Efruxifermin improved markers of portal hypertension as evaluated by Baveno VII criteria in compensated cirrhosis due to MASH: results from a 96-week, placebo-controlled, phase 2b trial (SYMMETRY)

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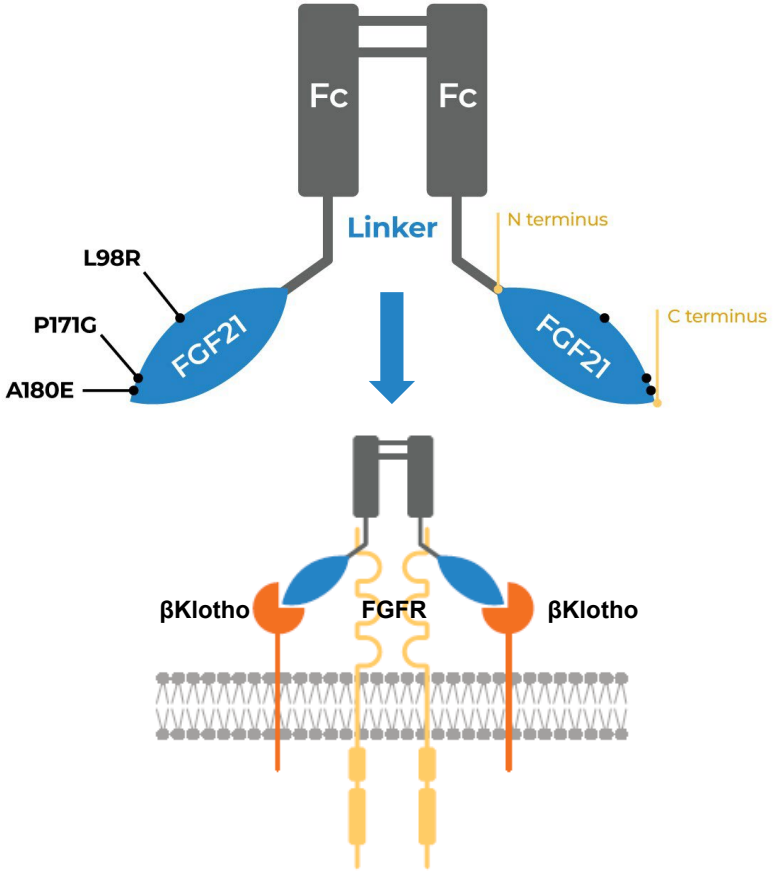
9 November 2025, Washington DC

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.*

Comprehensive Phase 3 SYNCHRONY Program in ~3500 Participants with MASH

Builds on two biopsy-based Phase 2b studies (N ~300) in corresponding populations treated for 96 weeks

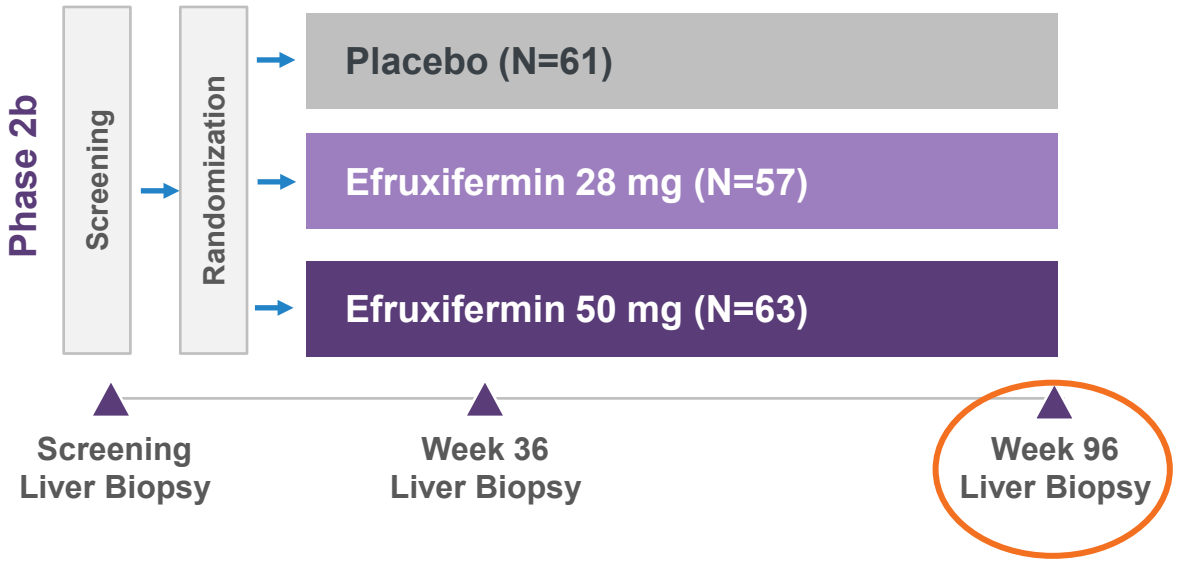
	HARMONY[1-3]	synchrony HISTOLOGY	symmetry FOR CIRRHOTIC NASH[4]	synchrony OUTCOMES
Fibrosis Stage	**F2-F3**	**F2-F3**	**F4c**	**F4c**
Phase	2b	3	2b	3
N	128	1650	182	1150
Weeks	96	240	96	~260

synchrony REAL-WORLD	*Phase 3 study evaluating safety & tolerability in ~700 clinically-diagnosed participants (F1 to F4, compensated) for 52 weeks* *Recruitment Complete*

[1] Harrison (2023) *Lancet Gastroenterol Hepatol;* [2] Harrison (2024) *Clin Gastroenterol Hepatol*; [3] Noureddin (2025) *Lancet;* [4] Noureddin (2025) *N Engl J Med*.

