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For Study of The Liver
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Efruxifermin improved fibrosis due to MASH in participants with F2/F3 fibrosis or compensated cirrhosis due to MASH: results of two 96-week, randomized, double-blind, placebo-controlled, phase 2b trials

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9 August 2025

Efruxifermin Background and Rationale

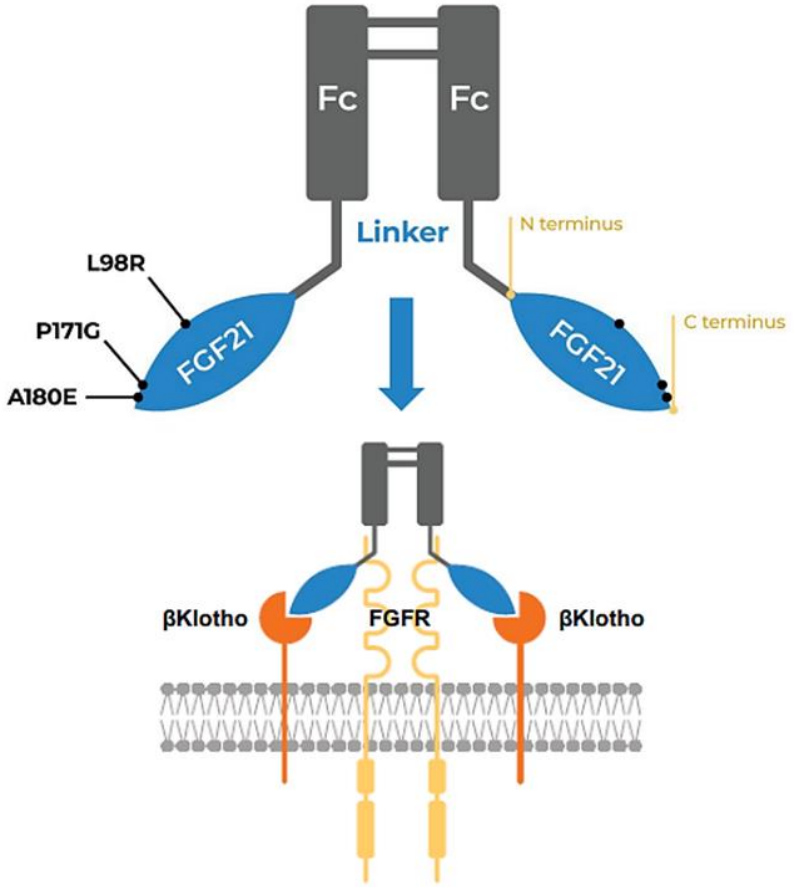
Efruxifermin is a long-acting, bivalent Fc-FGF21 fusion protein designed to mimic biology of native FGF21

Key structure/activity attributes of efruxifermin:

- Increased half-life to ~3 days, supporting once-weekly dosing
- Balanced agonism of FGFR1c, 2c, and 3c, no activity at FGFR4
- Bivalent structure enhances binding to target cells
- Sustained biomarker response over 96-week dosing

Rationale for efruxifermin in MASH and advanced fibrosis:

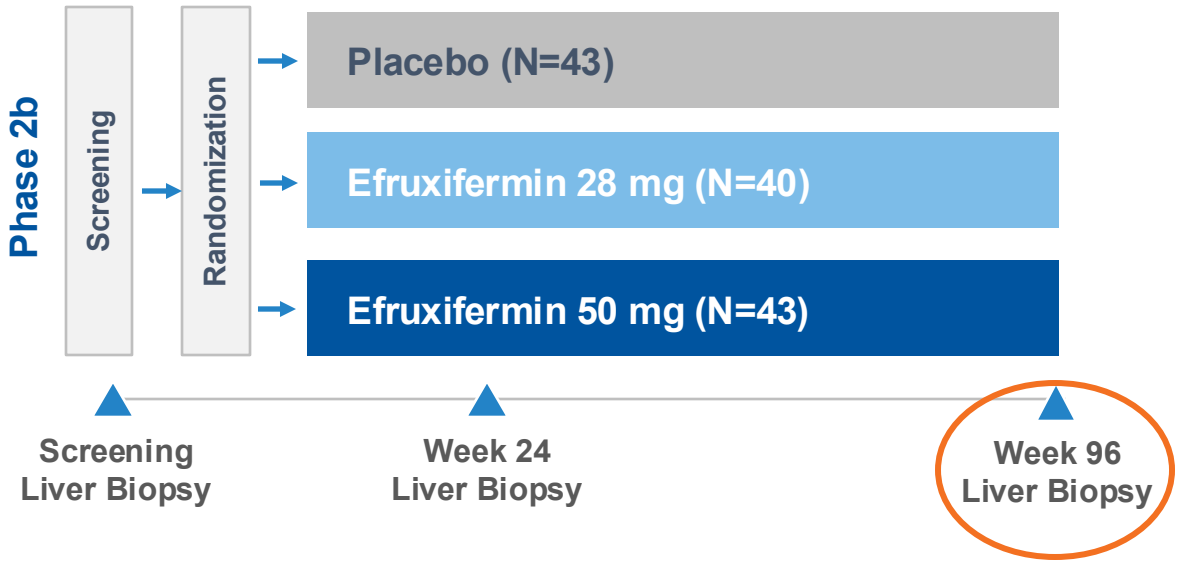
- Reduces liver fat and lipotoxicity
- Direct antifibrotic effects
- Increases insulin sensitivity (increased adiponectin, decreased C-peptide)



