Updated Early and Week 52 Biomarker (MRI-PDFF, ALT, MRE and PRO-C3) Responses to Resmetirom Associate With Improvements in MASH and Liver Fibrosis

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Introduction

- MASH with fibrosis progresses to cirrhosis, and fibrosis stage drives liver-related outcomes
- Resmetirom, an oral THR-β agonist, **resolved MASH and improved fibrosis relative to placebo** at Week 52 in the phase 3 MAESTRO-NASH trial[1]
- Resmetirom is approved by the accelerated approval pathway for the treatment of patients with noncirrhotic MASH with stages F2-F3 fibrosis in conjunction with diet and exercise[2]
- Treatment response was confirmed by liver biopsy,[1] which is rarely used to diagnose MASH in clinical practice
- **MASH-related blood biomarkers and imaging** can show treatment-related changes earlier than 52 weeks, but their associations with histologic response to resmetirom need to be established

F2-F3, moderate to advanced fibrosis; MASH, metabolic dysfunction–associated steatohepatitis; THR-β, thyroid hormone receptor β.

1. Harrison SA, et al. *N Engl J Med.* 2024;390:497-509. 2. Rezdiffra (resmetirom) tablets, for oral use. Prescribing information. Madrigal Pharmaceuticals Inc.; 2025.

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Key Question

In a patient taking resmetirom, what early treatment-related changes in biomarkers or imaging are associated with histologic responses at Week 52?

Week 0	Start resmetirom 80 or 100 mg daily, or placebo
Starting Week 12	**Early changes from baseline assessed**[a] ALT ≥20%↓ MRI-PDFF ≥30%↓ MRE ≥15%↓ and PRO-C3[b] ≥10%↓
Week 52	**Histologic benefit on biopsy** ≥1-stage fibrosis improvement; MASH resolution

Why it matters

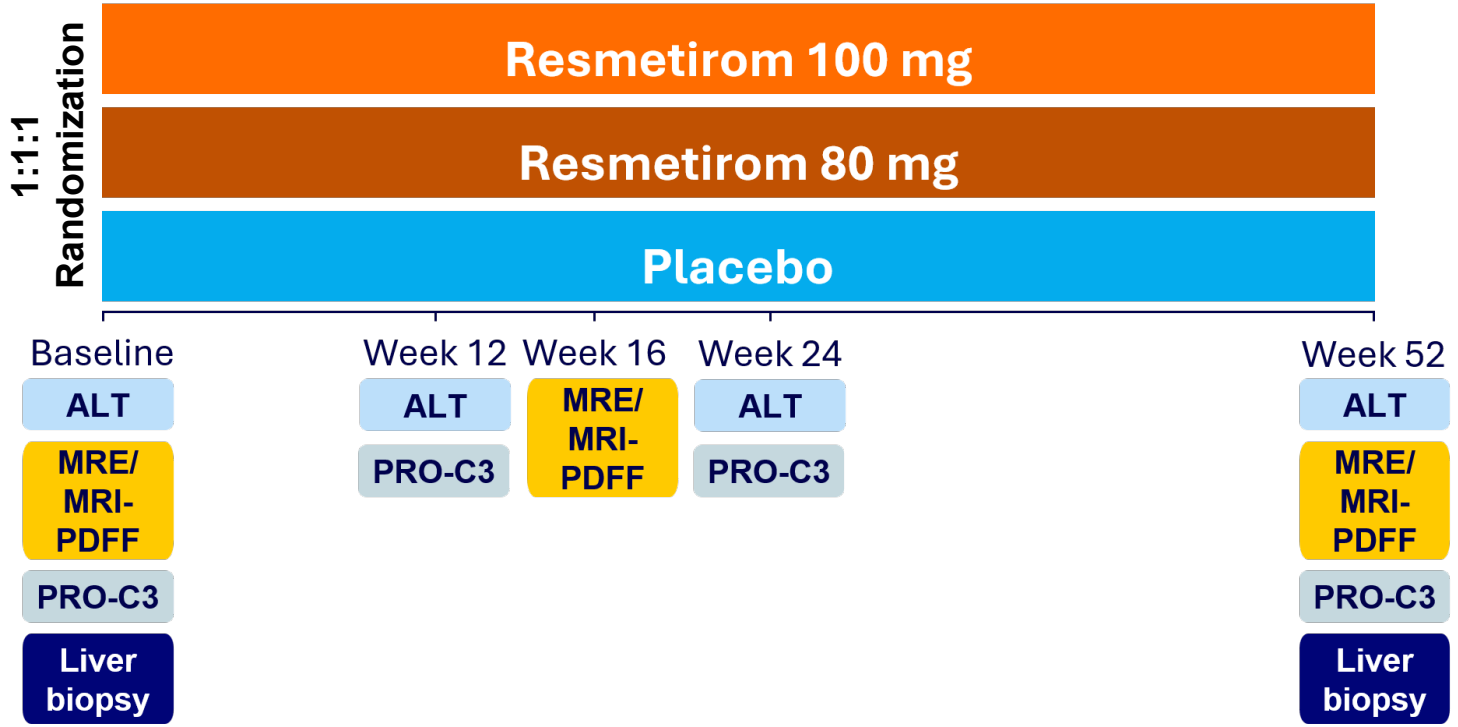
- The physician may be able to counsel patients and plan follow-up based on changes in tests that occur early in treatment
- Confidence in these biomarker changes will be gained by showing alignment with improvement in histology at 52 weeks

[a]Thresholds are relative reductions from baseline.
[b]PRO-C3 assessed in F3.
ALT, alanine aminotransferase; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; PRO-C3, N-terminal propeptide of type III collagen.
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Study Design

- MAESTRO-NASH (NCT03900429) is an ongoing phase 3, randomized, double-blind, placebo-controlled trial
  - Patients aged ≥18 years with at least 3 metabolic risk factors and biopsy-confirmed MASH, with fibrosis stages F2/F3 at baseline[a]
  - Week 52 biopsy data supported FDA accelerated approval; confirmatory 54-month outcomes portion ongoing



[a]A small number of patients had F1B fibrosis, which was shown to be consistent with F2 in this study.
ALT, alanine aminotransferase; F, fibrosis stage (F1B: mild fibrosis [substage B], F2: moderate fibrosis, F3, advanced fibrosis); FDA, Food and Drug Administration; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; PRO-C3, N-terminal propeptide of type III collagen.