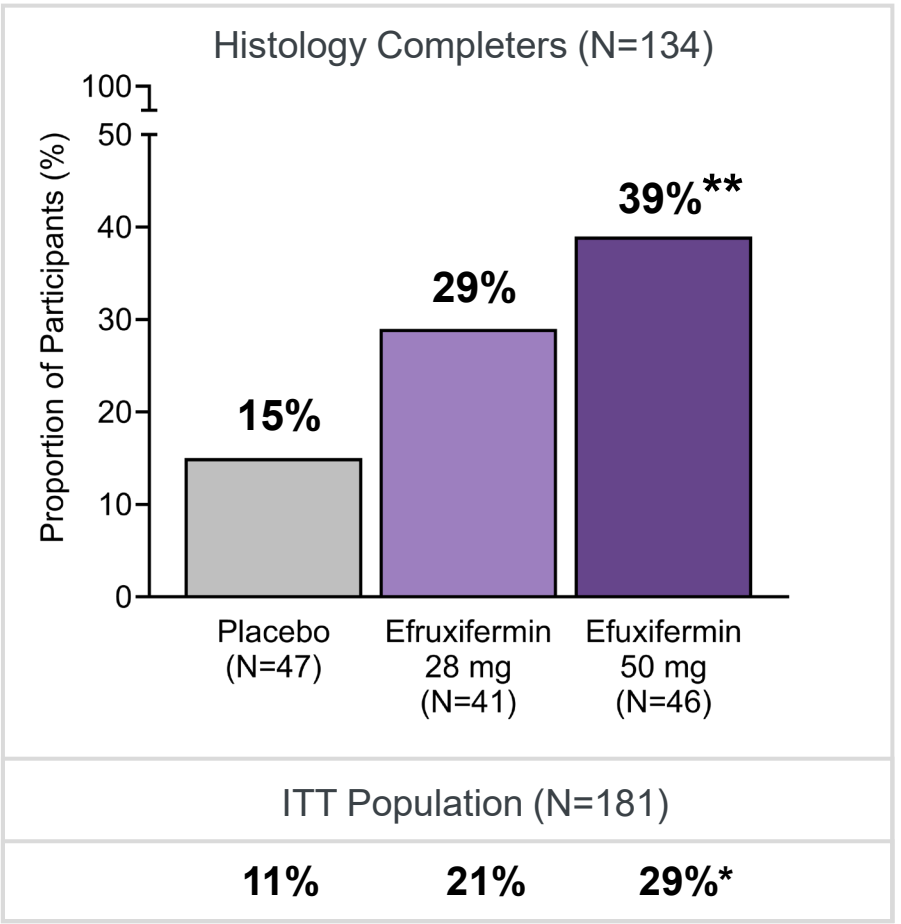
SYMMETRY: Efruxifermin in Compensated Cirrhosis (F4c) due to MASH

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.

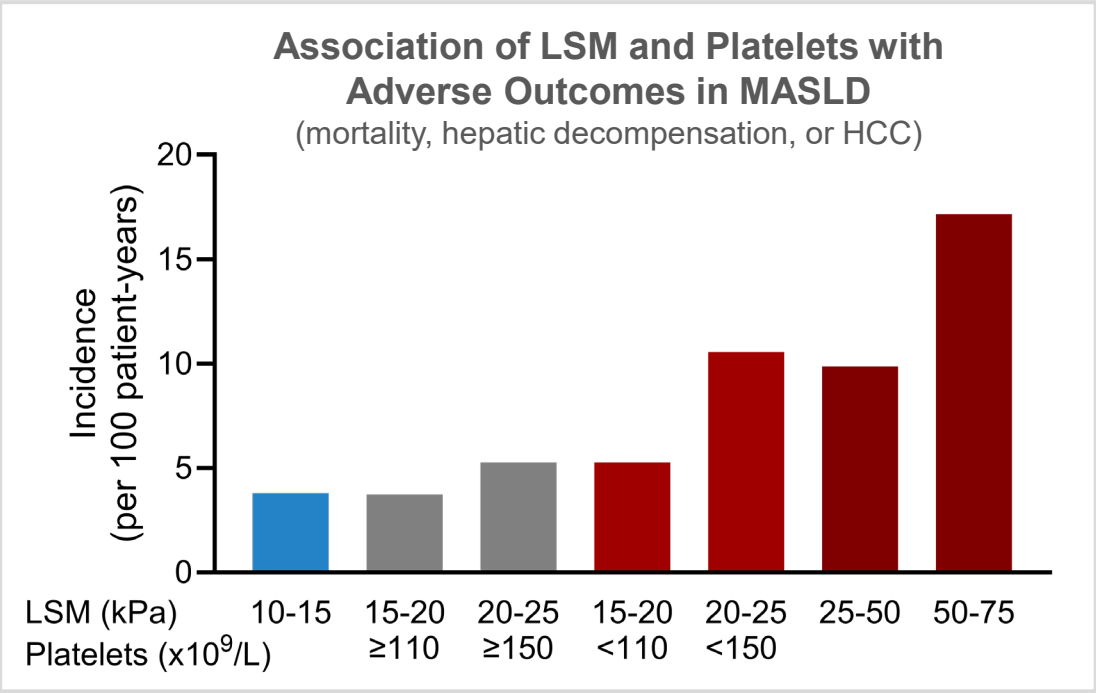
Aims

Evaluate if fibrosis improvement observed with efruxifermin in SYMMETRY is associated with improvements in noninvasive test of liver function, such as clinically significant portal hypertension (CSPH).

1. Classify participants at baseline by risk of having CSPH based on Baveno VII criteria.
2. Evaluate changes in CSPH risk criteria from baseline to Week 96 with efruxifermin.
3. Evaluate effect of efruxifermin in participants with higher risk of CSPH at baseline.
4. Evaluate if fibrosis regression with efruxifermin improves other measures associated with risk of liver-related outcomes: LSM and Agile 4.

Noninvasive Evaluation of CSPH Risk (Baveno) and Correlation with Liver-Related Outcomes and Mortality

- Baveno VII criteria estimate risk of developing clinically significant portal hypertension (CSPH) and varices based on LSM and platelet count.
- Patients classified as having CSPH by Baveno criteria have increased incidence of liver-related outcomes.



De Franchis (2022) *J Hepatol;* Figure adapted from Vutien (2025) *Hepatology*

CSPH Risk at Baseline in SYMMETRY Overall Population (N=135)

Baveno Risk Category		% (n) of Participants
CSPH	LSM ≥25	**29%** (39)
Probable CSPH	LSM 15–20 and platelets <110	**8%** (11)
	LSM 20–25 and platelets <150	
Indeterminate	All other	**54%** (73)
Rule out CSPH	LSM <15 and platelets ≥150	**9%** (12)

Overall Population includes participants with paired Baseline and Week 96 data (N=135).

