Phase 3 MAESTRO Clinical Development Program

*For Educational Purposes Only upon request of Liver Forum

MED-AT-MGL-3196-2200024 | November 2025

Phase 3 MAESTRO Clinical Development Program

MAESTRO clinical trials are intended to provide a comprehensive dataset in patients with MASH

MAESTRO NAFLD-1[1]	MAESTRO NAFLD-OLE[2,3]	MAESTRO NASH[4]	MAESTRO NASH OUTCOMES[5]
Safety and tolerability as measured by incidence of TEAEs	Safety and tolerability as measured by incidence of TEAEs (extension to MAESTRO-NAFLD-1)	MASH resolution and/or fibrosis improvement on liver biopsy and composite clinical events	Event-driven trial evaluating progression to hepatic decompensation in patients with well-compensated MASH cirrhosis
52 weeks (completed)	52 weeks (ongoing)	52 weeks biopsy (completed); 54 months clinical outcomes (ongoing)	~36 months (ongoing)
1143 patients	1000 patients (estimated)	1050 patients (52 weeks) 1759 patients (54 months)	845 patients

Resmetirom is not approved by the United States Food and Drug Administration to treat cirrhosis and the safety and effectiveness of resmetirom for the treatment of cirrhosis has not been established.
aNo efficacy or safety data available yet. The study duration is expected to be 2-3 years for accrual of the required number of composite clinical outcome events.
MASH, metabolic dysfunction–associated steatohepatitis; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; OLE, open-label extension; TEAE, treatment-emergent adverse event.
1. Harrison SA et al. Nat Med. 2023;29(11):2919-2928. 2. Alkhouri N et al. Presented at EASL International Liver Congress: May 7-10 2025; Amsterdam, the Netherlands. 3. A Phase 3 Study to Evaluate Safety and Biomarkers of Resmetirom (MGL-3196) in Patients With Non-alcoholic Fatty Liver Disease (NAFLD), MAESTRO-NAFLD-Open-Label-Extension (MAESTRO-NAFLD-OLE). Updated August 3, 2025. Accessed August 12, 2025. https://clinicaltrials.gov/study/NCT04951219/ 4. Harrison SA et al. N Engl J Med. 2024;390:497-5096. 5. Schattenberg JM et al. Poster SAT-424. Presented at EASL International Liver Congress: May 7-10, 2025; Amsterdam, the Netherlands.