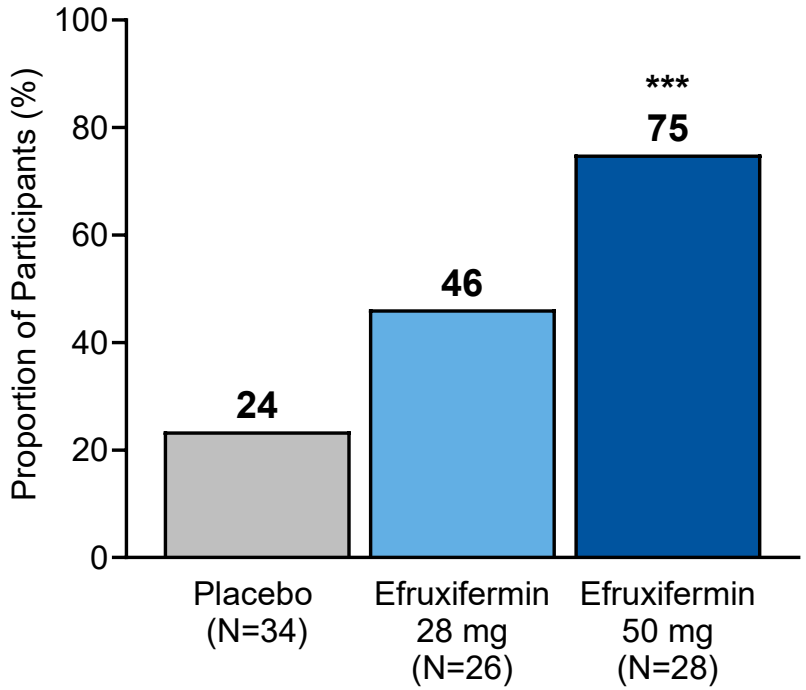
Tillman (2020) *Front Endocrinol*; Harrison (2023) *Lancet Gastroenterol Hepatol;* Noureddin (2025) *N Engl J Med;* Noureddin *Lancet (in press)*

HARMONY: Efruxifermin in Pre-Cirrhotic (F2/F3) MASH

Population	126 randomized and dosed 88 with Week 96 liver biopsy
Primary End Point	≥1-stage fibrosis improvement without MASH worsening
Participants	66% F3, age 55 years, 62% female 70% T2D, GLP-1 RA 16% BMI 38 kg/m^2



Fibrosis improvement ≥1 stage without MASH Worsening, Week 96 Completers



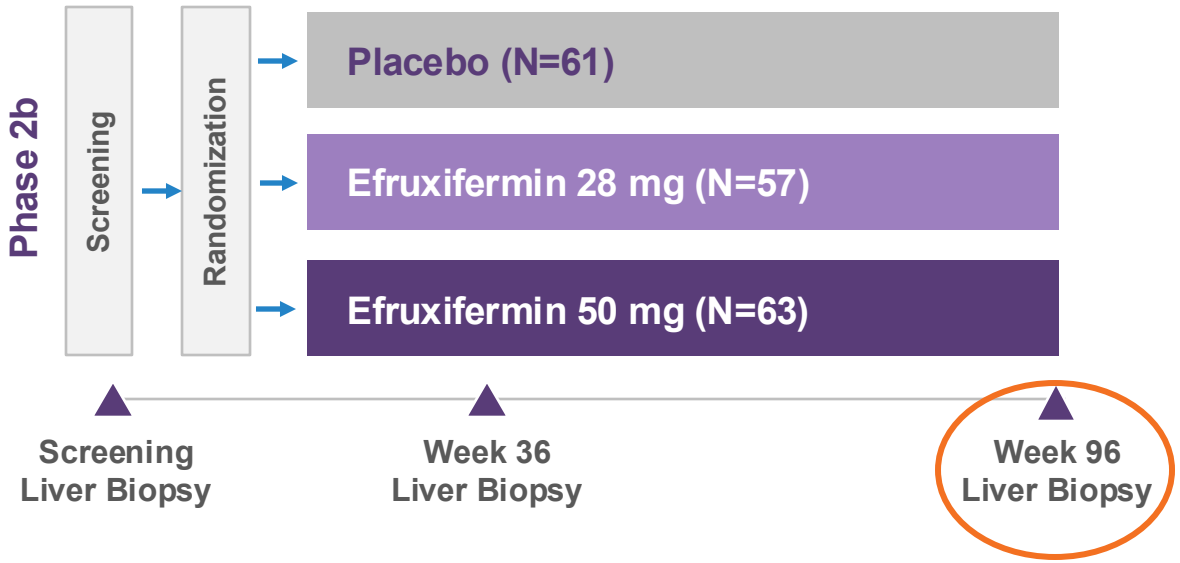
mITT Population	(N=43)	(N=40)	(N=43)
	19%	**30%**	**49%****

Harrison (2023) *Lancet Gastroenterol Hepatol;* Noureddin *Lancet (in press).*

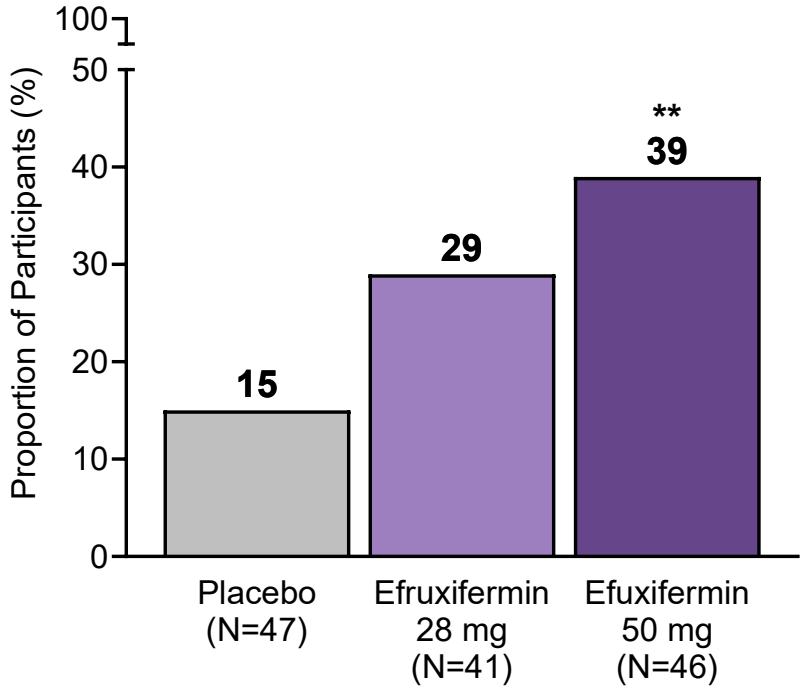
Missing biopsy imputed as non-response. *p<0.05, ***p<0.001 vs placebo.