Baseline Characteristics by CSPH Risk Category in SYMMETRY
Overall Population

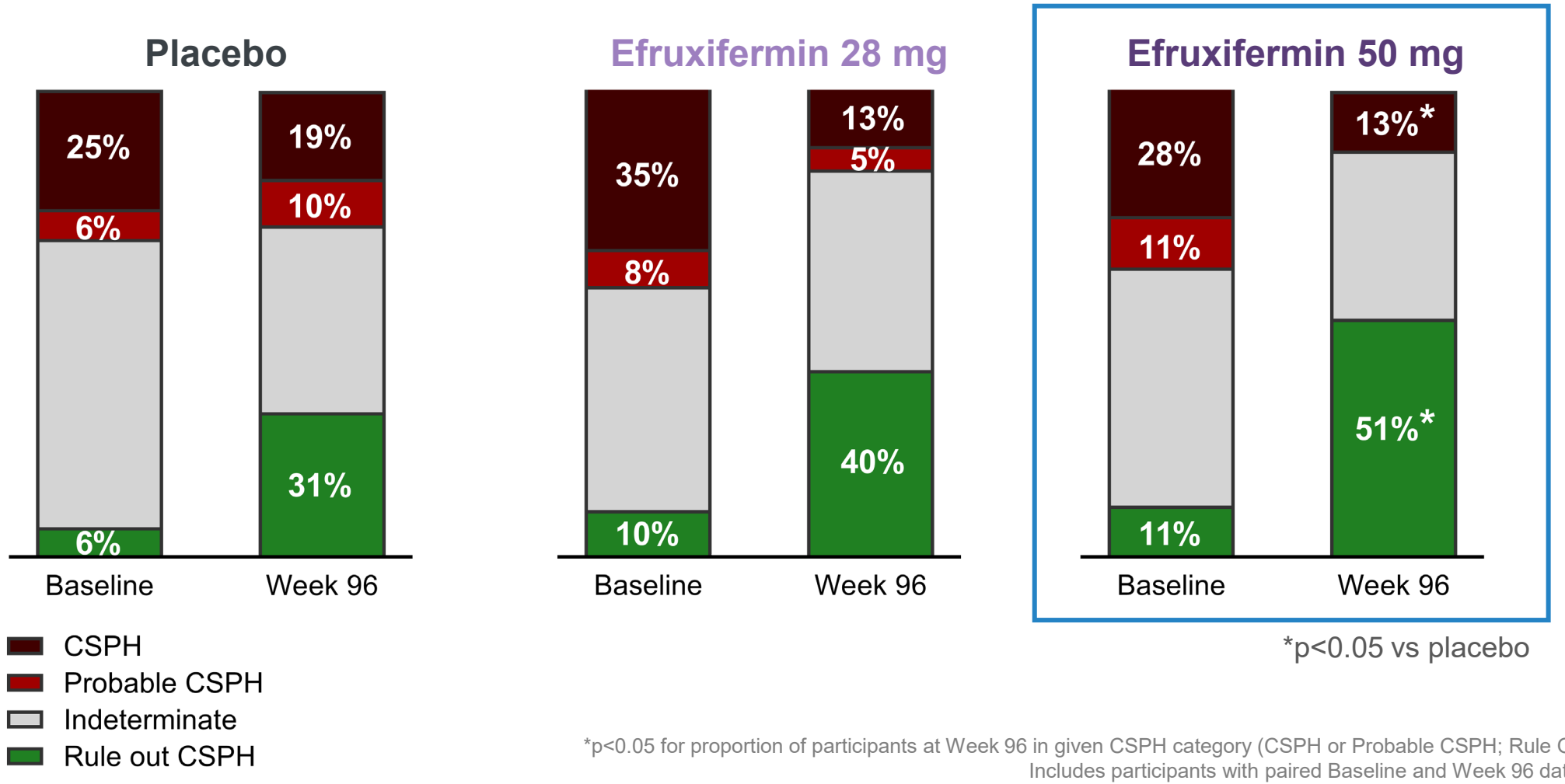
	CSPH / Probable CSPH	Indeterminate	Rule out CSPH
% of participants	**37%**	**54%**	**9%**
Age, years	59	60	61
% Female	76%	67%	67%
% with T2D	82%	77%	83%
LSM (kPa)	**35*** **	**19*** **	**11**
ELF	**10.9****	**10.4**	**10.1**
ALT (U/L)	40	39	38
AST (U/L)	41	35	32
AST / ALT ratio	1.09	0.99	0.96
MELD Score	8.1	7.8	7.5
Platelets ($x10^9$/L)	**166*** **	**192****	**238**
PAI-1 (AU/mL)	15.7	14.5	19.8
Total Bilirubin (mg/dL)	0.7	0.7	0.7
Albumin (g/dL)	**4.2*** **	**4.3****	**4.6**

*p<0.05, **p<0.01, ***p<0.001 vs Rule out CSPH. Data are mean or % of participants, for participants with paired Baseline and Week 96 data (N=135).

Efruxifermin Significantly Improved CSPH Risk Profile
Overall Population

akero

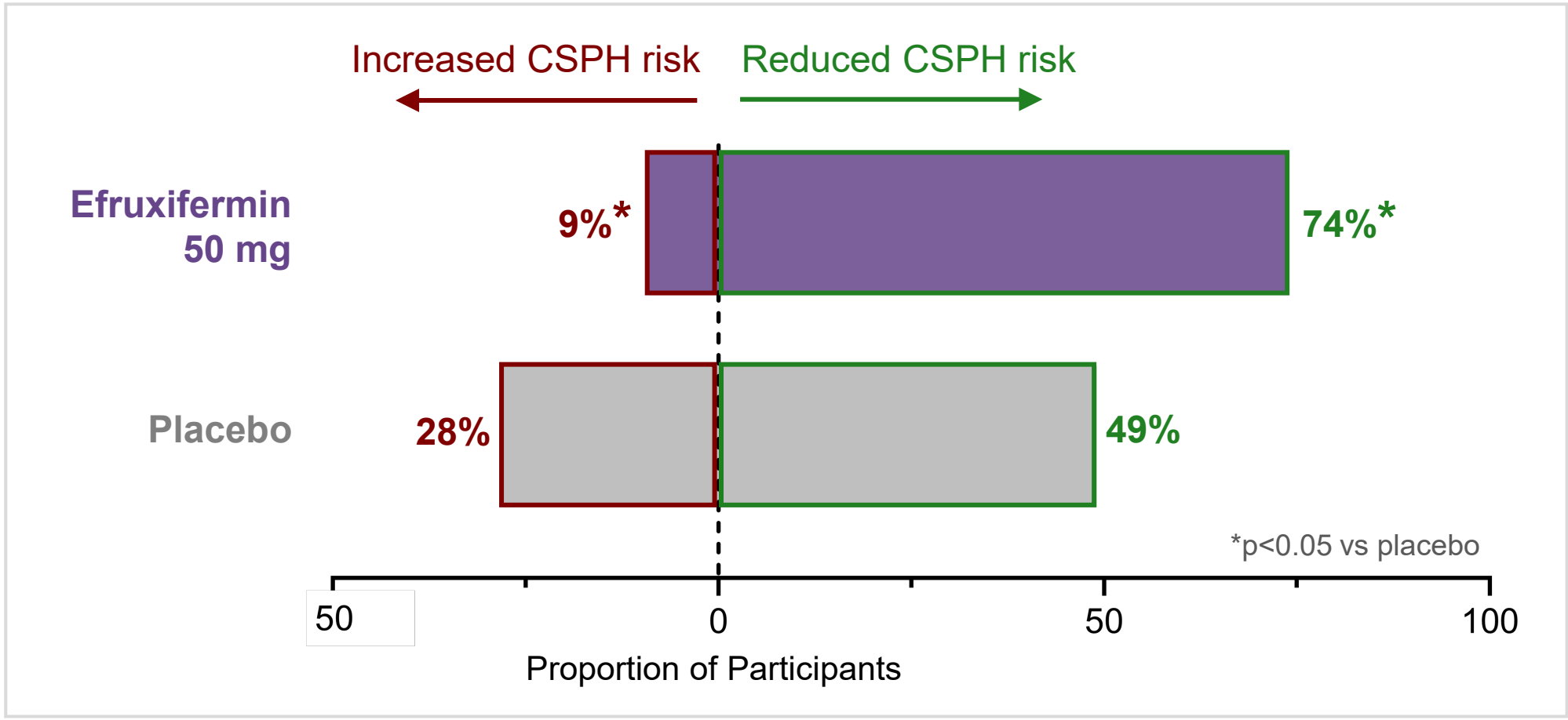
CSPH Could be Ruled Out for Over Half of Efruxifermin 50 mg Participants at Week 96



*p<0.05 vs placebo

*p<0.05 for proportion of participants at Week 96 in given CSPH category (CSPH or Probable CSPH; Rule Out CPSH).
Includes participants with paired Baseline and Week 96 data (N=135).

