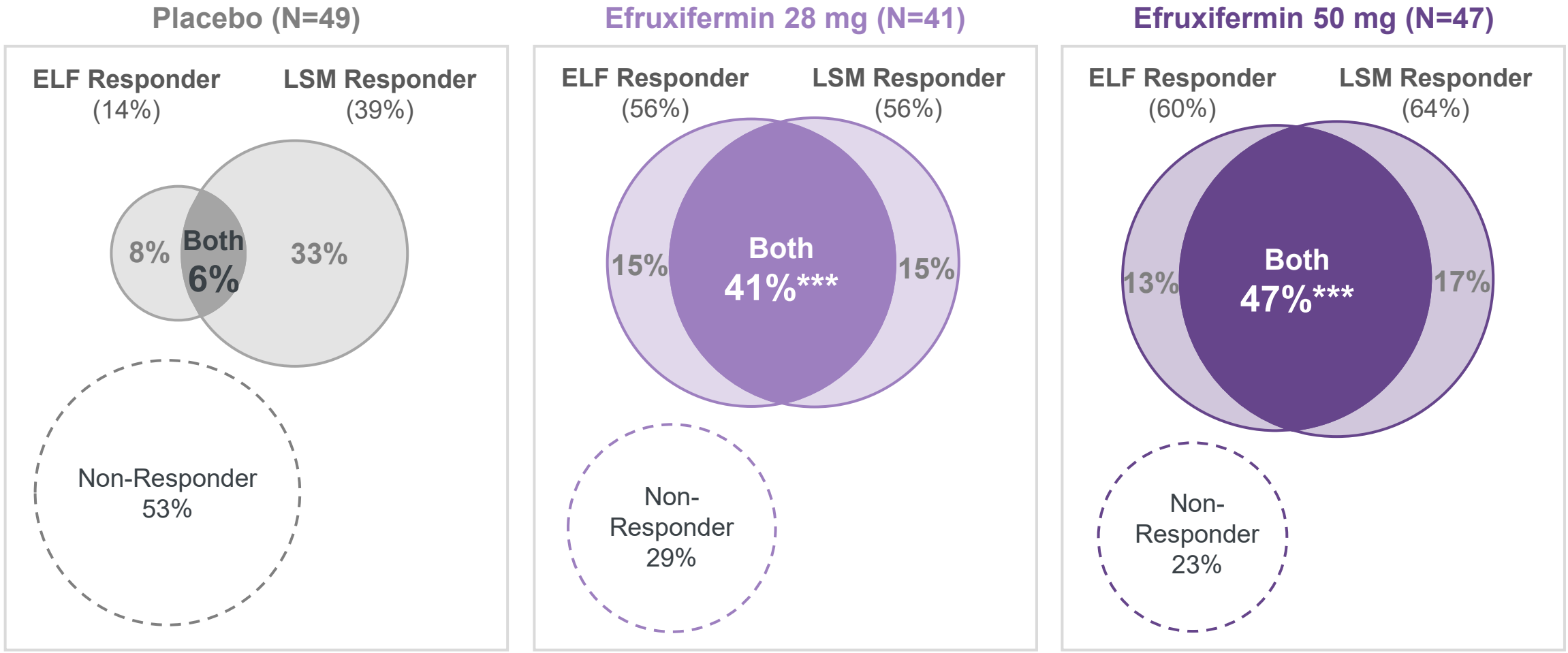
Aim 2: Changes in ELF at Week 96 Among Efruxifermin Participants Predict a Lower Risk of Liver-Related Events (LRE)



Sanyal (2019) *Hepatology*

*p<0.05, ***p<0.001 vs placebo. Figure shows absolute change from Baseline to Week 96 in ELF test score for the NIT population.