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



Fibrosis improvement ≥1 stage without MASH Worsening, Week 96 Completers



ITT Population	(N=61)	(N=57)	(N=63)
	12%	**21%**	**29%***

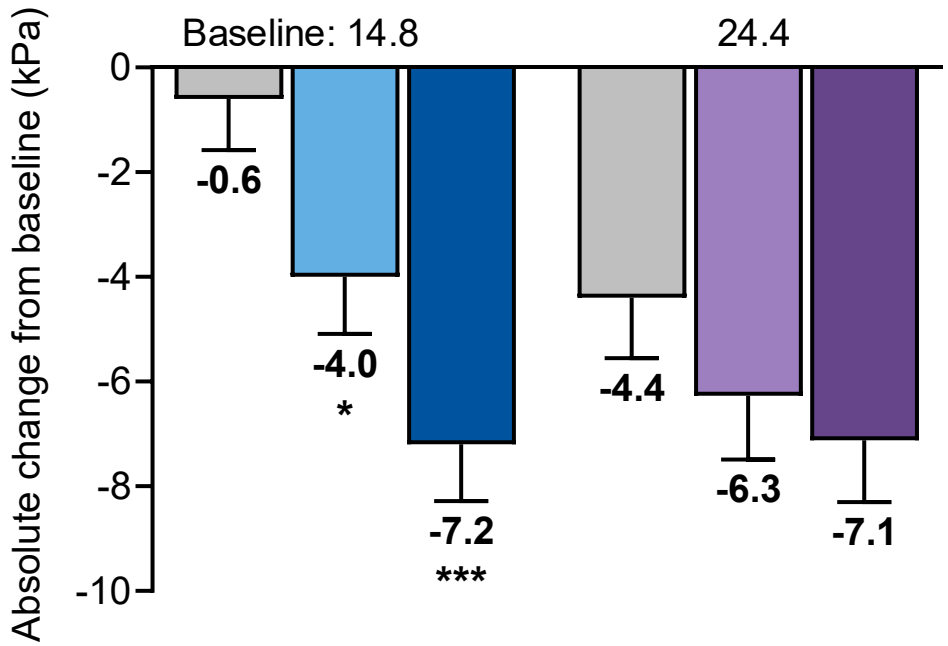
Noureddin (2025) *N Engl J Med.*

Missing biopsy imputed as non-response. *p<0.05,**p<0.01 vs placebo.

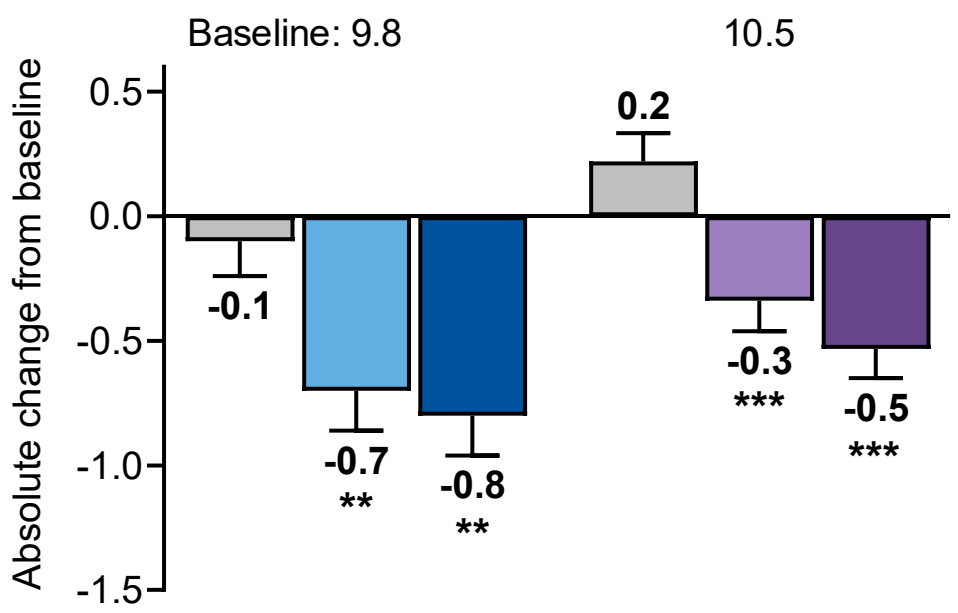
Efruxifermin Improved Noninvasive Measures of Fibrosis at Week 96

in Participants with Advanced Fibrosis (F2/F3) and Cirrhosis (F4c)