Efruxifermin for 96 Weeks Reduced CSPH Risk
Subgroups of Participants by Baseline CSPH Status



Increased CSPH risk analysis subgroup excluded participants who were in the CSPH category at baseline (placebo n=36; efruxifermin n=34).

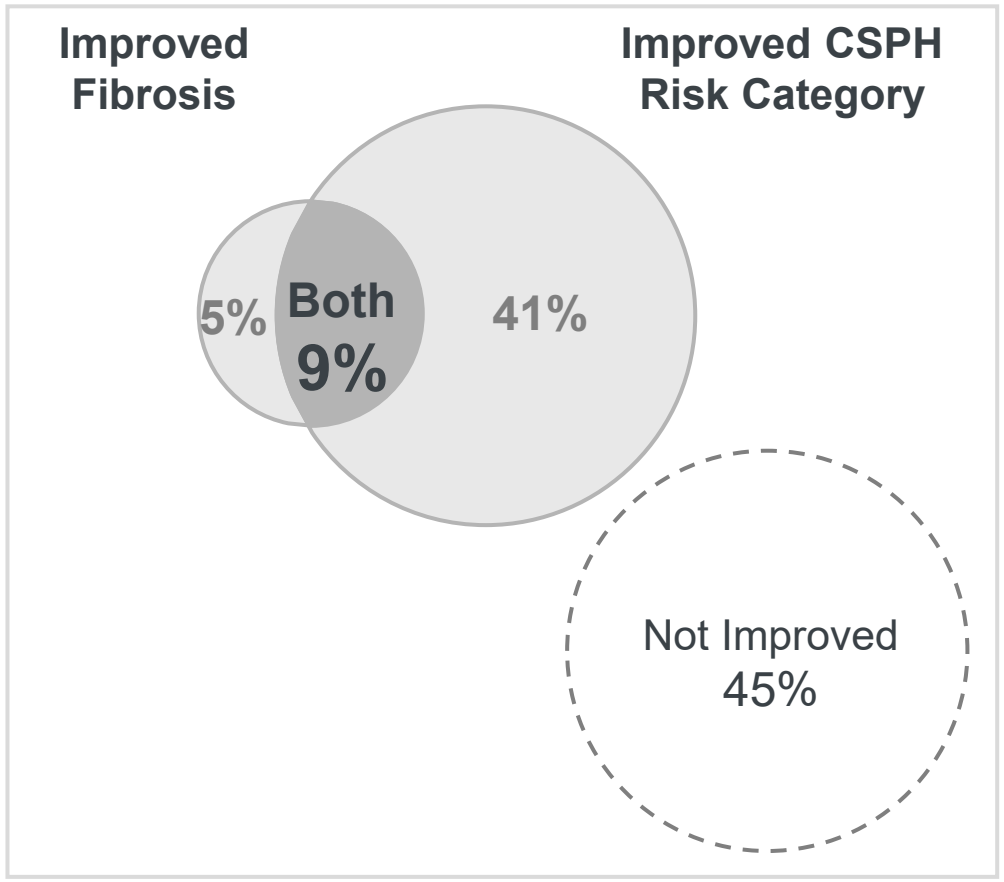
Reduced CSPH risk analysis subgroup excluded participants who were in the Rule Out CSPH category at baseline (placebo n=45; efruxifermin n=42).

Includes participants with paired Baseline and Week 96 data.

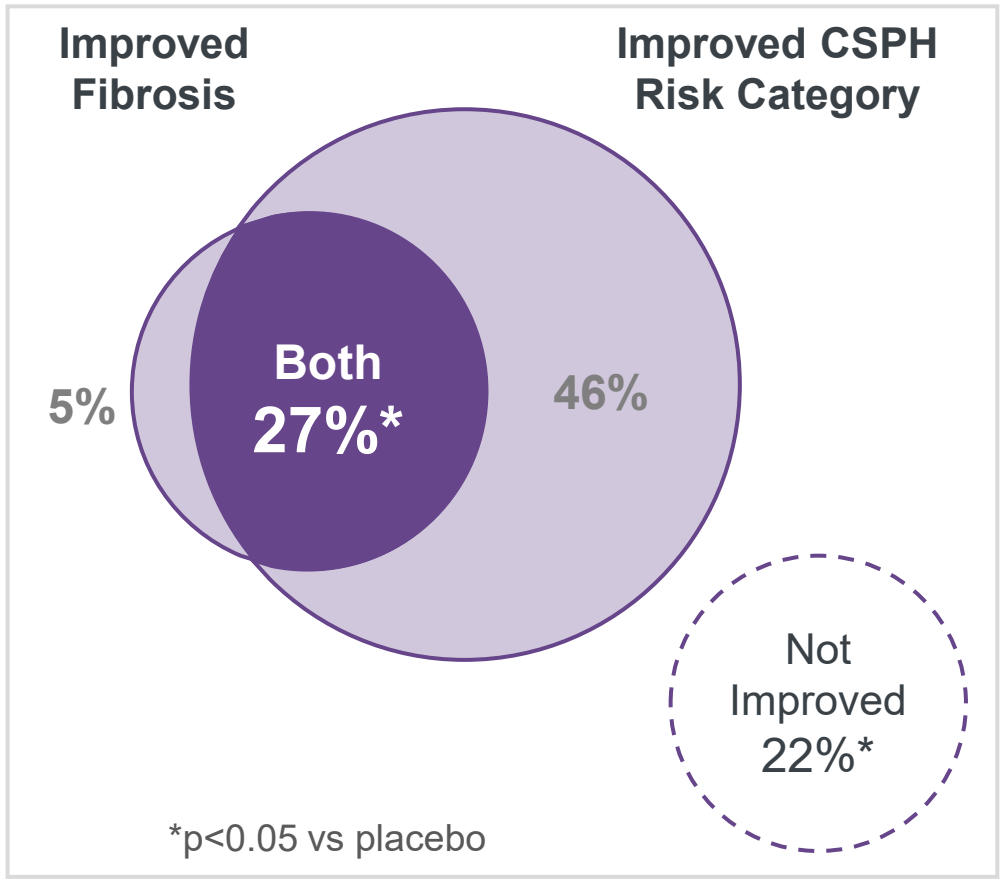
Efruxifermin Improved Both Fibrosis and CSPH Risk Category

Subgroup of Participants Not in Rule Out CSPH Category at Baseline

Placebo (n=44)