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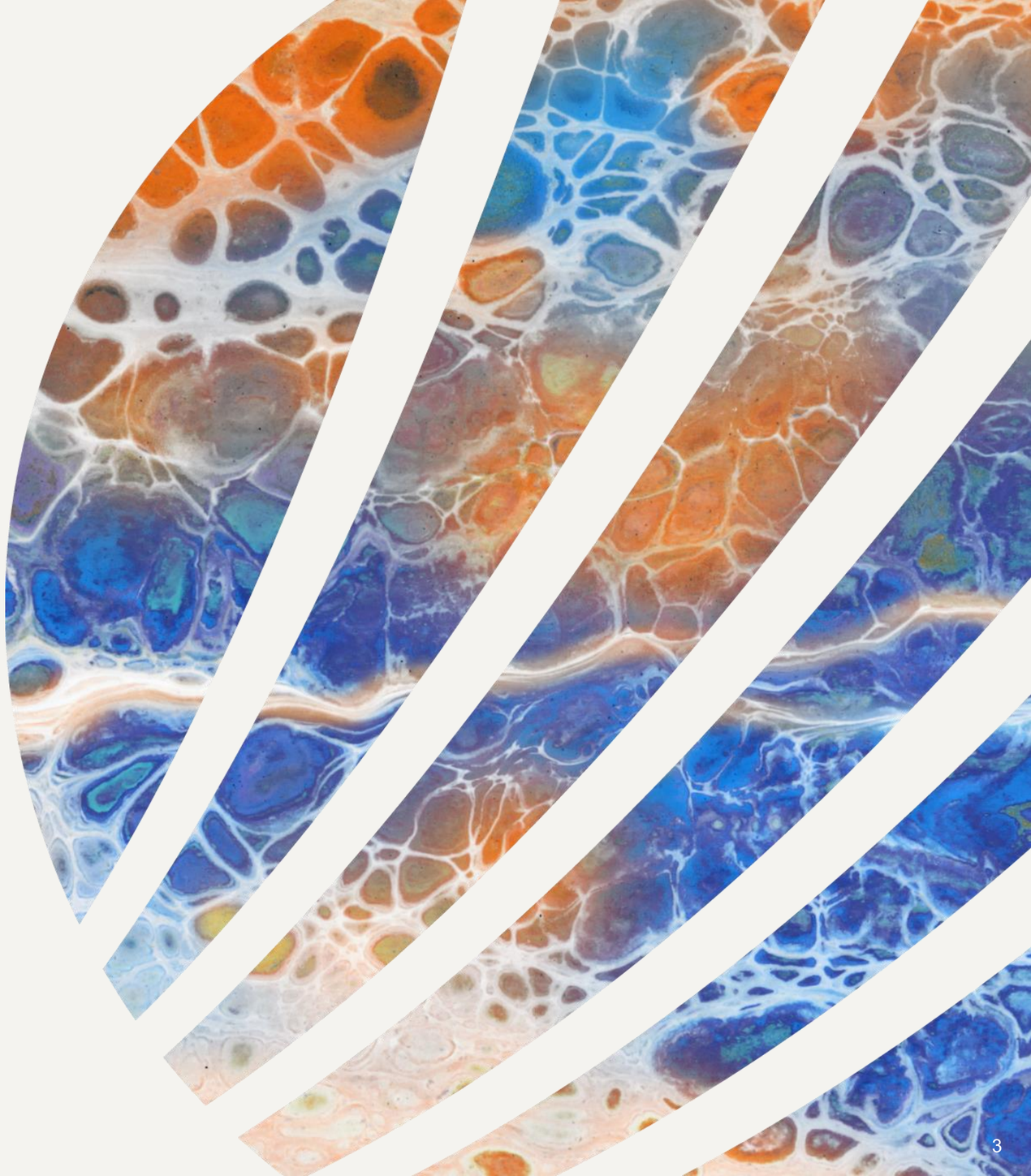
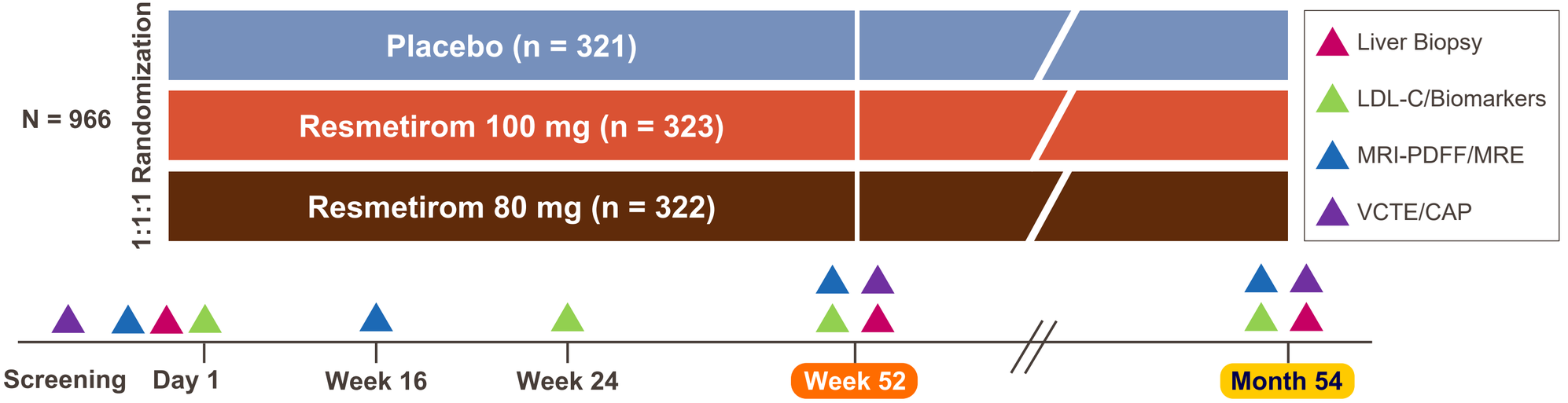
MAESTRO-NASH