LSM-VCTE



ELF Score



F2/3 MASH

- Placebo
- Efruxifermin 28 mg
- Efruxifermin 50 mg

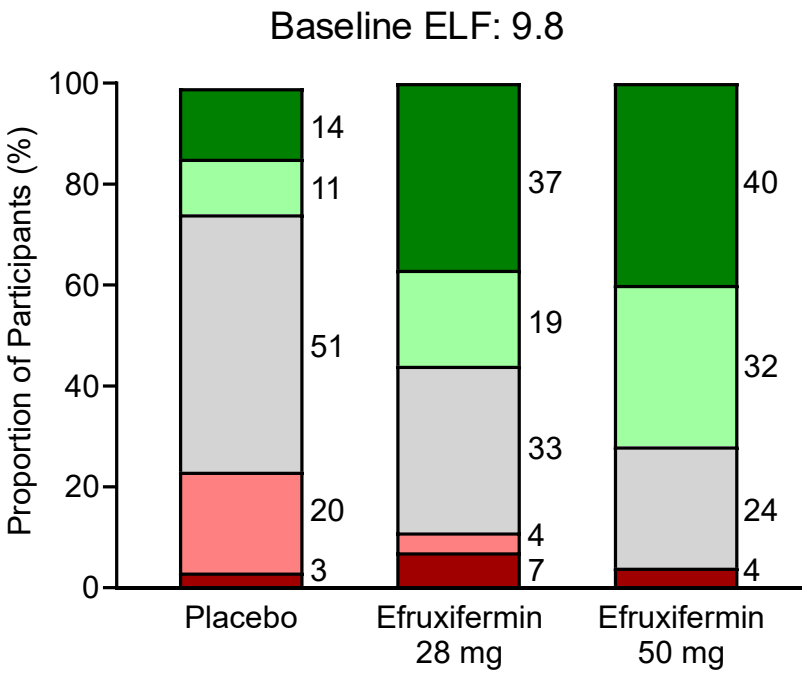
F4c MASH

- Placebo
- Efruxifermin 28 mg
- Efuxifermin 50 mg

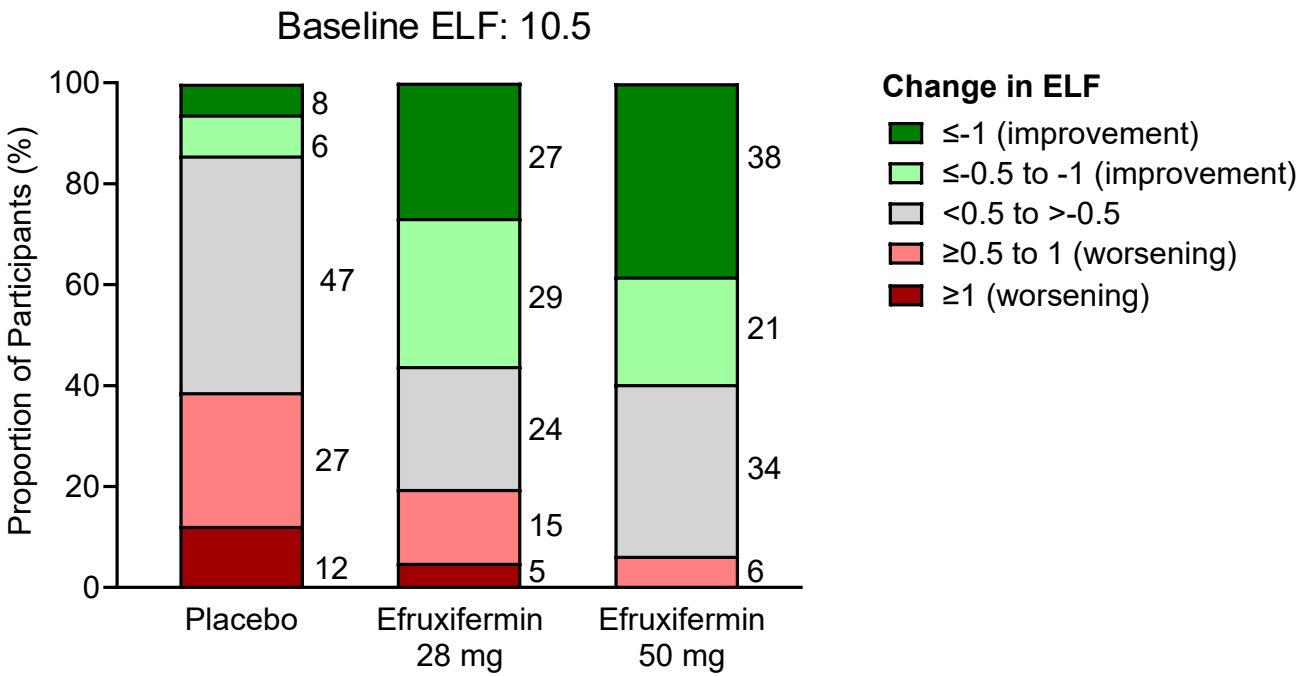
F2/3 MASH data are observed values for the mITT population (N=126) at Week 96 in HARMONY.
F4 MASH data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY.
LSM-VCTE=liver stiffness measurement by vibration-controlled transient elastography (FibroScan); ELF=Enhanced Liver Fibrosis score.
Baseline values are population mean; *p<0.05,**p<0.01, ***p<0.001 vs placebo.

Efruxifermin Improved ELF Score and Reduced Disease Progression
in Participants with Advanced Fibrosis and Cirrhosis