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Aims of Exploratory MAESTRO-NASH Analyses

1. **Evaluate the association** of early and Week 52 changes in ALT, MRE LSM, MRI-PDFF, and PRO-C3 (F3 patients only) with Week 52 MASH resolution and fibrosis improvement

2. **Test whether these associations hold** after adjusting for weight loss

3. **Compare odds of achieving biomarker responses and time to sustained responses** with resmetirom compared with placebo

Since Week 52 histologic response is required for this assessment, this analysis was conducted in the subset of patients from MAESTRO-NASH who had both a baseline and Week 52 biopsy available **(N = 782)**

ALT, alanine aminotransferase; F3, advanced fibrosis; LSM, liver stiffness measurement; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; PRO-C3, N-terminal propeptide of type III collagen.

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Patient Characteristics

Characteristic	Resmetirom (n = 506)	Placebo (n = 276)
Age, mean ± SD, years	56.2 (11.0)	57.0 (10.0)
Sex, male, n (%)	223 (44.1)	120 (43.5)
Race, n (%)		
Asian	12 (2.4)	8 (2.9)
Black	7 (1.4)	9 (3.3)
White	460 (90.9)	238 (86.2)
Other	27 (5.3)	21 (7.6)
Ethnicity, Hispanic or Latino, n (%)	121 (23.9)	47 (17.0)
CAP by VCTE, median (Q1, Q3), dB/m	350.0 (320.0, 380.0)	348.5 (321.5, 377.0)
LSM by VCTE, median (Q1, Q3), kPa	11.5 (9.4, 15.2)	11.7 (9.4, 14.5)
LSM by MRE, median (Q1, Q3), kPa	3.4 (2.9, 4.0)	3.4 (2.8, 4.0)
% liver fat by MRI-PDFF, median (Q1, Q3)	16.7 (12.8, 22.0)	16.9 (12.5, 22.4)
ALT, median (Q1, Q3), U/L	48.0 (34.0, 66.0)	46.0 (31.0, 70.0)
Fibrosis stage, n (%)		
F1B	24 (4.7)	18 (6.5)
F2	156 (30.8)	92 (33.3)
F3	326 (64.4)	166 (60.1)

Note: Resmetirom dose groups in the trial were combined in this analysis

ALT, alanine aminotransferase; CAP, controlled attenuation parameter; dB, decibel; F, fibrosis stage (F1B: mild fibrosis [substage B], F2: moderate fibrosis, F3: advanced fibrosis); kPa, kilopascal; LSM, liver stiffness measurement; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; Q, quartile; VCTE, vibration-controlled transient elastography.

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Three Noninvasive Tests Measuring Liver Injury, Inflammation, Fibrosis, and Fat

Hepatocyte injury

ALT



MEASURES

Hepatocellular injury and inflammation

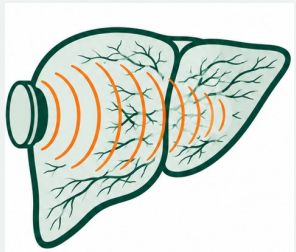
Can be checked at a routine visit; an early ALT drop predicted histologic response in MASH trials[1]

RESPONSE IN THIS ANALYSIS[a]

Defined as ≥20% reduction vs baseline

Fibrosis

MRE



MEASURES

Liver stiffness, from shear waves

Early decreases may measure inflammatory response; later responses associated with liver fibrosis decrease[2,b]

RESPONSE IN THIS ANALYSIS[a]

Defined as ≥15% reduction vs baseline

Liver fat

MRI-PDFF



MEASURES

Liver fat fraction across the whole liver

Resmetirom works in part by clearing liver fat, so PDFF can serve as a direct readout; a ≥30% drop is the established response[3] that has been shown to be correlated with histology

RESPONSE IN THIS ANALYSIS[a]

Defined as ≥30% reduction vs baseline

[a]Response thresholds are changes from baseline.
[b]In the 52-week double-blind period of the MAESTRO-NASH clinical trial, VCTE was only performed at Week 52.
ALT, alanine aminotransferase; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction. ALT, alanine aminotransferase; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; VCTE, vibration-controlled transient elastography.

1. Loomba R et al. *Gastroenterology*. 2019;156:88-95. 2. Park CC et al. *Gastroenterology*. 2017;152:598-607. 3. Stine JG et al. *Clin Gastroenterol Hepatol*. 2021;19:2274-2283.

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ALT Reduction ≥20% Associated With Week 52 Histologic Response With Both Resmetirom and Placebo Treatment

resmetirom N = 406 [both doses combined]; placebo N = 210

		Unadjusted				Adjusted for weight loss			
Outcome	Week	Resmetirom OR (95% CI)	P	Placebo OR (95% CI)	P	Resmetirom OR (95% CI)	P	Placebo OR (95% CI)	P
Fibrosis improvement	12	2.00 (1.27-3.18)	0.002	2.02 (0.81-4.95)	0.116	1.97 (1.28-3.07)	0.002	2.02 (0.87-4.57)	0.094
	24	2.22 (1.37-3.66)	<0.001	2.82 (1.15-7.17)	0.018	2.22 (1.40-3.57)	<0.001	2.61 (1.13-6.19)	0.025
	52	2.58 (1.50-4.57)	<0.001	2.75 (1.15-6.85)	0.014	2.41 (1.44-4.17)	<0.001	2.61 (1.12-6.26)	0.028
MASH resolution	12	1.78 (1.13-2.84)	0.011	1.24 (0.32-4.19)	0.770	1.83 (1.16-2.90)	0.010	1.22 (0.36-3.66)	0.731
	24	1.63 (1.01-2.67)	0.042	2.32 (0.73-7.68)	0.113	1.60 (1.00-2.58)	0.053	1.88 (0.65-5.60)	0.244
	52	3.23 (1.82-6.00)	<0.001	7.22 (1.89-40.81)	<0.001	2.60 (1.26-5.37)	0.007	5.70 (1.64-26.46)	0.011

Biomarker-histology association did not differ significantly by treatment arm for ALT or any subsequent biomarker, so the following slides pool resmetirom and placebo arms to summarize degree of association

ALT, alanine aminotransferase; MASH, metabolic dysfunction–associated steatohepatitis; OR, odds ratio.