MAESTRO-NASH (M-NASH) Trial Design[1,2]

Key inclusion criteria

- 18 years of age or older
- ≥3 metabolic risk factors
- VCTE-LSM ≥8.5 kPa, CAP ≥280 dB/m
- Biopsy confirmed MASH with fibrosis stage F1B, F2 and F3 (no more of 15% F1B)
- ELF ≥9
- ≥8% liver fat on MRI-PDFF



Week 52 Primary analysis

- **Dual primary endpoints**
  - MASH resolution: (ballooning = 0, inflammation =0/1), and ≥ 2 point improvement in NAS with no worsening of fibrosis
  - Fibrosis improvement ≥1 stage with no worsening of NAS
- **Key secondary endpoint**
  - LDL-C lowering at Week 24

Month 54 Primary Analysis

- **Composite Clinical Outcomes**
  - Hepatic decompensation events
  - Histologic progression to cirrhosis
  - All-cause mortality
  - MELD score increase < 12 to ≥15
  - Liver transplant

As the MAESTRO-NASH trial is ongoing, results at Week 52 are shown

[a]Patients were stratified at randomization by fibrosis stage (F2 or F3) or T2D status (present or absent) at baseline.
CAP, controlled attenuation parameter; ELF, enhanced liver fibrosis test; F, (F1: mild fibrosis, F2: moderate fibrosis, F3: advanced fibrosis); kPa, kilopascal; LDL-C, low-density lipoprotein cholesterol; LSM, liver stiffness measurement; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NAS, nonalcoholic fatty liver disease activity score; VCTE, vibration-controlled transient elastography.

1. Harrison SA et al. *N Engl J Med*. 2024;390:497-509. 2. Harrison SA et al. *Aliment Pharmacol Ther*. 2024;59(1):51-63.

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Demographic & Baseline Characteristics

Primary population (n = 966)[a]	Resmetirom 80 mg (n = 322)	Resmetirom 100 mg (n = 323)	Placebo (n = 321)
Age, mean years ± SD	55.9 ± 11.5	57.0 ± 10.8	57.1 ± 10.5
Sex, male, n (%)	140 (43.5)	141 (43.7)	143 (44.5)
Race, White, n (%)	291 (90.4)	291 (90.1)	281 (87.5)
Ethnicity, Hispanic or Latino, n (%)	71 (22.0)	81 (25.1)	52 (16.2)
Body weight, kg ±SD	100.1 ± 22.3	101.9 ± 22.9	100.2 ± 23.1
Body mass index, mean years ± SD	35.5 ± 6.4	36.2 ± 7.4	35.3 ± 6.5
T2D, n (%)	224 (69.6)	213 (65.9)	210 (65.4)
Hypertension, n (%)	243 (75.5)	254 (78.6)	257 (80.1)
Dyslipidemia, n (%)	229 (71.4)	236 (73.1)	224 (69.8)
Hypothyroidism, n (%)[b]	39 (12.1)	46 (14.2)	45 (14.0)
History of ASCVD, n (%)	20 (6.2)	23 (7.1)	14 (4.4)
LDL cholesterol level, mean mg/dL ± SD	106.6 ± 37.4	103.0 ± 36.8	106.8 ± 41.1

[a]Baseline characteristics shown in this table differ from the Prescribing Information.
[b]Patients on thyroxine replacement therapy at screening.
ASCVD, atherosclerotic cardiovascular disease; LDL, low-density lipoprotein; SD, standard deviation; T2D, type 2 diabetes.
Harrison SA et al. *N Engl J Med*. 2024;390:497-509.