F2/3 MASH



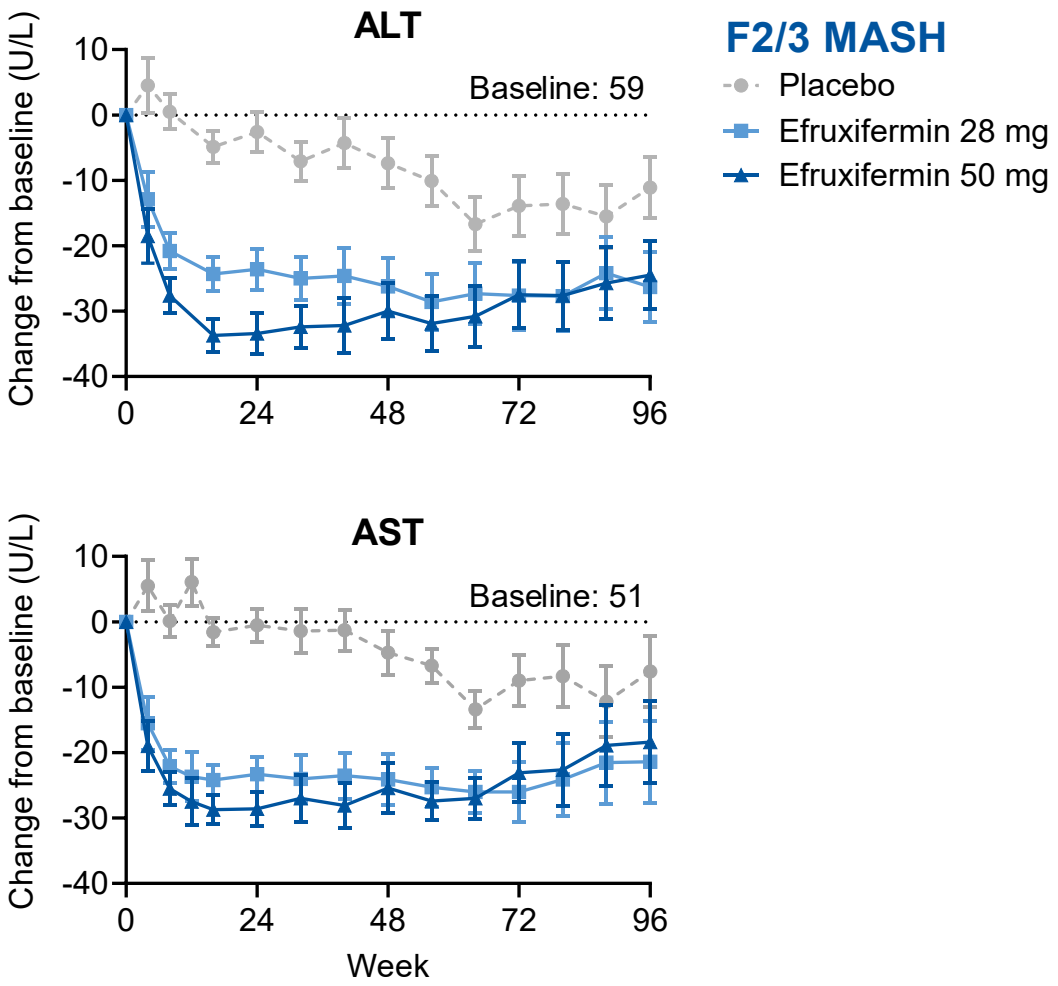
F4c MASH

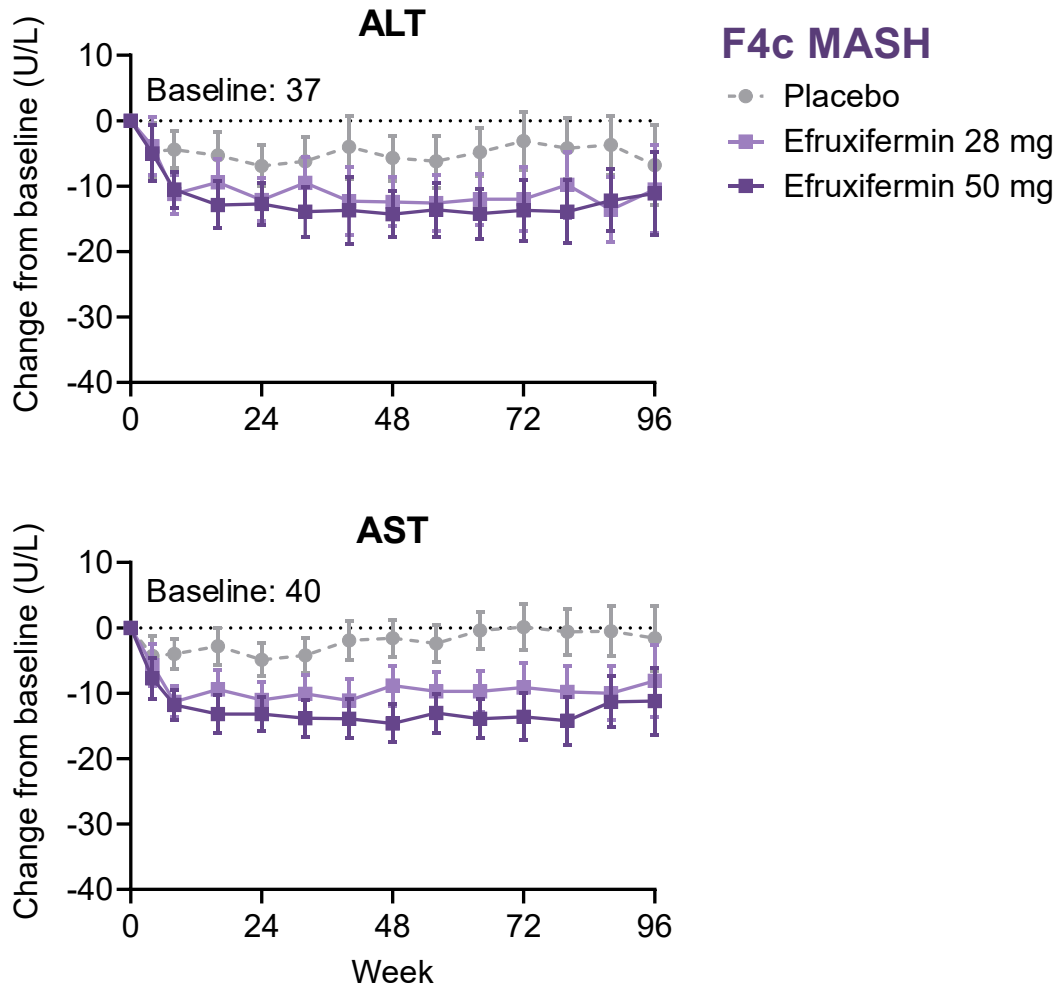


- More efruxifermin-treated participants had an improvement in ELF score of ≥0.5 or 1.
- Fewer efruxifermin-treated participants progressed or had worsened ELF score of ≥0.5 or 1.

F2/3 MASH data are observed values for the mITT population (N=126) at Week 96 in HARMONY.
F4 MASH data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY.
ELF=Enhanced Liver Fibrosis score. Baseline values are population mean; *p<0.05,**p<0.01, ***p<0.001 vs placebo.

Rapid and Sustained Improvement in Liver Enzymes
in Participants with Advanced Fibrosis and Cirrhosis





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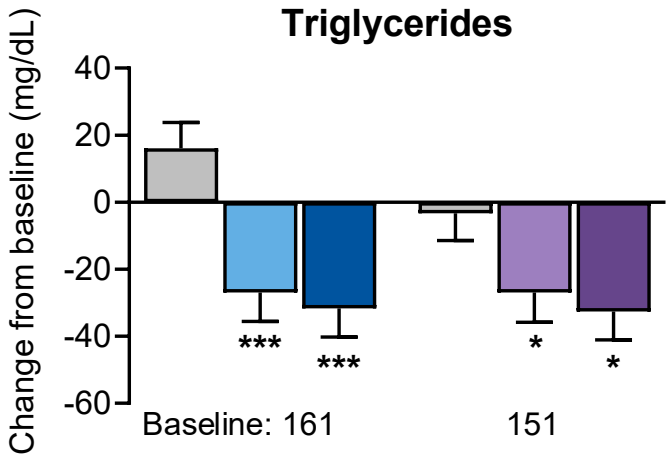
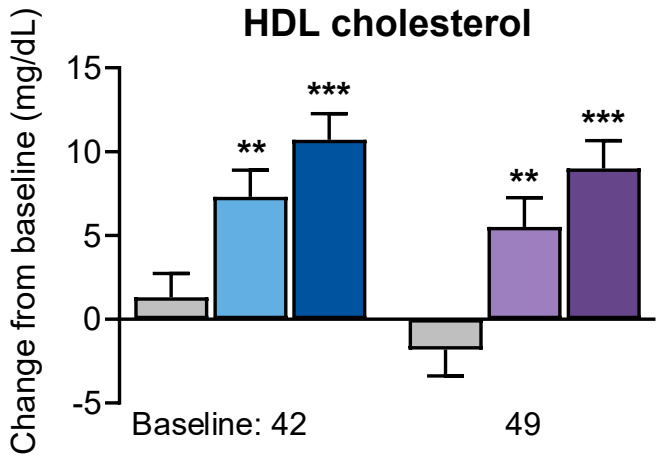
Baseline values are population mean.