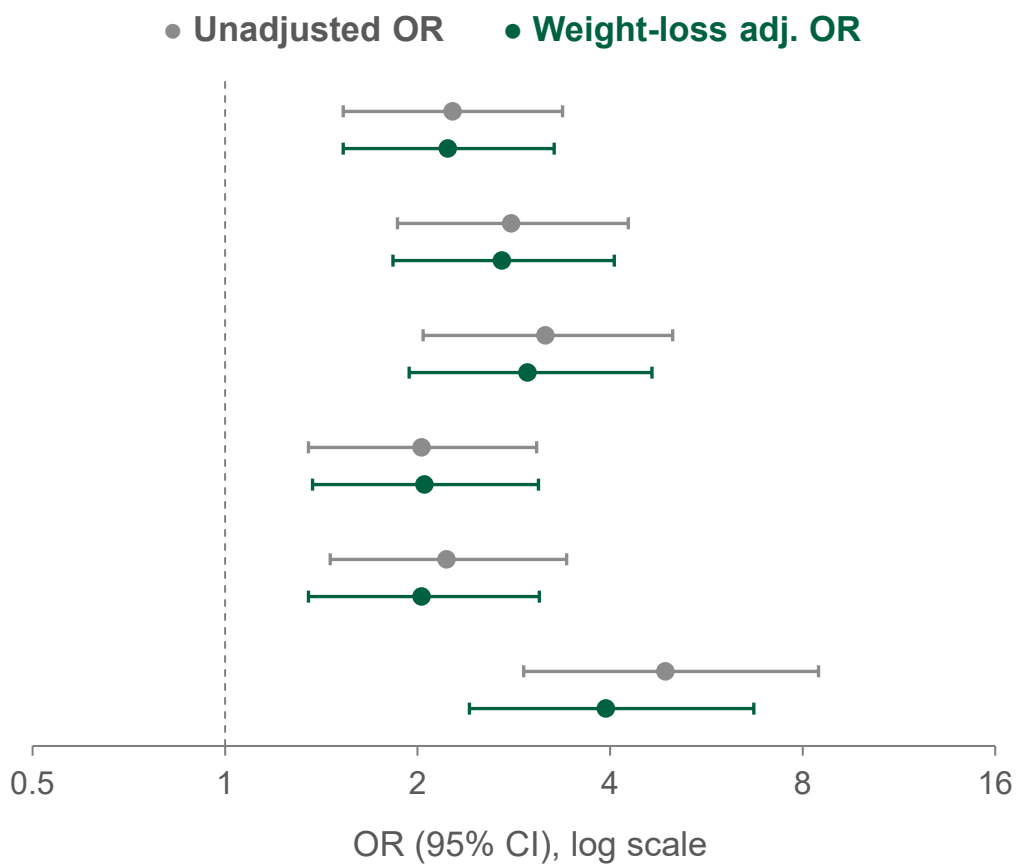
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ALT Reduction ≥20% Associated With Week 52 Histologic Response, Independent of Weight Loss

Pooled data from active and placebo arms in trial; N = 615

Outcome	Week	Unadjusted OR (95% CI)	Weight-loss adj. OR (95% CI)
Fibrosis improvement	12	2.27 (1.53-3.37)	2.23 (1.53-3.27)
	24	2.80 (1.86-4.27)	2.71 (1.83-4.06)
	52	3.17 (2.04-5.01)	2.97 (1.94-4.65)
MASH resolution	12	2.03 (1.35-3.07)	2.05 (1.37-3.09)
	24	2.22 (1.46-3.42)	2.03 (1.35-3.10)
	52	4.88 (2.93-8.47)	3.94 (2.41-6.71)

All P-values for unadjusted OR and weight-loss adjusted OR were P < 0.001.



ORs compare odds of Week 52 histologic response in ALT responders vs non-responders

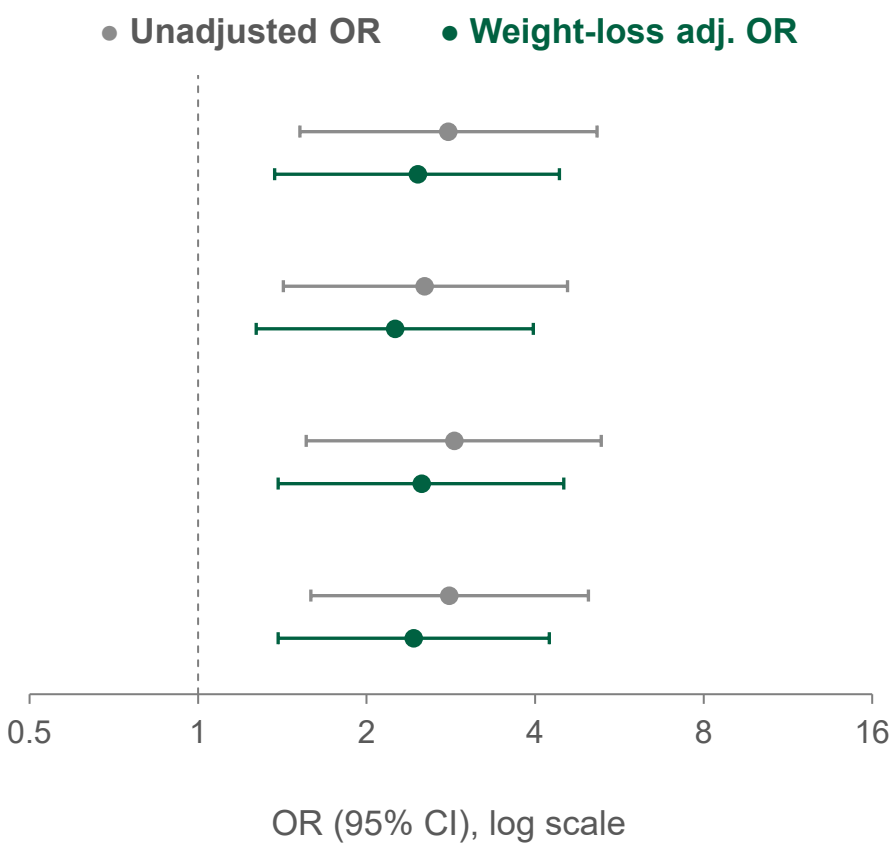
ALT, alanine aminotransferase; MASH, metabolic dysfunction–associated steatohepatitis; OR, odds ratio.