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Demographic & Baseline Characteristics

Primary population (n = 966)[a]	Resmetirom 80 mg (n = 322)	Resmetirom 100 mg (n = 323)	Placebo (n = 321)
VCTE/LSM, kPa	13.3 (6.8)	13.6 (7.1)	12.9 (5.5)
VCTE/CAP, dB/m	346.1 (37.2)	349.4 (38.7)	347.2 (37.0)
MRI-PDFF, % fat fraction	18.2 (6.8)	17.2 (6.6)	17.8 (6.8)
MRE, kPa	3.5 (0.9)	3.7 (1.1)	3.5 (1.0)
Baseline medications			
GLP-1 RA	54 (16.8)	41 (12.7)	42 (13.1)
Statin	149 (46.3)	166 (51.4)	157 (48.9)
ALT, U/L	52.8 ± 27.3	56.3 ± 34.0	54.7 ± 34.8
AST, U/L	38.2 ± 19.3	42.5 ± 25.2	40.7 ± 24.6
GGT, U/L	84.3 ± 111.3	84.6 ± 99.0	75.7 ± 85.0
Baseline liver biopsy			
NAS ≥5	266 (82.6)	288 (89.2)	253 (78.8)
F1B	16 (5.0)	15 (4.6)	18 (5.6)
F2	107 (33.2)	100 (31.0)	112 (34.9)
F3	194 (60.2)	203 (62.8)	186 (57.9)

Data are mean (SD) or n (%).
[a]Baseline characteristics shown in this table differ from the Prescribing Information
ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; dB, decibel; F, fibrosis stge (F1: mild fibrosis [substage B: dense zone 3 perisinusoidal fibrosis], F2: moderate fibrosis, F3: advanced fibrosis); GGT, gamma-glutamyltransferase; GLP-1 RA, glucagon-like peptide-1 receptor agonist; kPa, kilopascal; LSM, liver stiffness measurement; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NAS, nonalcoholic fatty liver disease activity score; VCTE, vibration-controlled transient elastography.
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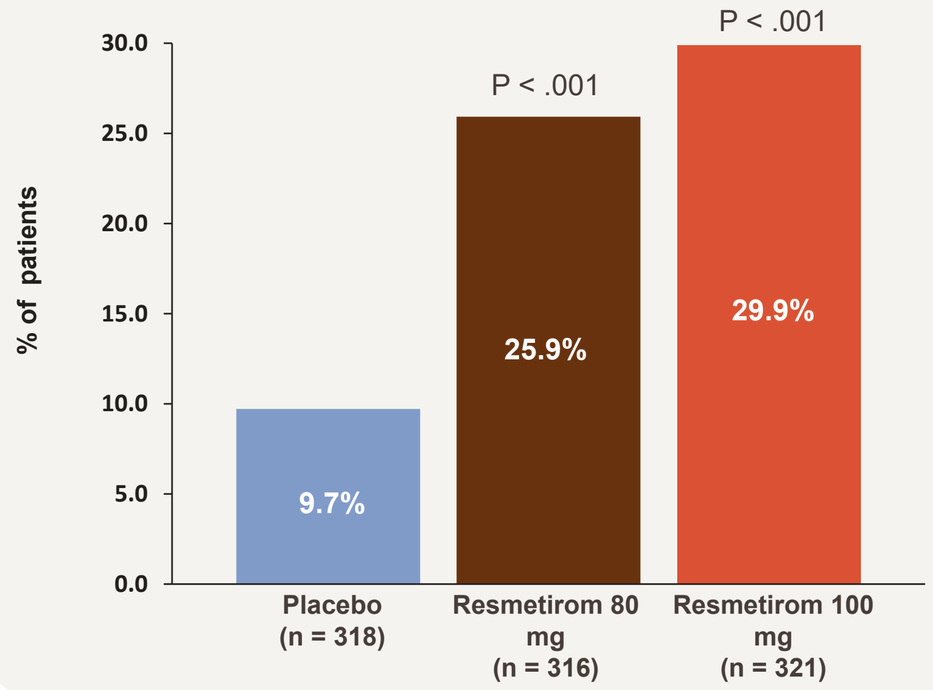
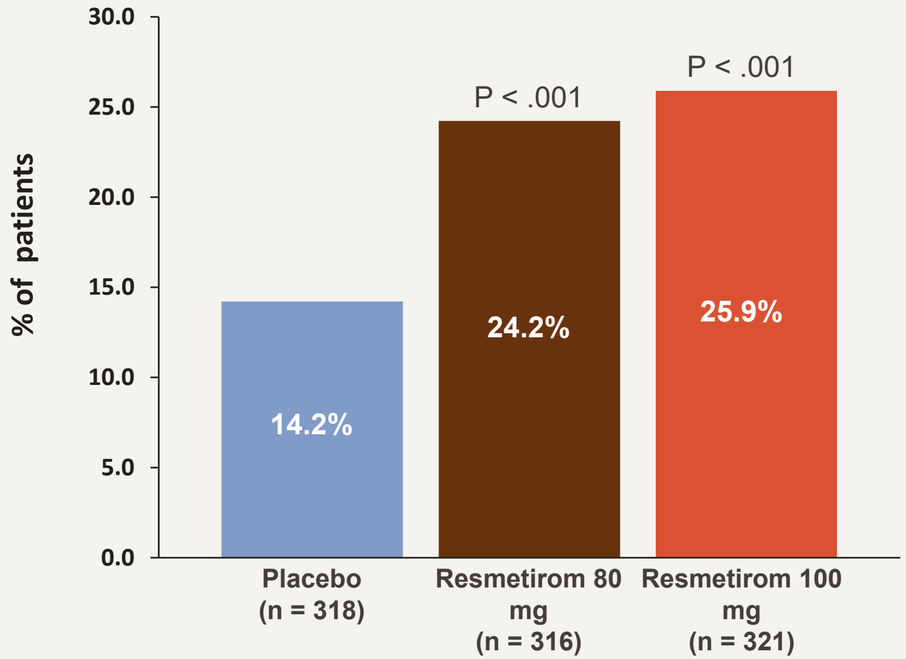
Dual Primary Endpoints (Week 52)