Improvement in Lipid Profile at Week 96
in Participants with Advanced Fibrosis and Cirrhosis





F2/F3 MASH
- Placebo
- Efruxifermin 28 mg
- Efruxifermin 50 mg

F4c MASH
- Placebo
- Efruxifermin 28 mg
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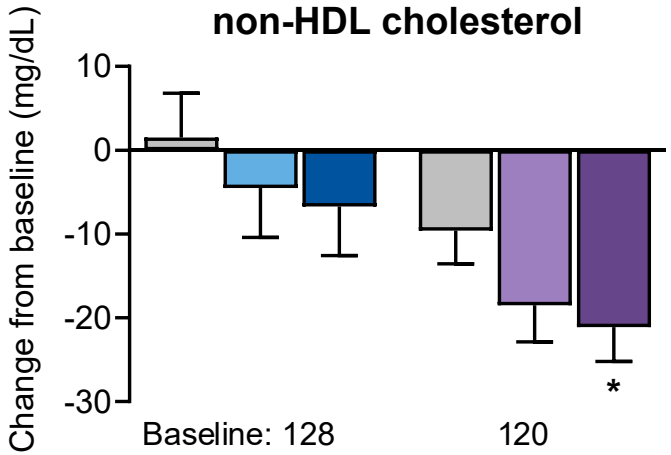

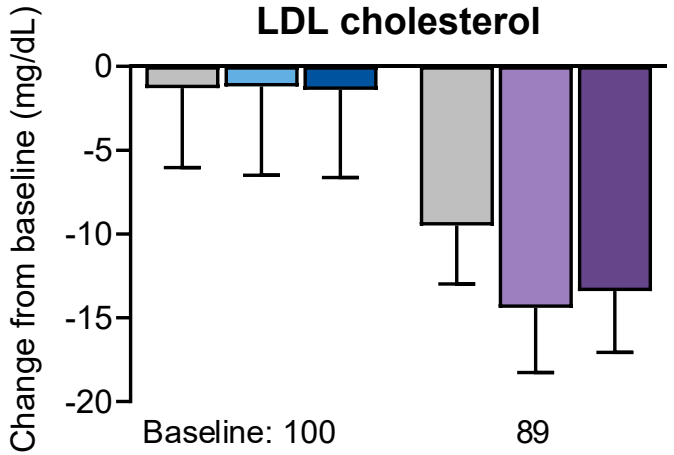

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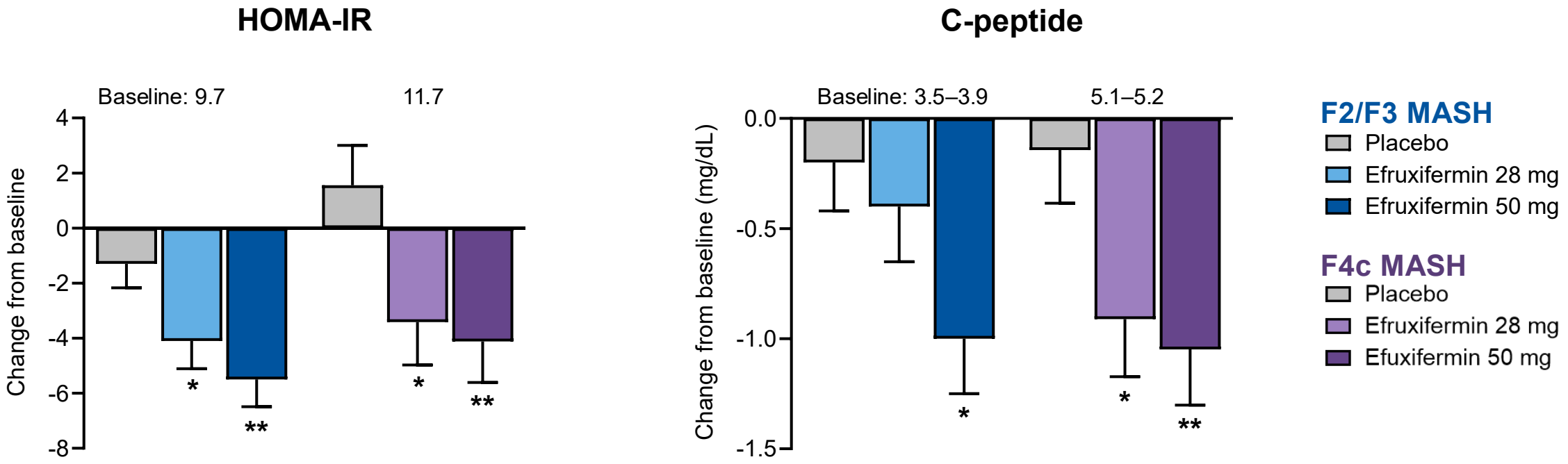
F4 MASH data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY.
Baseline values are population mean; *p<0.05,**p<0.01, ***p<0.001 vs placebo.

Improvement in Measures of Insulin Sensitivity
in Participants with Advanced Fibrosis and Cirrhosis



- HbA1C at Week 96 was generally unchanged from baseline in all treatment groups in both F2-F3 and F4c MASH.

F2/3 MASH data are observed values for the mITT population (N=126) at Week 96 in HARMONY.
F4c MASH data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY.
Baseline values are population mean or range of group means; *p<0.05,**p<0.01 vs placebo.

Safety and Tolerability of Efruxifermin Across Phase 2b Trials
in Participants with Advanced Fibrosis and Cirrhosis

- Most common AEs were gastrointestinal, mild-to-moderate, transient, and generally occurred early in treatment.
- Incidence and pattern of SAEs was consistent with prevalent comorbidities of the population.
- Small but statistically significant reductions in BMD after 96 weeks, clinical relevance to be determined. No increase in fractures.
- No reported events of DILI.
- Markers of liver function and hemostasis remained stable.