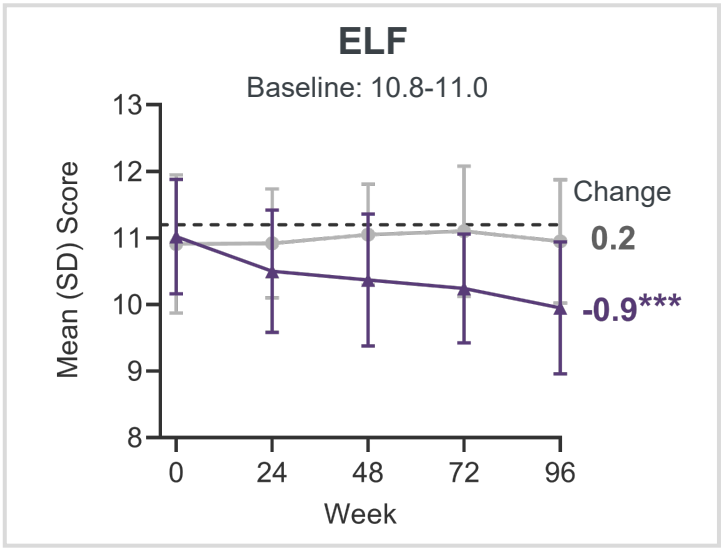
Efruxifermin 50 mg (n=41)

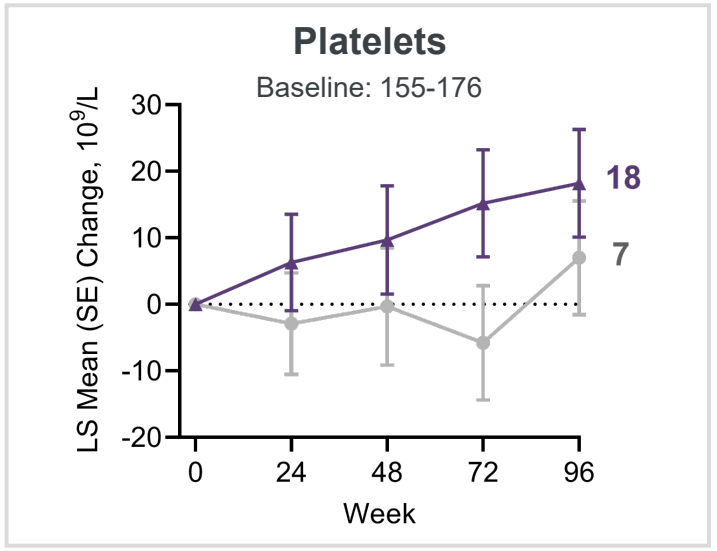


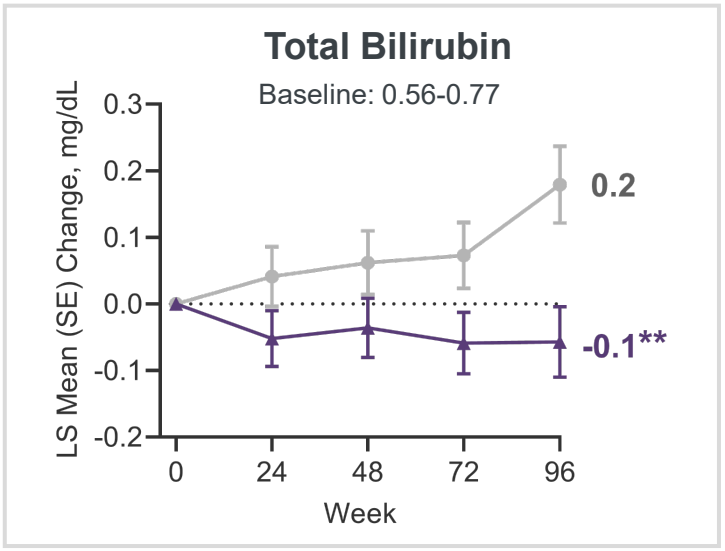
Improved fibrosis defined as ≥1 stage fibrosis improvement without MASH worsening. Improved CSPH Risk Category defined as improvement in CSPH risk category, of those that were not rule-out at baseline. None indicates participants who did not meet either response definition. Includes participants with paired Baseline and Week 96 data.

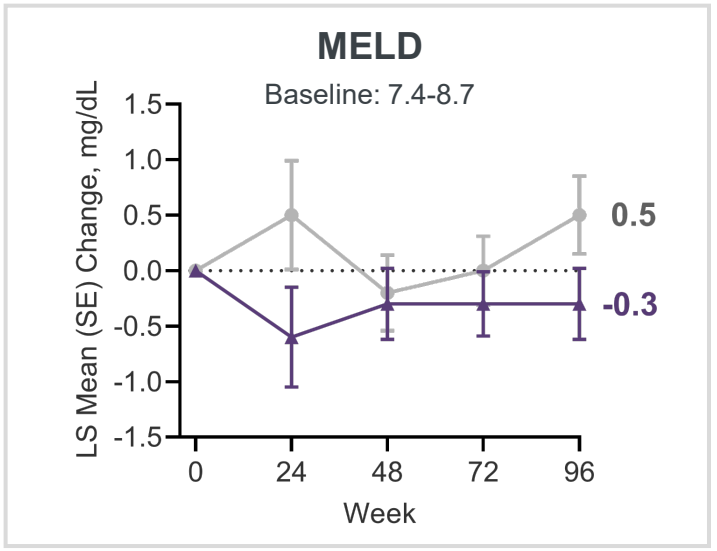
Efruxifermin Improved Markers of Fibrosis and Liver Function

Subgroup of Participants with Higher Baseline CSPH Risk (CSPH or Probable CSPH)









Placebo (n=15)
Efruxifermin 50 mg (n=18)