Resolution of MASH with no worsening of liver fibrosis



Fibrosis improvement with no worsening of NAS



Based on the dual primary endpoints at Week 52, both doses of resmetirom demonstrated improvement of MASH and fibrosis improvement vs placebo.

NAS is assessed on a scale of 0 to 8, with higher scores indicating more severe disease; the components of this measure are steatosis (assessed on a scale of 0 to 3), lobular inflammation (assessed on a scale of 0 to 3), and hepatocellular ballooning (assessed on a scale of 0 to 2). MASH resolution was defined as achievement of a hepatocellular ballooning score of 0, a lobular inflammation score of 0 or 1, and a reduction in NAS by at least 2 points. Fibrosis stages range from F0 to F4. A total of 11 patients had a delay in their Week 52 biopsy due to coronavirus disease 2019–related closure of the biopsy site or related reasons and were removed from the primary analysis population for liver-biopsy analyses.
F0-F4, fibrosis stage (F0: no fibrosis, F1: mild fibrosis, F2: moderate fibrosis, F3: advanced fibrosis, F4: cirrhosis); LDL, low-density lipoprotein; MASH, metabolic dysfunction–associated steatohepatitis; NAS, nonalcoholic fatty liver disease activity score.
Figures adapted from Harrison et al. 2024.
Harrison SA et al. *N Engl J Med*. 2024;390:497-509.