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MRE LSM Reduction ≥15% Was Associated With Week 52 Histologic Response, Independent of Weight Loss

Pooled data from active and placebo arms in trial; N = 320

Outcome	Week	Unadjusted OR (95% CI)	*P*	Weight-loss adj. OR (95% CI)	*P*
Fibrosis improvement	16	2.80 (1.52-5.16)	<0.001	2.47 (1.37-4.42)	0.003
	52	2.54 (1.42-4.57)	0.001	2.25 (1.27-3.97)	0.005
MASH resolution	16	2.87 (1.56-5.25)	<0.001	2.51 (1.39-4.50)	0.002
	52	2.81 (1.59-4.98)	<0.001	2.43 (1.39-4.24)	0.002



MASH, metabolic dysfunction–associated steatohepatitis; MRE LSM, magnetic resonance elastography liver stiffness measurement; OR, odds ratio.

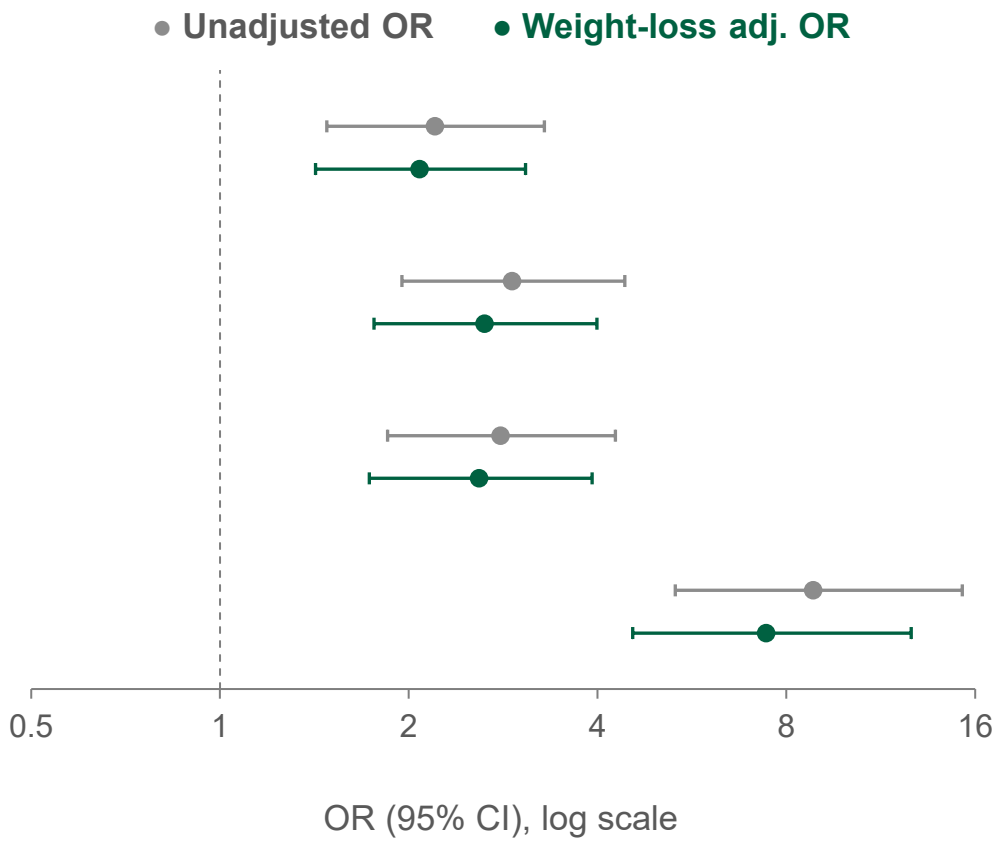
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MRI-PDFF Reduction ≥30% Was Associated With Week 52 Histologic Response, Independent of Weight Loss

Pooled data from active and placebo arms in trial; N = 635

Outcome	Week	Unadjusted OR (95% CI)	Weight-loss adj. OR (95% CI)
Fibrosis improvement	16	2.20 (1.48-3.29)	2.08 (1.42-3.07)
	52	2.92 (1.95-4.42)	2.64 (1.76-3.99)
MASH resolution	16	2.80 (1.85-4.27)	2.59 (1.73-3.92)
	52	8.83 (5.32-15.26)	7.43 (4.55-12.65)

All P-values for unadjusted OR and weight-loss adjusted OR were P < 0.001.



MASH, metabolic dysfunction–associated steatohepatitis; MRI-PDFF, magnetic resonance imaging proton density fat fraction; OR, odds ratio.

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Across All 3 Tests, Early Response Was Associated With Favorable Week 52 Histology Assessment

- **ALT**, **MRE LSM**, and **MRI-PDFF** responses were each associated with fibrosis improvement and MASH resolution at Week 52
- ORs ranged from **2.03 to 8.83** (all $P \leq 0.001$) in pooled resmetirom and placebo arms
- Associations held **after adjusting for weight loss** (ORs, 2.03-7.43; all $P \leq 0.005$)