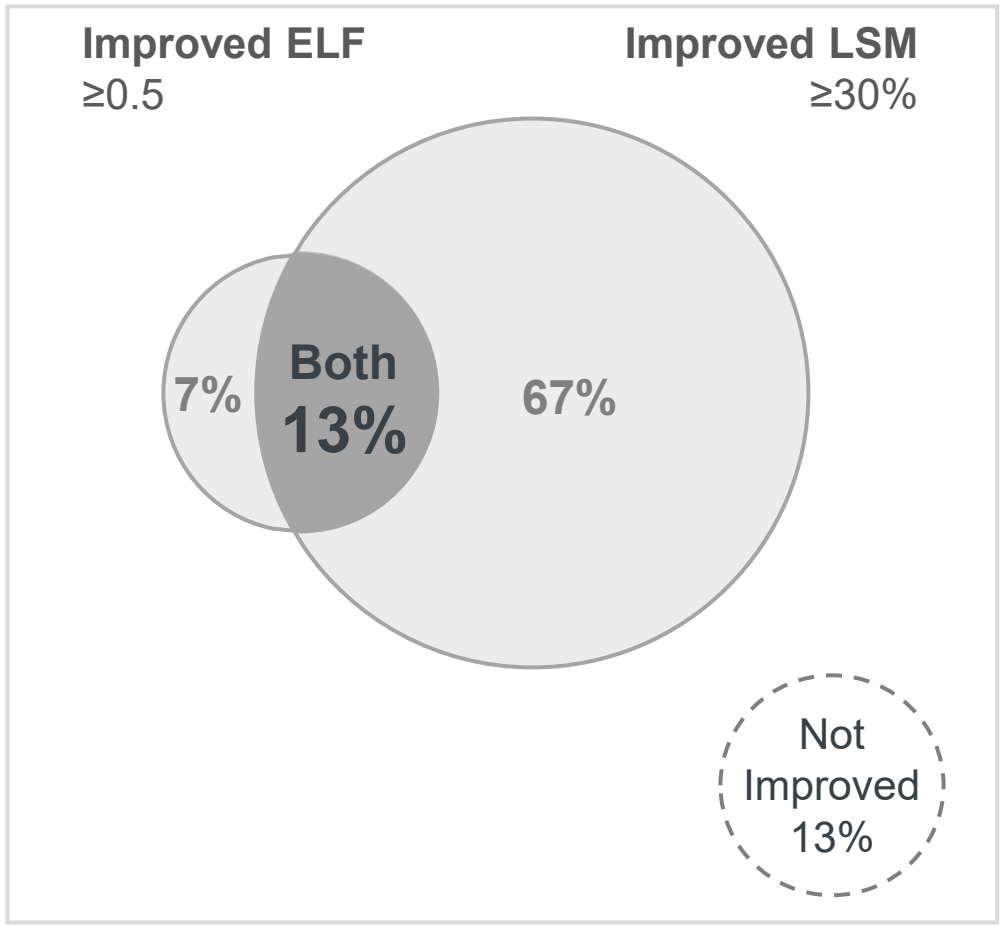
**p<0.01, ***p<0.001 vs placebo at Week 96.
Figures show mean score (ELF) or LS mean change from baseline. Numbers are LS Mean change from Baseline and Week 96. Data are for the subgroup of participants in CSPH or Probable CSPH risk categories with paired Baseline and Week 96 data.

Overlap of Responders for LSM and ELF with Efruxifermin

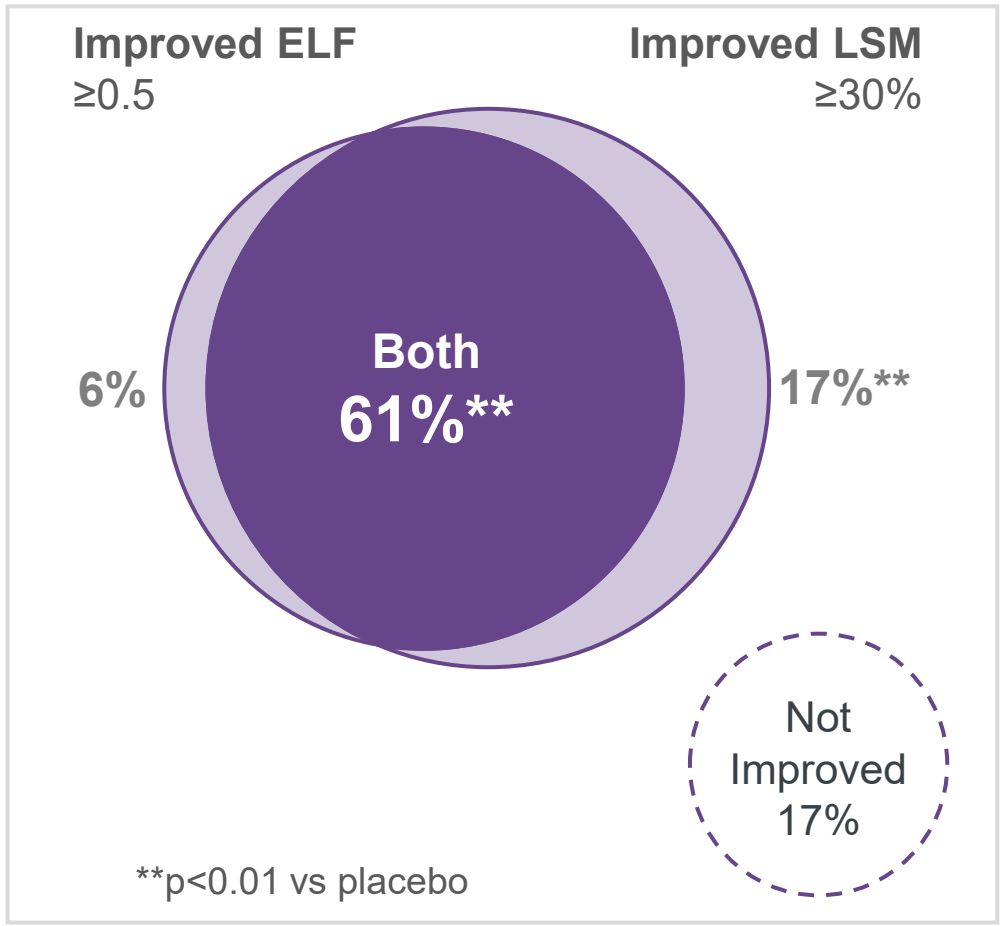
Subgroup of Participants with Higher Baseline CSPH Risk (CSPH or Probable CSPH)

akero

Placebo (n=15)