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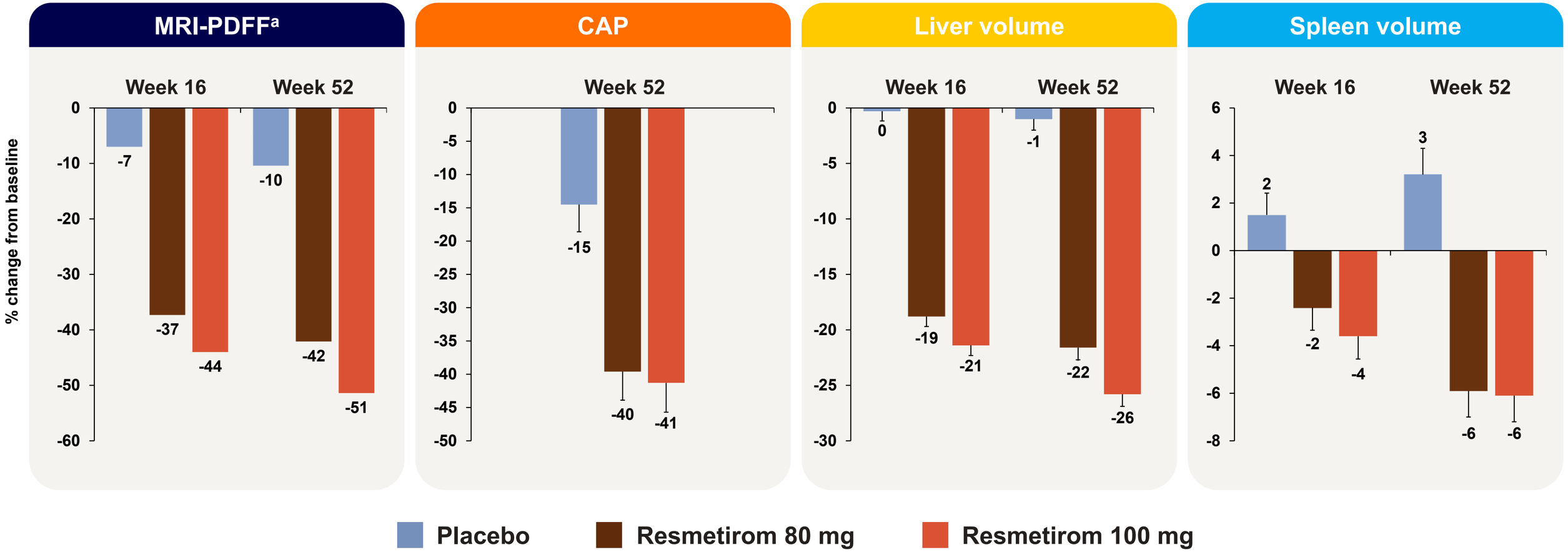
Secondary Endpoints: MRI-PDFF, CAP, Liver and Spleen Volume



[a]Median % change from baseline shown.
CAP, controlled attenuation parameter; MRI-PDFF, magnetic resonance imaging proton density fat fraction.
Figures adapted from Harrison et al. 2024.
Harrison SA et al. *N Engl J Med*. 2024;390:497-509.

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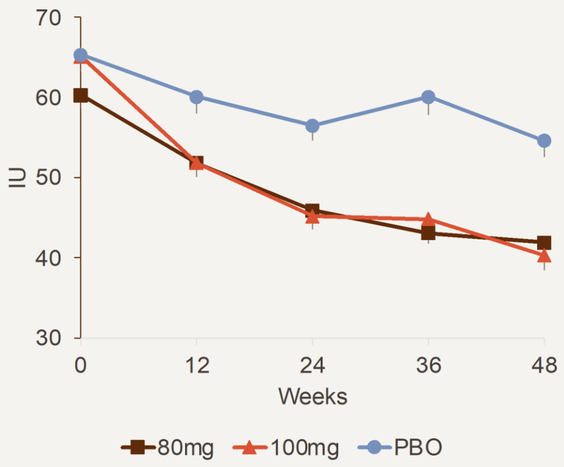
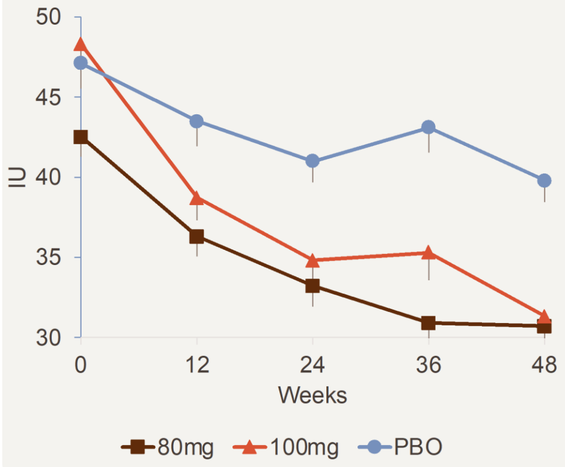
Change from Baseline in Liver Enzymes[a] and SHBG

