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Efruxifermin improved fibrosis in participants with MASH cirrhosis and multiple cardiometabolic comorbidities: a post hoc analysis of the SYMMETRY phase 2b trial

Poster 3548

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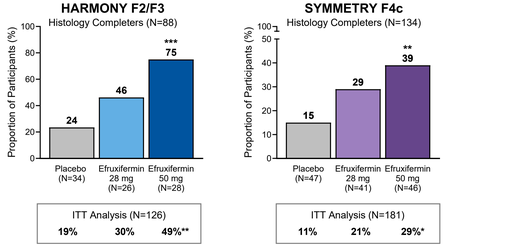
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https://sciencehub.novonordisk.com/congresses/aasld2026/rinella.html

Background

- Individuals with MASH and compensated cirrhosis are more likely to have multiple cardiometabolic risk factors and a higher risk of clinical outcomes.
- Efruxifermin is a bivalent FGF21 analog with balanced agonism of FGFR1c, 2c, and 3c that is in development for treatment of MASH.
- In Phase 2b trials, efruxifermin improved fibrosis and cardiometabolic markers in participants with MASH and moderate to advanced (F2/F3) fibrosis or compensated cirrhosis (F4c) (Figure 1).[1,2]
- Efruxifermin was generally well tolerated.[1,2] Mild to moderate gastrointestinal adverse events were more common with efruxifermin than placebo.

Figure 1. Efruxifermin improved histology-defined fibrosis at Week 96 in phase 2b trials in MASH[1,2]



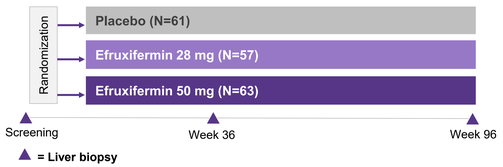
*p<0.05, **p<0.01, ***p<0.001 vs placebo (Cochran-Mantel-Haenszel test). The Histology Completers analysis included all participants with baseline and Week 96 liver biopsies. The ITT analyses included all randomized and dosed participants, with Week 96 missing biopsy imputed as nonresponse. Fibrosis response was defined as participants with ≥1-stage fibrosis improvement and no worsening of MASH. Abbreviations: ITT, intent to treat.

Aim

- **Evaluate if the presence of multiple cardiometabolic comorbidities affected the response to efruxifermin in participants with compensated cirrhosis (F4c) due to MASH.**

SYMMETRY Study Design

- **Population**: 181 randomized and dosed; 134 with Week 96 liver biopsy
- **Primary end point**: ≥1-stage fibrosis improvement without MASH worsening



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References: [1] Noureddin et al. Lancet. 2025;406(10504):719–730; [2] Noureddin et al. N Engl J Med. 2025;392(24):2413–2424.

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Methods

- This post hoc analysis included participants with MASH and biopsy-defined F4c from the SYMMETRY randomized placebo-controlled trial (NCT05039450).
- Participants were grouped by the number of baseline cardiometabolic comorbidities:

Comorbidity	Definition
Obesity	Baseline BMI ≥30 kg/m^2
T2D	Medical history of T2D or baseline HbA1c ≥6.5
Hypertension	Medical history of hypertension or baseline SBP ≥140 mmHg or DBP ≥90 mmHg
Hyperlipidemia	Medical history of hyperlipidemia or baseline LDL-C ≥100 mg/dL

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; T2D, type 2 diabetes.

Results

- At baseline, 40/181 participants had 1 or 2 cardiometabolic comorbidities, and 141/181 participants had 3 or 4 cardiometabolic comorbidities.
- The most prevalent cardiometabolic comorbidities were obesity, type 2 diabetes, and hypertension (Table 1).

Table 1. Overall Baseline Characteristics

Baseline Characteristics	N=181
Age, years	61 (8)
Female	121 (67%)
T2D	145 (80%)
Obesity	145 (80%)
Hypertension	146 (80%)
Hyperlipidemia	78 (43%)
Baseline Medication Use	
GLP1-RA	48 (27%)
Statin	85 (47%)
Number of cardiometabolic comorbidities[†]	
1	5 (3%)
2	35 (19%)
3	62 (34%)
4	79 (44%)

Data are mean (SD) or n (%). Percentages may not add up to 100 due to rounding. [†] To be eligible, participants were required to have a previous history or presence of T2D or 2 out of 4 components of metabolic syndrome (obesity, dyslipidemia, elevated blood pressure, elevated fasting glucose). Abbreviations GLP1-RA, glucagon-like peptide-1 receptor agonist ; T2D, type 2 diabetes.