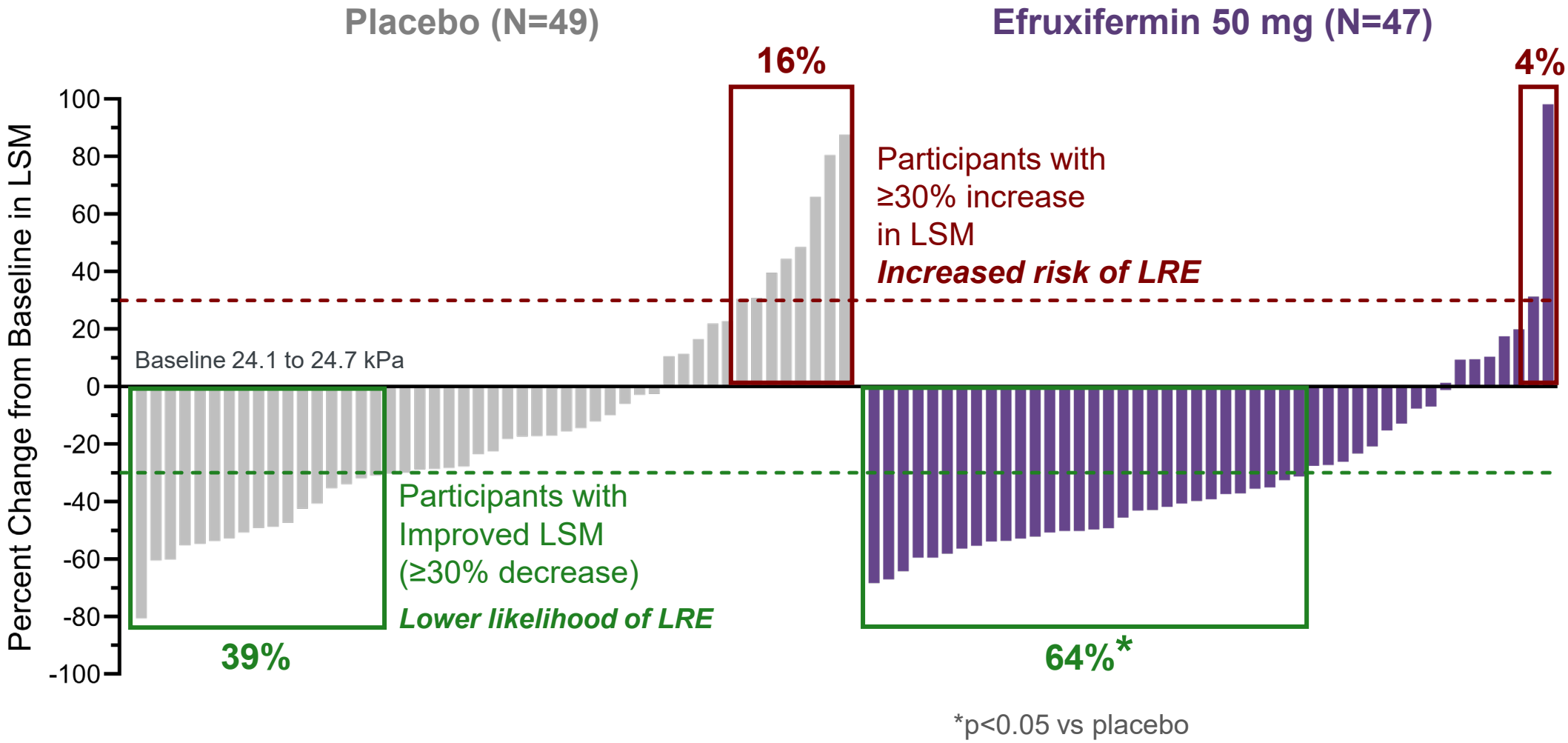


Efruxifermin 50 mg (n=18)



Improvements are based on the change from baseline to week 96: ELF score ≥0.5 improvement (decrease); LSM ≥30% improvement (decrease).
Data are for the subgroup of participants in CSPH / Probable CSPH risk categories with paired Baseline and Week 96 data.

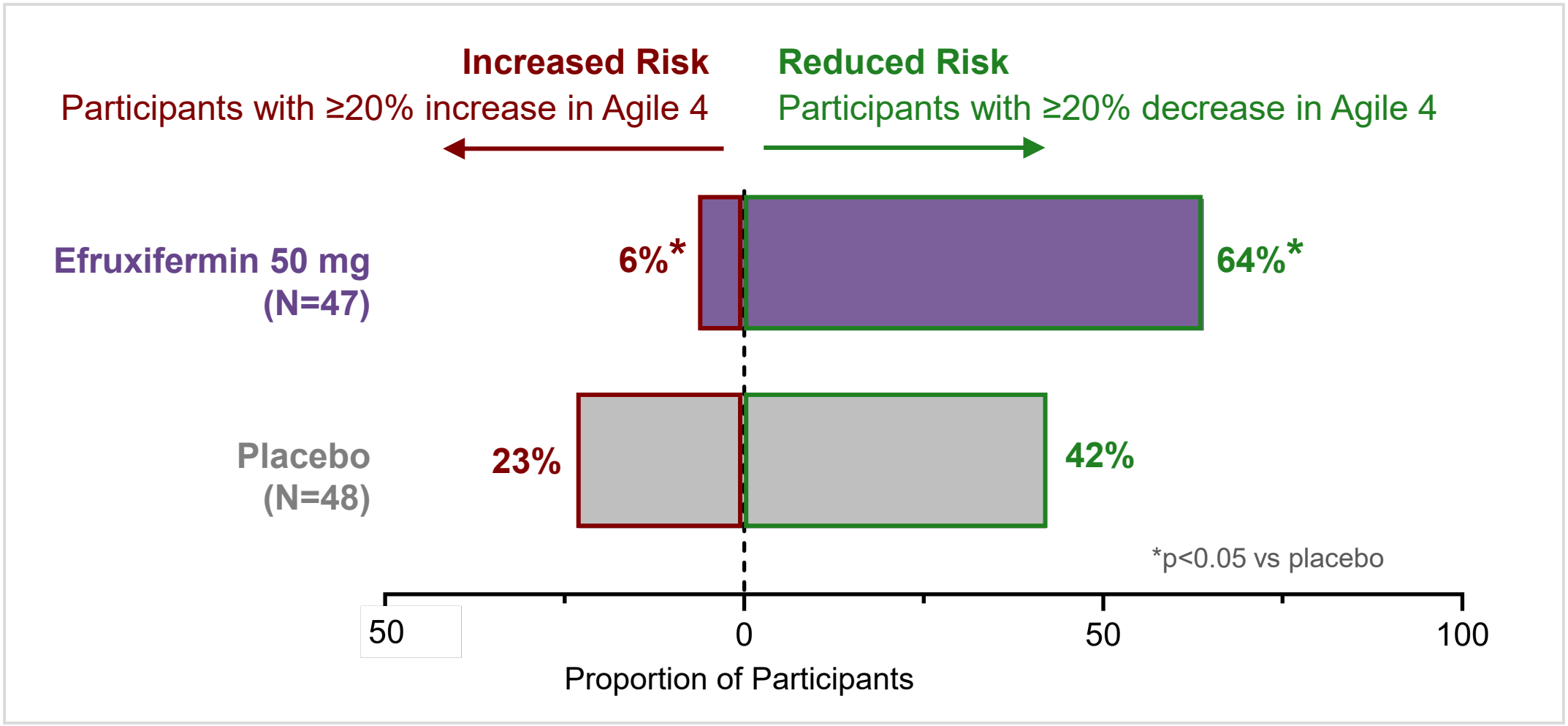
Changes in LSM Among Efruxifermin Participants Predict a Lower Risk of Liver-Related Events (LRE), Overall Population



Lin (2024) *JAMA*

Figure shows percent change from Baseline at Week 96 in LSM by VCTE. Includes participants with paired Baseline and Week 96 data.