- Reduction of liver enzymes relative to placebo, both percentage change and absolute reduction
- Associated with the neutral biomarker SHBG that increases in proportion to resmetirom target engagement (exposure)

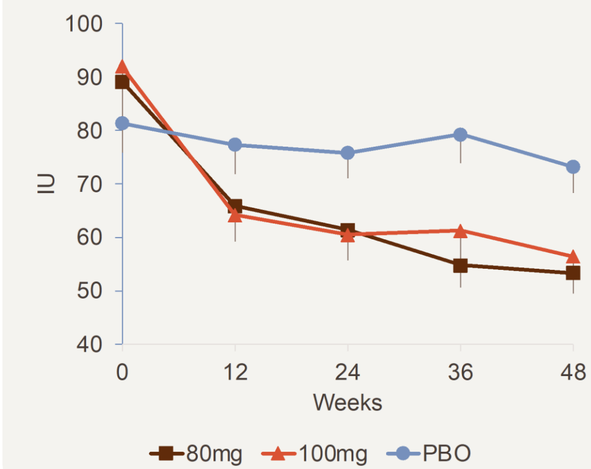
ALT



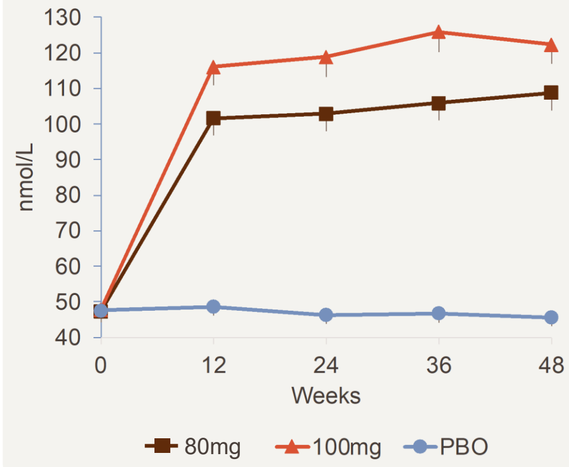
AST



GGT



SHBG



[a]Evaluated in patients with baseline ALT ≥30 IU.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; IU, international unit; PBO, placebo; SHBG, sex hormone–binding globulin.
Figures adapted from Harrison et al. 2023.
Harrison SA, et al. Abstract GS-001. Presented at EASL International Liver Congress: June 22, 2023; Vienna, Austria.