HARMONY: F2/F3 MASH

Most Frequent Drug-Related Adverse Events	Placebo (N=43)	Efruxifermin 28mg (N=40)	Efruxifermin 50mg (N=43)
Diarrhea	7 (16%)	16 (40%)	16 (37%)
Nausea	5 (12%)	12 (30%)	14 (33%)
Increased Appetite	3 (7%)	7 (18%)	10 (23%)
Injection Site Erythema	6 (14%)	8 (20%)	7 (16%)
Injection Site Bruising	2 (5%)	6 (15%)	3 (7%)

SYMMETRY: F4 MASH

Most Frequent Drug-Related Adverse Events	Placebo (N=61)	Efruxifermin 28mg (N=57)	Efruxifermin 50mg (N=63)
Diarrhea	10 (16%)	11 (19%)	19 (30%)
Nausea	8 (13%)	11 (19%)	18 (29%)
Increased Appetite	3 (5%)	7 (12%)	18 (29%)
Injection Site Erythema	5 (8%)	10 (18%)	14 (22%)
Injection Site Bruising	4 (7%)	5 (9%)	6 (10%)

Data are for the HARMONY and SYMMETRY safety populations.

Conclusions and Phase 3 Trials of Efruxifermin

Across populations with MASH and advanced fibrosis (F2/F3) or compensated cirrhosis (F4c), efruxifermin resulted in:

- Improved fibrosis by liver histology and noninvasive tests. Early fibrosis response was sustained through week 96 and additional responders observed at week 96.
- Improvements in disease drivers: MASH, lipids, insulin sensitivity.
- Acceptable safety & tolerability profile with AEs predominantly gastrointestinal and transient.

Phase 3 program currently enrolling individuals with MASH and fibrosis or cirrhosis

synchrony HISTOLOGY	synchrony OUTCOMES
• **Currently enrolling:** NCT06215716 • Biopsy confirmed fibrosis (F2/F3) and MASH • 28 and 50 mg efruxifermin	• **Currently enrolling:** NCT06528314 • Biopsy confirmed compensated cirrhosis (F4) and MASH • 50 mg efruxifermin

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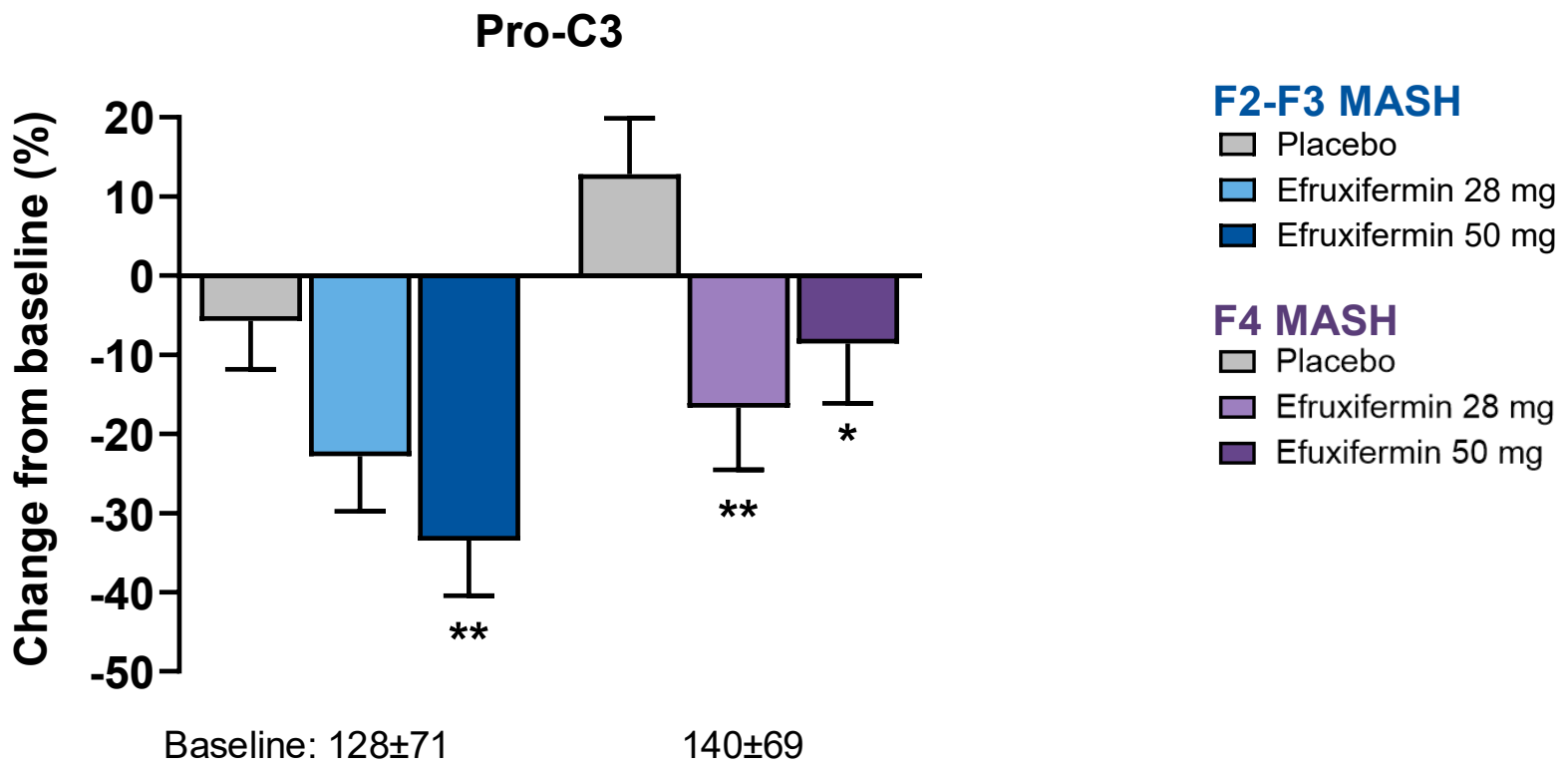
Thank you