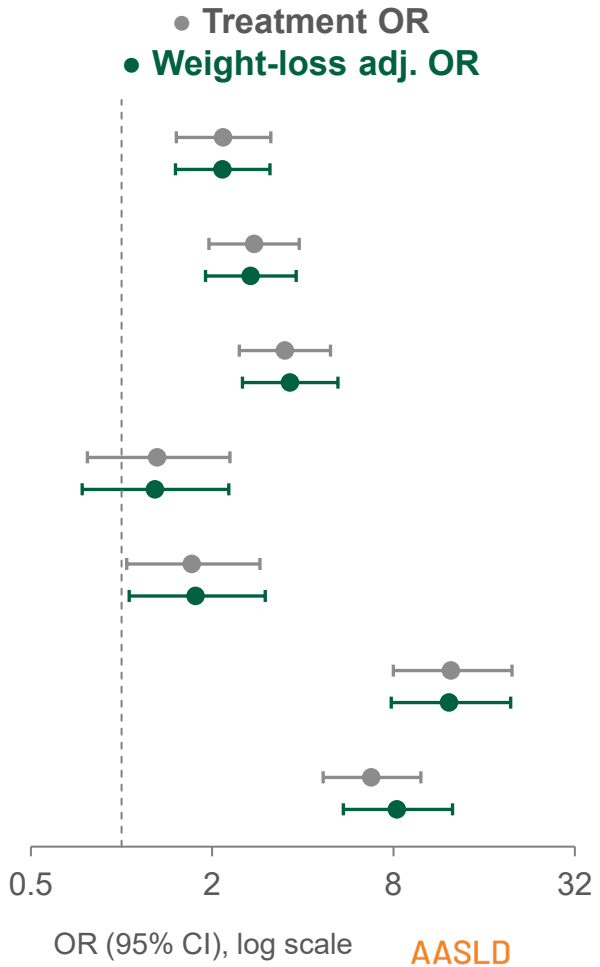
Blood and imaging tests as early as Weeks 12-16 each gave an early signal of association with Week 52 histologic response, independent of weight loss

ALT, alanine aminotransferase; F3, advanced fibrosis; LSM, liver stiffness measurement; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging-proton density fat fraction; OR, odds ratio.

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Resmetirom Increased Odds of Response by ALT, MRI-PDFF as Early as Weeks 12-16 and MRE LSM at Week 52

Biomarker	Week	Resmetirom n (%)	Placebo n (%)	Treatment OR (95% CI)	*P*	Weight-loss adj. OR (95% CI)	*P*
ALT ≥20% reduction	12	184 (47.2)	60 (29.1)	2.17 (1.52-3.13)	<0.001	2.16 (1.51-3.11)	<0.001
	24	245 (61.9)	78 (37.1)	2.75 (1.95-3.89)	<0.001	2.68 (1.90-3.80)	<0.001
	52	286 (70.4)	85 (40.7)	3.48 (2.46-4.94)	<0.001	3.62 (2.52-5.23)	<0.001
MRE LSM ≥15% reduction	16	55 (28.4)	25 (23.1)	1.31 (0.77-2.29)	0.327	1.29 (0.74-2.27)	0.375
	52	76 (36.9)	29 (25.4)	1.71 (1.04-2.88)	0.038	1.76 (1.06-3.00)	0.033
MRI-PDFF ≥30% reduction	16	253 (66.6)	28 (13.9)	12.38 (7.99-19.79)	<0.001	12.22 (7.86-19.59)	<0.001
	52	283 (67.9)	52 (23.9)	6.74 (4.67-9.86)	<0.001	8.19 (5.45-12.56)	<0.001



ALT, alanine aminotransferase; LSM, liver stiffness measurement; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; OR, odds ratio.

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PRO-C3: A Research Biomarker of Active Fibrogenesis

Fibrogenesis

PRO-C3



N-terminal propeptide of type III collagen, measured in serum

What it measures	**Fibrosis is an active process** Released when type III collagen forms, so it reflects active scarring rather than fibrosis already present
Why F3 only	**Enough signal to see a change** PRO-C3 rises with fibrosis stage; lower baseline levels in earlier stages leaves very little range to detect a meaningful reduction
In this analysis	**Response defined as ≥10% reduction from baseline** Measured at Weeks 0, 12, 24, and 52 in patients with F3 fibrosis
In practice	**A research assay, early commercial stage** Used in clinical trials and research; may not yet be in routine clinical care

F3, advanced fibrosis; PRO-C3, N-terminal propeptide of type III collagen.

Luo Y et al. *Sci Rep*. 2018;8:12414.

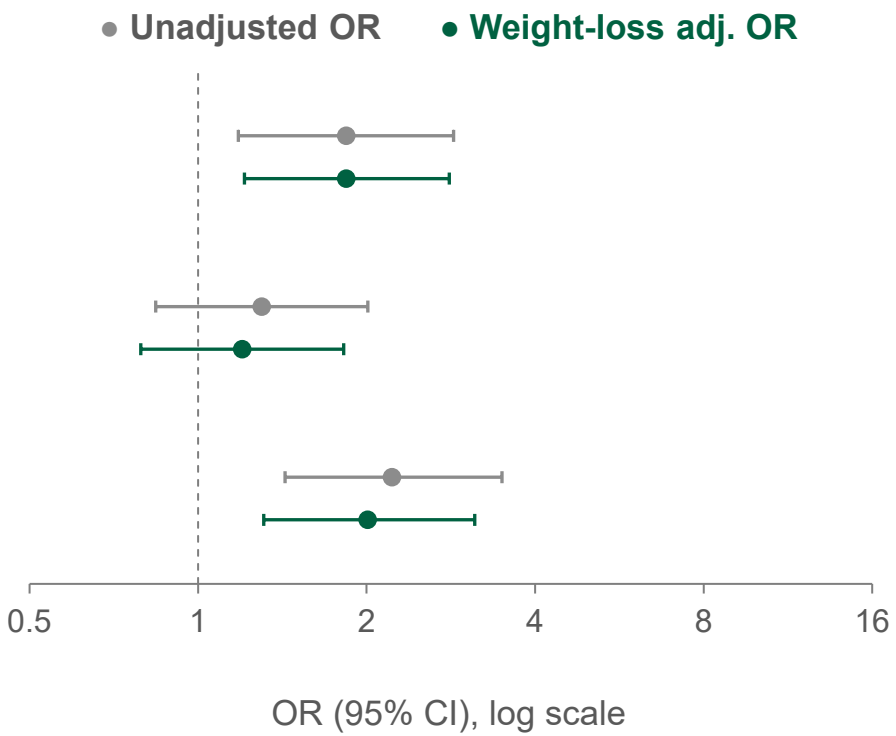
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In Patients With F3, PRO-C3 Reduction ≥10% at Weeks 12 and 52 Was Associated With Fibrosis Improvement

Pooled data from active and placebo arms in trial; F3 only; N = 486

Outcome	Week	Unadjusted OR (95% CI)	*P*	Weight-loss adj. OR (95% CI)	*P*
Fibrosis improvement	12	1.84 (1.18-2.86)	0.005	1.84 (1.21-2.81)	0.005
	24	1.30 (0.84-2.01)	0.247	1.20 (0.79-1.82)	0.398
	52	2.22 (1.43-3.49)	<0.001	2.01 (1.31-3.12)	0.001