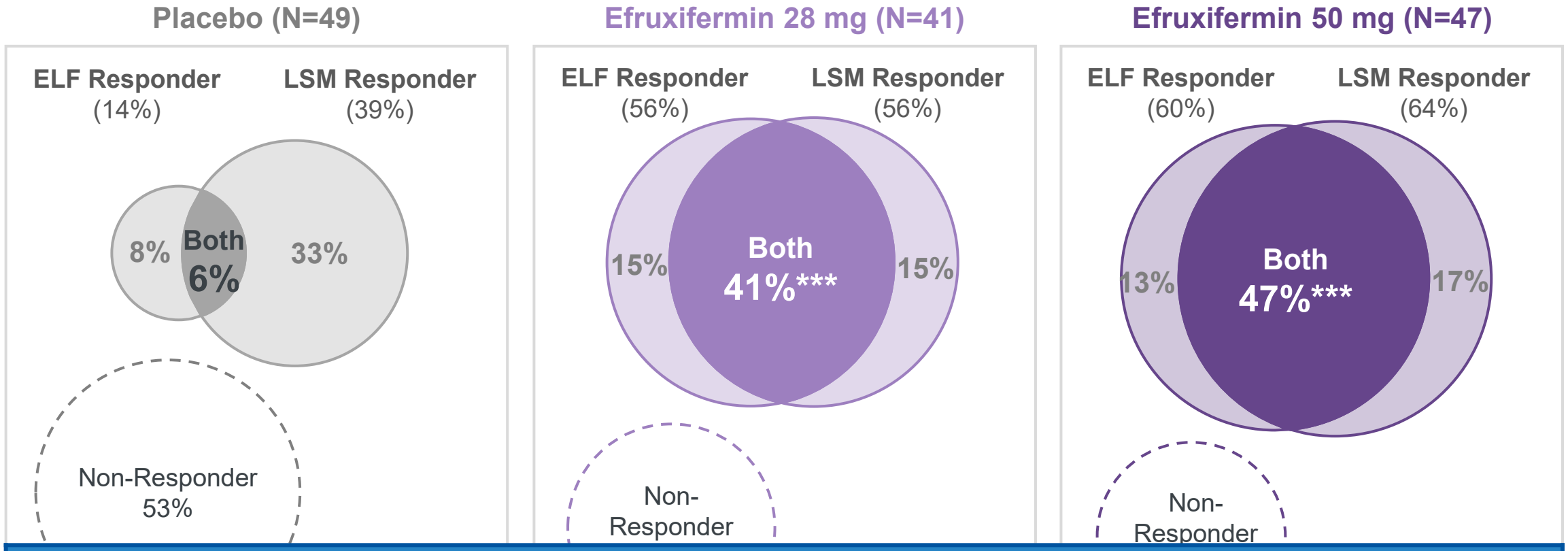
Aim 3: Participants Meeting Response Thresholds for NITs at Week 96



***p<0.001 vs placebo.

ELF Responder=participants with ≥0.5 decrease from baseline to Week 96; LSM Responder=participants with ≥30% decrease from baseline to Week 96; Data are for NIT population.

Aim 4: Definition of Fibrosis Response based on Composite NITs



Proposed definition of fibrosis response based on composite NITs:

Both ≥30% decrease in LSM and ≥0.5 decrease in ELF

Summary and Conclusions

- The SYMMETRY trial enrolled participants with MASH and compensated cirrhosis (F4c). More participants in efruxifermin groups vs placebo met thresholds for clinically meaningful improvement in
  - Fibrosis by liver biopsy using NASH CRN criteria
  - Noninvasive tests of fibrosis: LSM and ELF
  - Findings were corroborated by Agile 4, which indicated reduced likelihood of cirrhosis.
- For the majority of participants, the magnitude of reduction of NITs with efruxifermin was within the range shown to improve risk of liver-related events.
- The high level of overlap between noninvasive tests highlights the antifibrotic effect of efruxifermin.
- Combined response in noninvasive tests such as LSM and ELF may be useful in monitoring fibrosis response.
  - Combined LSM + ELF is being prospectively evaluated in the Phase 3 SYNCHRONY Real World clinical trial (Results expected 1H 2026).

Acknowledgements

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