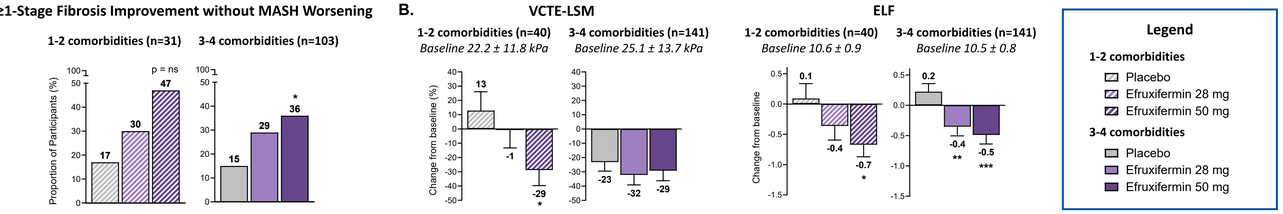
Safety and Tolerability

- There were no meaningful differences in the frequency of adverse events across comorbidity groups.

Improvement in Fibrosis, Lipid Profile, and Markers of Glycemic Control

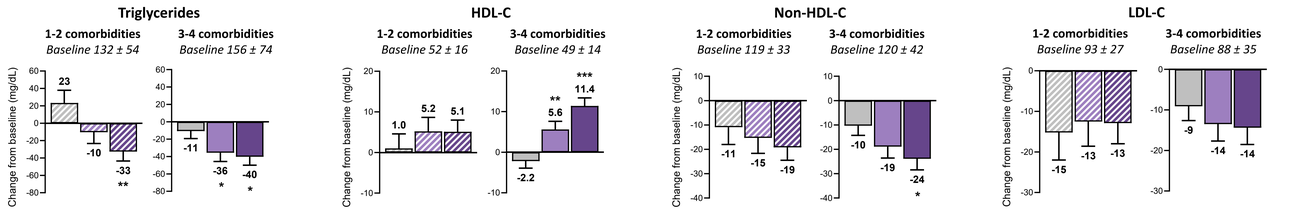
- In participants with F4c MASH and multiple cardiometabolic comorbidities, efruxifermin improved fibrosis (Figure 2), lipid profile (Figure 3), and measures of insulin sensitivity (Figure 4) at Week 96.

Figure 2. Improvement in Histology-Defined and Noninvasive Measures of Fibrosis at Week 96



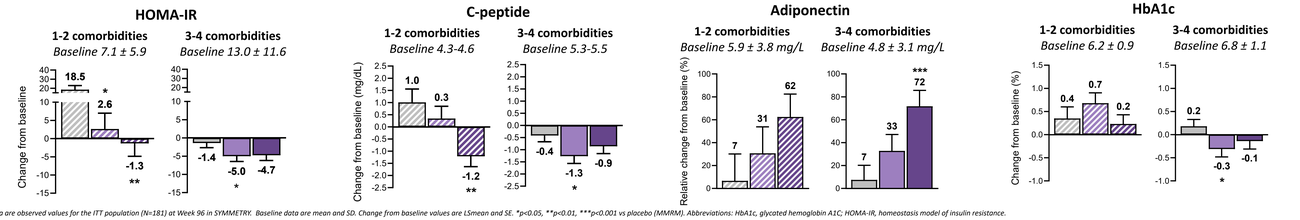
*(A) Fibrosis response data are for participants with baseline and Week 96 liver biopsies (N=134). Fibrosis response was defined as participants with ≥1-stage fibrosis improvement and no worsening of MASH. *p<0.05 vs placebo (Cochran-Mantel-Haenszel test). (B) LSM and ELF data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY. Baseline data are mean and SD. Change from baseline values are LSmean and SE. *p<0.05, **p<0.01, ***p<0.001 vs placebo (MMRM). Abbreviations: ELF, Enhanced Liver Fibrosis test; LSM, liver stiffness measurement by vibration-controlled transient elastography (Fibroscan).*

Figure 3. Improvement in Lipid Profile at Week 96



*Data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY. Baseline data are mean and SD. Change from baseline values are LSmean and SE. *p<0.05, **p<0.01, ***p<0.001 vs placebo (MMRM). Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.*

Figure 4. Improvement in Markers of Glycemic Control at Week 96



*Data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY. Baseline data are mean and SD. Change from baseline values are LSmean and SE. *p<0.05, **p<0.01, ***p<0.001 vs placebo (MMRM). Abbreviations: HbA1c, glycated hemoglobin A1C; HOMA-IR, homeostasis model of insulin resistance.*

Summary and Conclusions

- **Most of the participants in the SYMMETRY trial (78%) had 3 to 4 cardiometabolic comorbidities.**
- **In this post hoc analysis, efruxifermin improved fibrosis, lipid profile, and glycemic control in participants with F4c MASH, regardless of the number of cardiometabolic comorbidities.**
- **Phase 3 trials of efruxifermin in MASH with moderate to severe (F2/F3) fibrosis or compensated cirrhosis are ongoing.**

synchrony HISTOLOGY

- **Currently enrolling:** NCT06215716
- **F2/F3 MASH:** Biopsy-defined moderate to advanced fibrosis
- Efruxifermin 28 and 50 mg

synchrony OUTCOMES

- **Currently enrolling:** NCT06528314
- **F4c MASH:** Biopsy-defined or ***noninvasively diagnosed*** compensated cirrhosis due to MASH
- Efruxifermin 50 mg

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