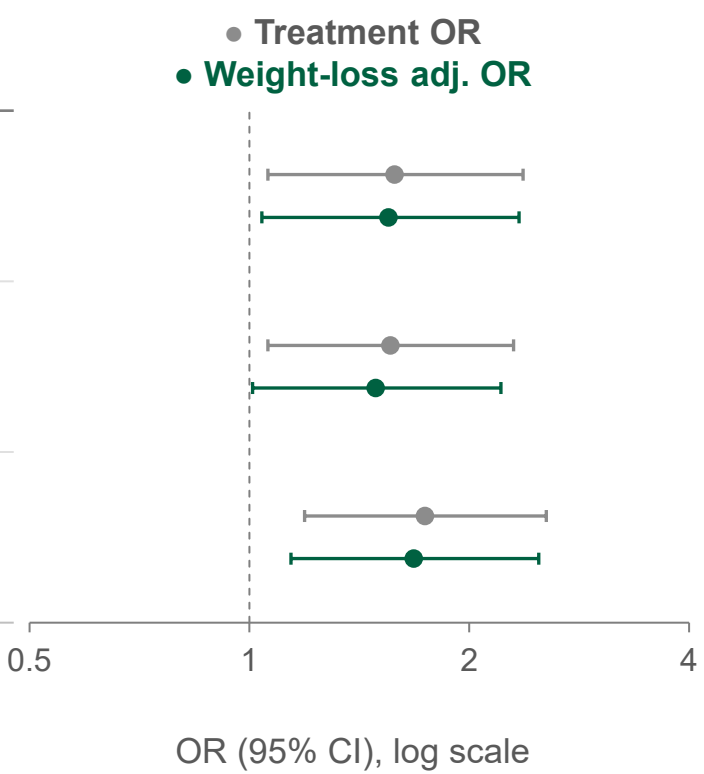


F3, advanced fibrosis; OR, odds ratio; PRO-C3, N-terminal propeptide of type III collagen.

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Resmetirom Increased PRO-C3 Response vs Placebo at Weeks 12, 24, and 52, Independent of Weight Loss (F3)

Week	Resmetirom n (%)	Placebo n (%)	Treatment OR (95% CI)	*P*	Weight-loss adj. OR (95% CI)	*P*
12	127 (41.1)	50 (30.7)	1.58 (1.06-2.37)	0.027	1.55 (1.04-2.34)	0.033
24	156 (48.8)	61 (37.9)	1.56 (1.06-2.30)	0.024	1.49 (1.01-2.21)	0.045
52	175 (54.2)	66 (40.5)	1.74 (1.19-2.55)	0.005	1.68 (1.14-2.49)	0.009

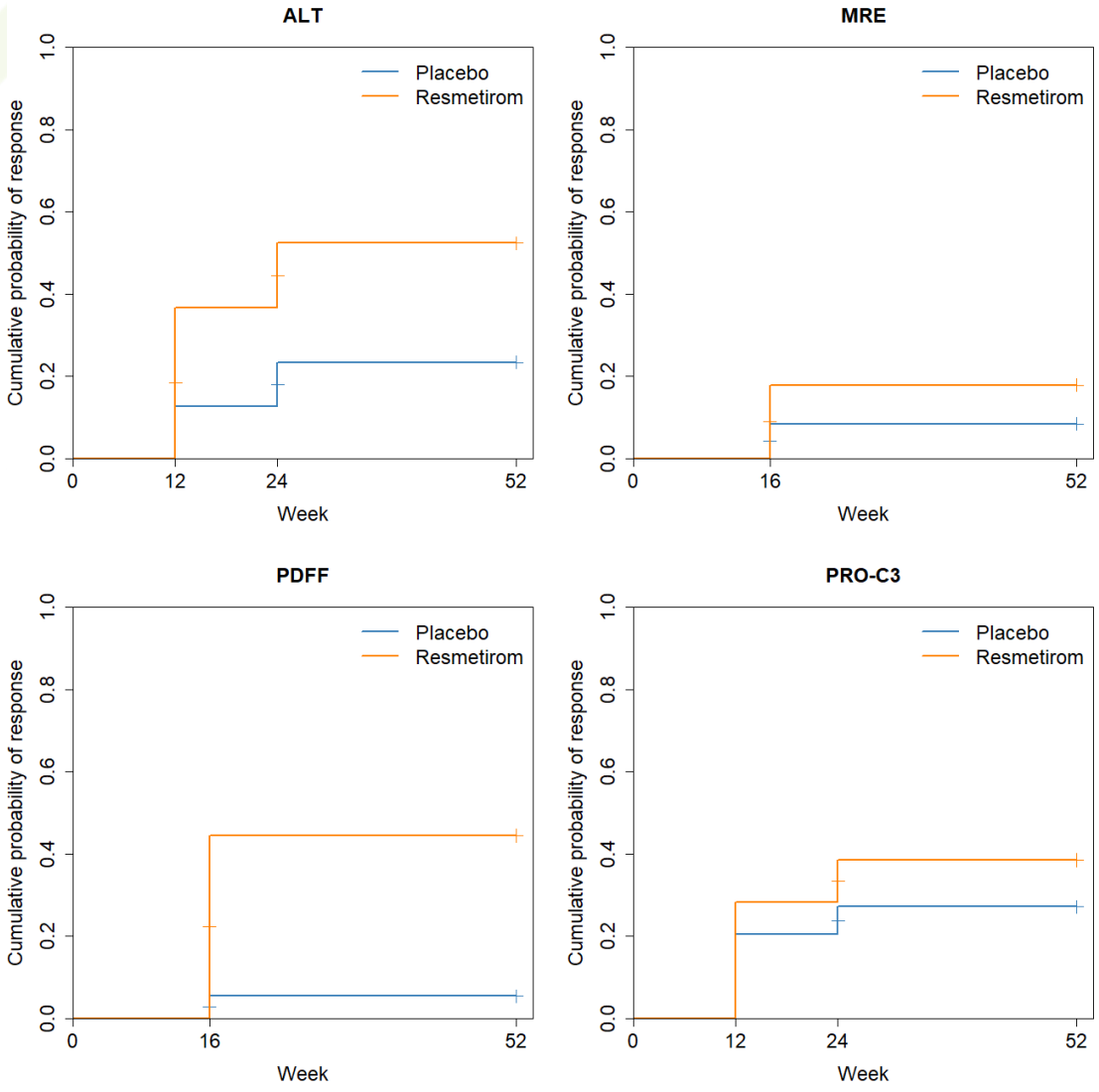


Early separation from placebo suggests that fibrogenesis is quickly blunted by resmetirom