Agile 4 Predicts Lower Risk of Liver-Related Events with Efruxifermin, Overall Population

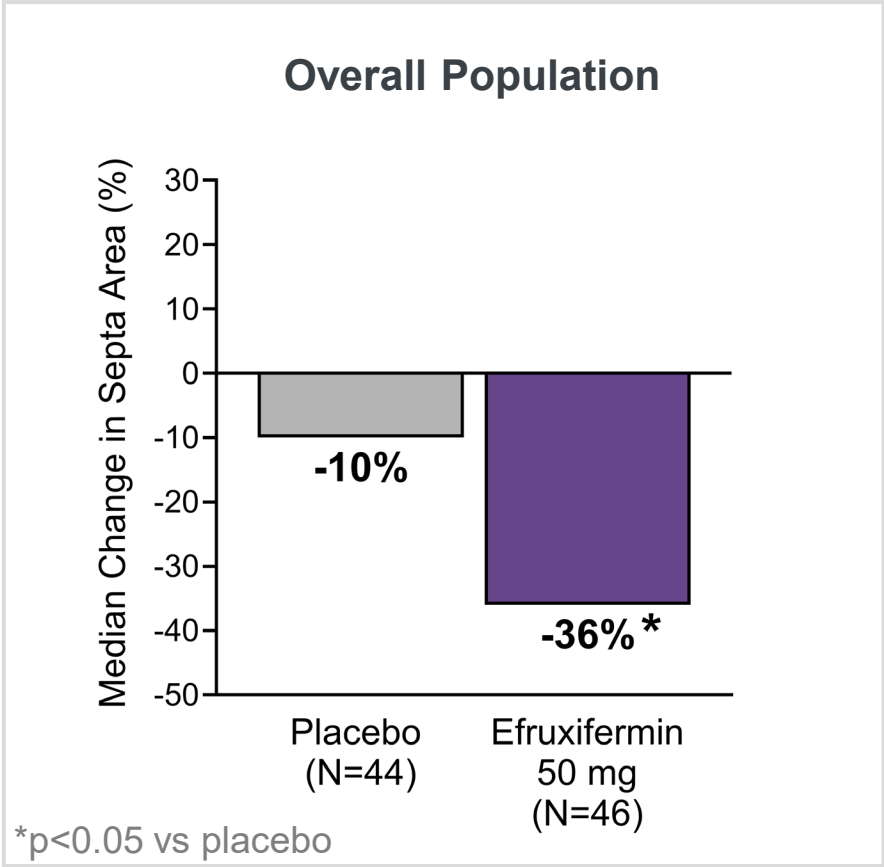


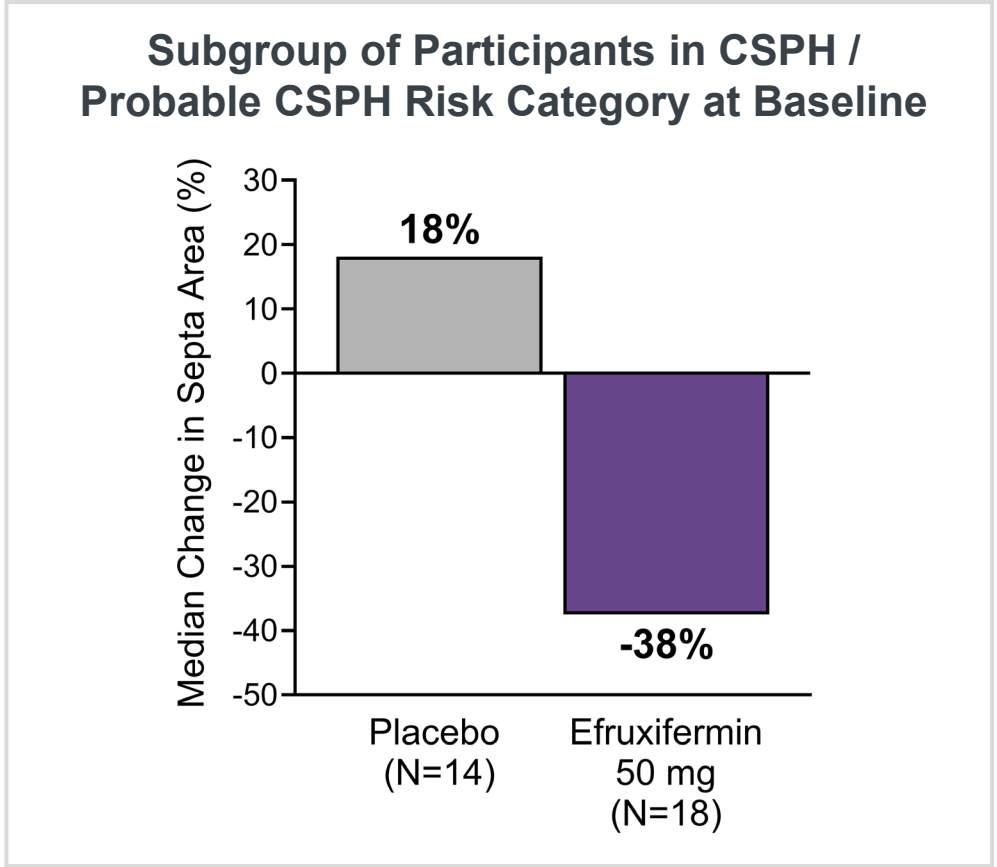
Includes participants with paired Baseline and Week 96 data.

Sanyal (2023) *J Hepatol;* Lin (2024) *JAMA*

Efruxifermin Reduced Septa Area by AI-Based Digital Pathology
Overall Population and Subgroup with Higher Baseline CSPH Risk

Relative Change in Septa Area from Baseline to Week 96
(Poster #5024)





Median septa area change from Baseline at Week 96 evaluated by qSepta.
Includes participants with paired Baseline and Week 96 data.

Goodman (2024) *Liver Int Commun;* Noureddin (2024) *Aliment Pharmacol Ther.*

Summary and Conclusions

- In the SYMMETRY trial that enrolled participants with MASH and compensated cirrhosis (F4c), efruxifermin improved fibrosis by histology at Week 96.
- Fibrosis improvement with efruxifermin was accompanied by changes in noninvasive tests consistent with improved liver function.
  - Reduced risk of portal hypertension (CSPH) and potentially improved hemodynamics
  - Reduced fibrosis burden in participants with more advanced disease at baseline
  - Improvements in Agile 4
- Efruxifermin may prevent progression to decompensation and liver-related events in patients with compensated cirrhosis.
- The Phase 3 clinical trial of efruxifermin in individuals with compensated cirrhosis is currently enrolling.
  - SYNCHRONY Outcomes: NCT06528314

Acknowledgements

We thank the participants and their families, the investigators, and staff who participated in the SYMMETRY trial.

Investigators: *Mazen Noureddin and the SUMMIT Network* • *Gary Abrams • Naim Alkhouri • Duane C Anderson • Victor Ankoma-Sey • Amon Asgharpour • Robert Barish • Jacques Benun • Bal Raj Bhandari • Sureka Bollepalli • Shekhar Challa • Laura Cisneros • Sudhanshu Gogia • Saeid Goshtasbi • Colby Grossman • Nadege T. Gunn • Stephen Harrison • Anita Kohli • Alma Laura Ladron de Guevara Cetina • John Lowe • Kathryn J. Lucas • Matthew Mason • Fernando Membreno • Edward A. Mena • Ann Moore • Sam E. Moussa • Guy W. Neff • Grisell Ortiz-Lasanta • Pankaj Patel • Pavan Patel • Rashmee Patil • Narayan Peddanna • Gilberto Perez • Stephanie Pointer • John Poulos • Robert Rahimi • Gary Reiss • Jose Rodriguez • Manuel E. Rodriguez • Madhavi Rudraraju • Peter Ruane • William Sanchez • Harry Sarles • Muhammad Sheikh • Mousab Tabbaa • Louis Wilson • Scott A. Wofford*