Serum Fibrosis Markers at Week 96



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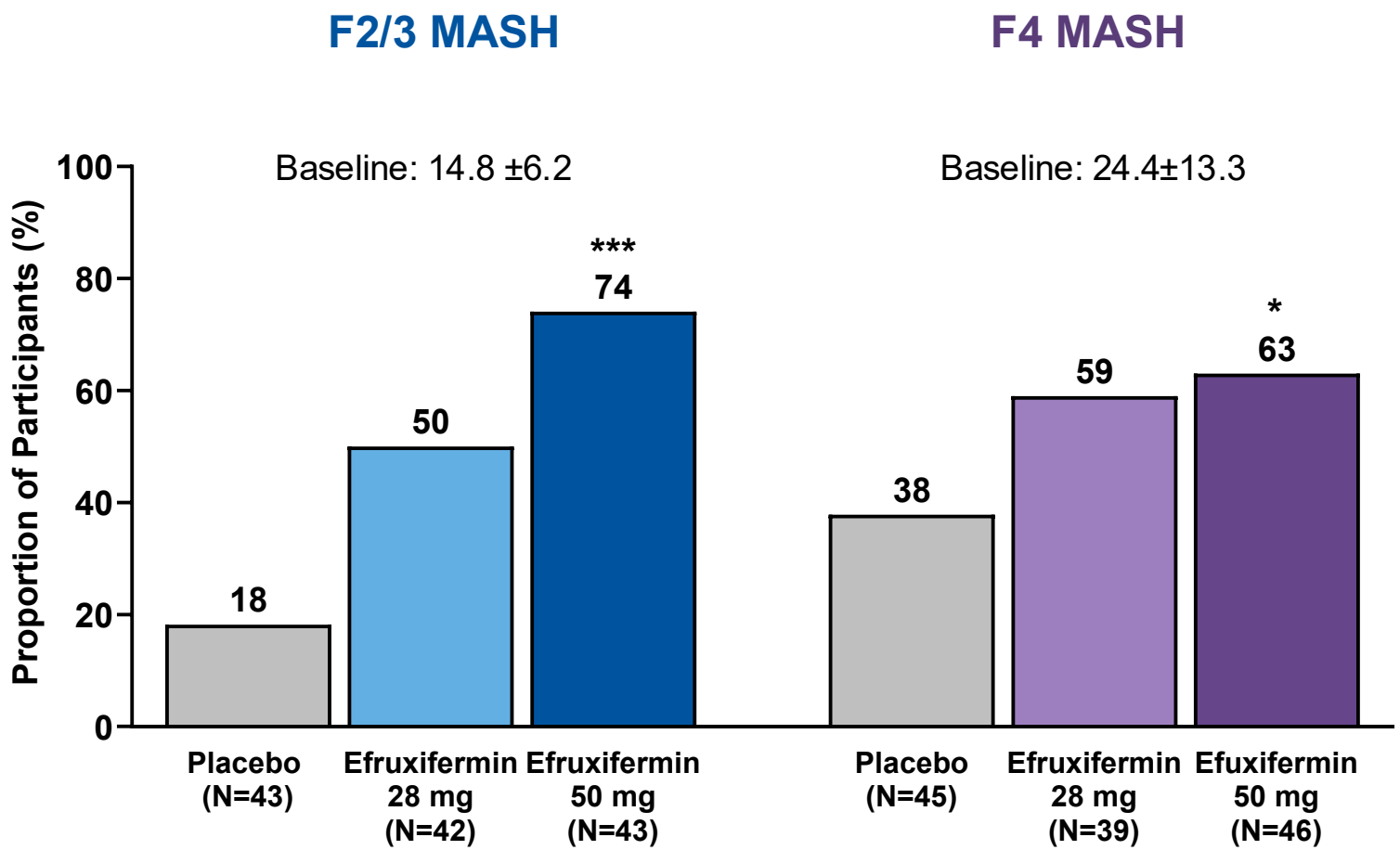
LSM-VCTE=liver stiffness measurement by vibration-controlled transient elastography (FIbroScan)

Participants with ≥30% Reduction in LSM at Week 96



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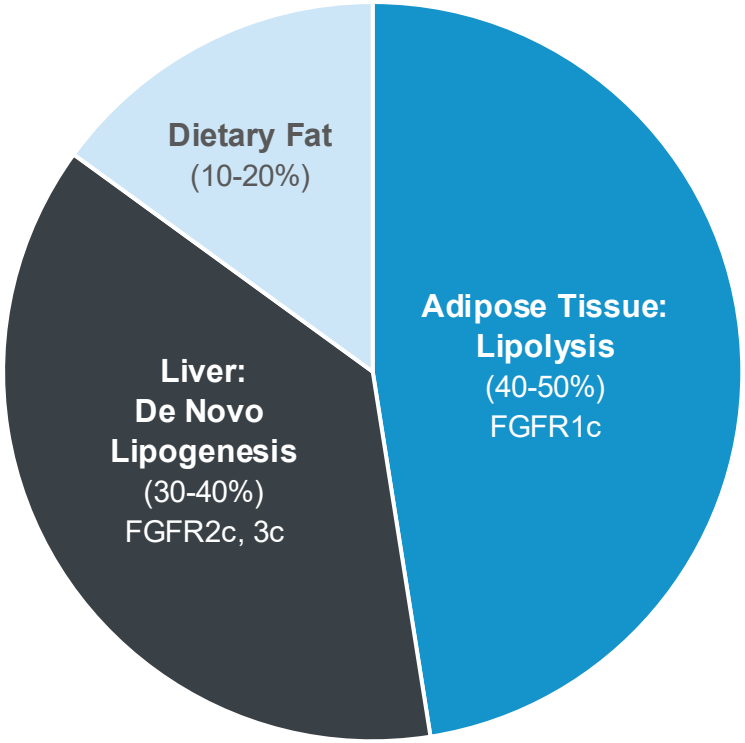
EFX Acts on Two Major Sources of Liver Fat: Potential for Optimal Reduction

Sources of Fat Flowing into and Through Liver for Patients with MASH



Acting on both hepatic and peripheral sources of liver fat is key to optimizing liver fat reduction

Source of Liver Fat	FGF Receptor	EFX Activity
Lipolysis	FGFR1c	✓
De Novo Lipogenesis	FGFR2c FGFR3c	✓