F3 population: N = 492 (326 resmetirom, 166 placebo).
F3, advanced fibrosis; OR, odds ratio; PRO-C3, N-terminal propeptide of type III collagen.
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Resmetirom Shortened Time to Sustained Response for All 4 Biomarkers, Independent of Weight Loss



Question	Do patients on resmetirom reach a sustained biomarker response sooner than patients on placebo?
Approach	Time to sustained response: Kaplan-Meier, log-rank *P*; Cox HRs adjusted for weight loss

Biomarker	Treatment HR (95% CI)	Weight-loss adj. HR (95% CI)	Log-rank *P*
MRI-PDFF	**10.57 (5.90-18.95)**	**10.24 (5.71-18.36)**	<0.001
ALT	**2.83 (2.08-3.85)**	**2.75 (2.02-3.74)**	<0.001
MRE LSM	**2.23 (1.11-4.47)**	**2.11 (1.05-4.23)**	0.019
PRO-C3	**1.52 (1.08-2.14)**	**1.44 (1.02-2.03)**	0.014

Sustained response: Reaching the biomarker response threshold and maintaining it through Week 52. Kaplan-Meier curves and log-rank *P* are unadjusted; weight-loss adjusted HRs from Cox models adjusted for weight loss.
ALT, alanine aminotransferase; HR, hazard ratio; LSM, liver stiffness measurement; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; PRO-C3, N-terminal propeptide of type III collagen.

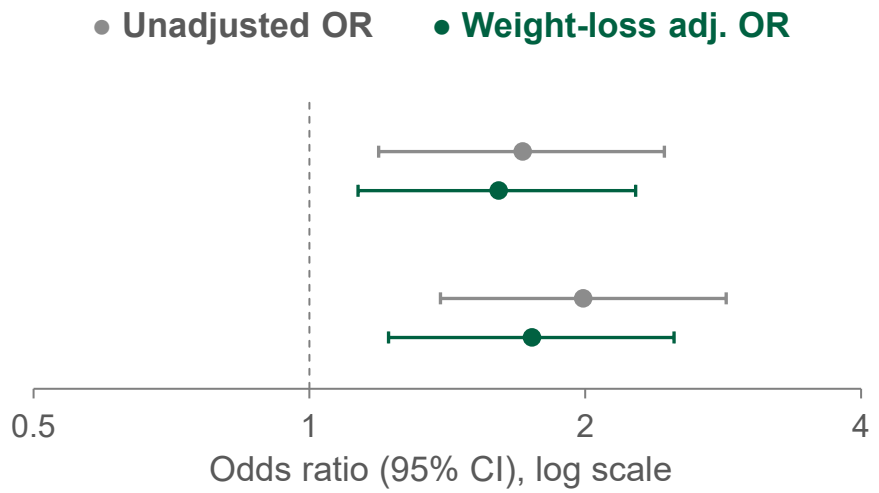
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VCTE-LSM reduction ≥25% was associated with Week 52 histologic response, independent of weight loss

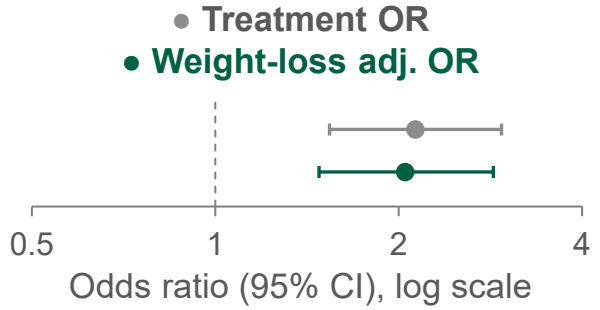
Pooled data from active and placebo arms in trial; N = 726

Outcome	Week	Unadjusted OR (95% CI)	P	Weight-loss adj. OR (95% CI)	P
Fibrosis improvement	**52**	**1.71 (1.19-2.44)**	**0.003**	**1.61 (1.13-2.27)**	**0.008**
MASH resolution	**52**	**1.99 (1.39-2.85)**	**<0.001**	**1.75 (1.22-2.50)**	**0.002**



Resmetirom increased odds of VCTE-LSM response at Week 52

Biomarker	Week	Resmetirom n (%)	Placebo n (%)	Treatment OR (95% CI)	P	Weight-loss adj. OR (95% CI)	P
VCTE-LSM ≥25% reduction	**52**	**219 (46.5%)**	**74 (29.0%)**	**2.13 (1.54-2.95)**	**<0.001**	**2.05 (1.48-2.86)**	**<0.001**



MASH, metabolic dysfunction-associated steatohepatitis; MRE LSM, magnetic resonance elastography liver stiffness measurement; OR, odds ratio.

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Conclusions

- In Week 52 data from MAESTRO-NASH, **early (Weeks 12-16) responses in ALT, MRE LSM, MRI-PDFF, and PRO-C3 in F3**, were associated with Week 52 MASH resolution and fibrosis improvement
- These associations **remain after adjusting for weight loss**
- Compared with placebo, resmetirom **increased ALT and MRI-PDFF response from Weeks 12-16**, MRE LSM response at Week 52, PRO-C3 response at all time points, and **shortened time to sustained response** for all 4 tests

Early changes in blood and imaging biomarkers may give clinicians a noninvasive signal of response to resmetirom treatment, without a biopsy

- **Limitations:** post hoc analysis of a single trial with pooled arms; associations do not indicate causality; liver stiffness not measured by VCTE before Week 52

ALT, alanine aminotransferase; F3, advanced fibrosis; LSM, liver stiffness measurement; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; PRO-C3, N-terminal propeptide of type III collagen; VCTE, vibration-controlled transient elastography.

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Thank You

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Each Test Can Answer a Question Clinicians Ask During Treatment

ALT	**Can be checked at a routine visit** An early ALT drop predicted histologic response in MASH trials[1]
MRE	**MRE** is the most accurate imaging test of liver stiffness[2]
MRI-PDFF	**Is the drug acting on the liver?** Resmetirom works in part by clearing liver fat, so PDFF can serve as a direct readout; a ≥30% drop is the established fat response[3]

Why not VCTE?

VCTE is a liver stiffness test many hepatologists already use.

MAESTRO-NASH did not measure liver stiffness by VCTE before Week 52, so it could not be tested as an early on-treatment signal in this analysis.

ALT, alanine aminotransferase; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; VCTE, vibration-controlled transient elastography.

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Week 52 Histologic Response by ALT Reduction (≥20%) by Treatment

Resmetirom, N = 406; placebo, N = 210

		Unadjusted				Adjusted for weight loss			
Outcome	Week	Resmetirom OR (95% CI)	*P*	Placebo OR (95% CI)	*P*	Resmetirom OR (95% CI)	*P*	Placebo OR (95% CI)	*P*
Fibrosis improvement	12	2.00 (1.27-3.18)	0.002	2.02 (0.81-4.95)	0.116	1.97 (1.28-3.07)	0.002	2.02 (0.87-4.57)	0.094
	24	2.22 (1.37-3.66)	<0.001	2.82 (1.15-7.17)	0.018	2.22 (1.40-3.57)	<0.001	2.61 (1.13-6.19)	0.025
	52	2.58 (1.50-4.57)	<0.001	2.75 (1.15-6.85)	0.014	2.41 (1.44-4.17)	<0.001	2.61 (1.12-6.26)	0.028
MASH resolution	12	1.78 (1.13-2.84)	0.011	1.24 (0.32-4.19)	0.770	1.83 (1.16-2.90)	0.010	1.22 (0.36-3.66)	0.731
	24	1.63 (1.01-2.67)	0.042	2.32 (0.73-7.68)	0.113	1.60 (1.00-2.59)	0.053	1.88 (0.65-5.60)	0.244
	52	3.23 (1.82-6.00)	<0.001	7.22 (1.89-40.81)	<0.001	2.60 (1.50-4.71)	0.001	5.70 (1.64-26.46)	0.011

ALT, alanine aminotransferase; MASH, metabolic dysfunction–associated steatohepatitis; OR, odds ratio.

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Week 52 Histologic Response by MRE Reduction (≥15%) by Treatment

Resmetirom, N = 206; placebo, N = 114

		Unadjusted				Adjusted for weight loss			
Outcome	Week	Resmetirom OR (95% CI)	*P*	Placebo OR (95% CI)	*P*	Resmetirom OR (95% CI)	*P*	Placebo OR (95% CI)	*P*
Fibrosis improvement	16	2.60 (1.26-5.37)	0.007	3.16 (0.87-11.07)	0.052	2.37 (1.19-4.71)	0.013	2.51 (0.76-7.97)	0.121
	52	2.30 (1.16-4.62)	0.012	2.66 (0.75-9.12)	0.117	2.12 (1.10-4.08)	0.025	2.01 (0.57-6.54)	0.254
MASH resolution	16	2.46 (1.22-4.97)	0.007	6.51 (1.16-45.46)	0.016	2.22 (1.13-4.36)	0.020	5.01 (1.06-27.17)	0.044
	52	1.94 (1.02-3.70)	0.043	12.82 (2.24-135.07)	<0.001	1.72 (0.92-3.21)	0.090	11.01 (2.24-80.68)	0.006

MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; OR, odds ratio.

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Week 52 Histologic Response by MRI-PDFF Reduction (≥30%) by Treatment

Resmetirom, N = 417; placebo, N = 218

		Unadjusted				Adjusted for weight loss			
Outcome	Week	Resmetirom OR (95% CI)	*P*	Placebo OR (95% CI)	*P*	Resmetirom OR (95% CI)	*P*	Placebo OR (95% CI)	*P*
Fibrosis improvement	16	1.88 (1.13-3.21)	0.013	1.42 (0.43-4.05)	0.585	1.80 (1.11-3.00)	0.020	1.29 (0.44-3.35)	0.620
	52	2.95 (1.73-5.21)	<0.001	1.48 (0.58-3.54)	0.377	2.63 (1.56-4.60)	<0.001	1.27 (0.50-3.02)	0.599
MASH resolution	16	1.63 (0.99-2.70)	0.049	1.90 (0.42-6.74)	0.285	1.52 (0.93-2.50)	0.099	1.81 (0.48-5.63)	0.334
	52	6.47 (3.49-12.80)	<0.001	6.73 (2.28-21.58)	<0.001	4.94 (2.72-9.53)	<0.001	7.92 (2.74-24.57)	<0.001

MASH, metabolic dysfunction–associated steatohepatitis; MRI-PDFF, magnetic resonance imaging proton density fat fraction; OR, odds ratio.

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Week 52 Histologic Response by PRO-C3 Reduction (≥10%) by Treatment

Resmetirom, N = 323; placebo, N = 163

		Unadjusted				Adjusted for weight loss			
Outcome	**Week**	**Resmetirom OR** (95% CI)	***P***	**Placebo OR** (95% CI)	***P***	**Resmetirom OR** (95% CI)	***P***	**Placebo OR** (95% CI)	***P***
Fibrosis improvement	12	1.76 (1.05-2.94)	0.026	1.55 (0.55-4.20)	0.340	1.79 (1.10-2.93)	0.019	1.50 (0.58-3.72)	0.390
	24	1.08 (0.65-1.77)	0.810	1.77 (0.65-4.87)	0.241	1.02 (0.63-1.64)	0.951	1.59 (0.62-4.03)	0.328
	52	2.03 (1.21-3.43)	0.005	2.12 (0.80-5.83)	0.110	1.87 (1.14-3.10)	0.014	1.86 (0.73-4.84)	0.192

F3 population: N = 492 (326 resmetirom, 166 placebo).
F3, advanced fibrosis; OR, odds ratio; PRO-C3, N-terminal propeptide of type III collagen.
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