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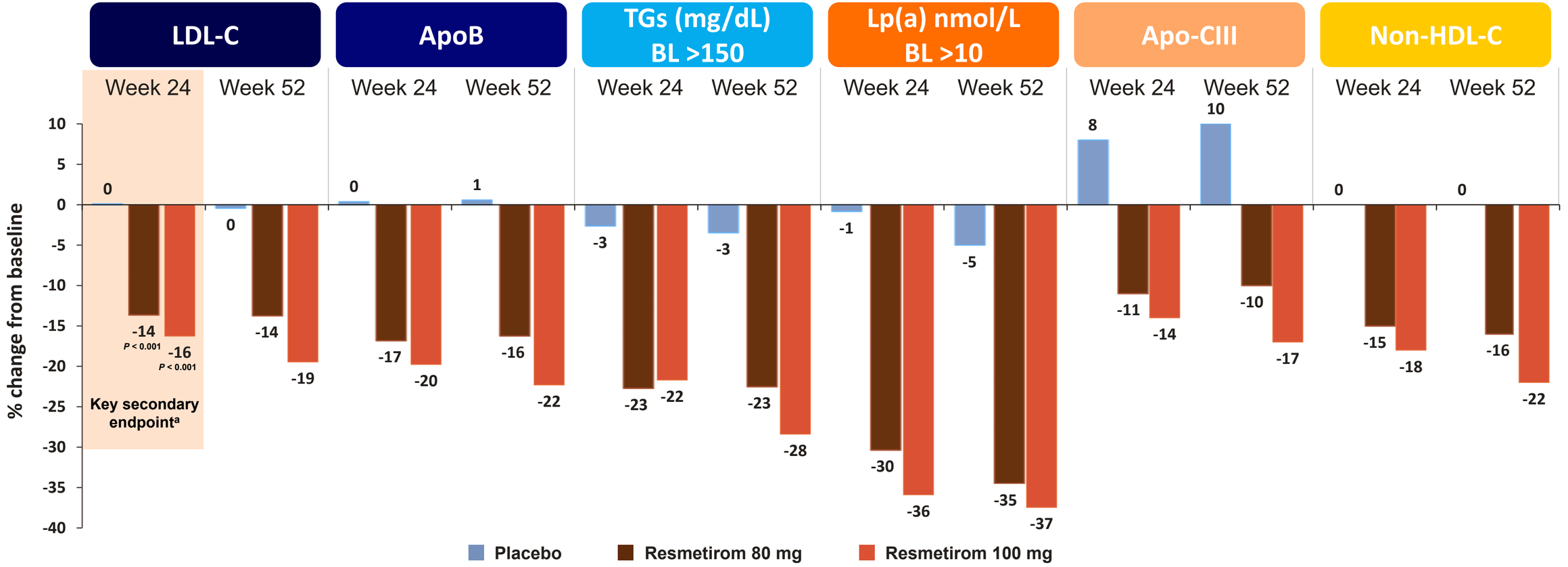
Key Secondary and Other Secondary Endpoints: Lipids and Lipoproteins



Key secondary endpoint met (LDL-C lowering)

- Significant effect of resmetirom 80 and 100 mg at Week 24

[a]Key secondary endpoint: Percent change from baseline in LDL at Week 24 vs placebo; all other measures were secondary endpoints.
ApoB, apolipoprotein B; apo-CIII, apolipoprotein C-III; BL, baseline; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); TG, triglyceride.
Figures adapted from Harrison et al. 2024.

Harrison SA et al. *N Engl J Med*. 2024;390:497-509.

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Safety Overview

- Study discontinuations were higher in the resmetirom 100 mg group at Week 52 compared to placebo and the 80 mg group; after 52 weeks, trial discontinuations were similar across treatment arms

n (%)	Resmetirom 80 mg (n = 322)	Resmetirom 100 mg (n = 323)	Placebo (n = 321)
≥1 TEAE(s)	**296 (91.9)**	**296 (91.6)**	**269 (92.2)**
Grade 1 (mild)	73 (22.7)	66 (20.4)	77 (24.0)
Grade 2 (moderate)	180 (55.9)	183 (56.7)	169 (52.6)
≥Grade 3 (severe)	43 (13.4)	47 (14.6)	52 (16.2)
≥1 TEAE attributed to resmetirom or placebo[a]	124 (38.5)	134 (41.5)	88 (27.4)
≥1 serious TEAEs	**35 (10.9)**	**41 (12.7)**	**37 (11.5)**
≥1 serious TEAE attributed to resmetirom or placebo[a]	2 (0.6)	0	1 (0.3)
TEAEs leading to study discontinuation (before 52 weeks)	**6 (1.9)**	**22 (6.8)**	**7 (2.2)**
Fatal TEAE	**1 (0.3)**	**1 (0.3)**	**1 (0.3)**
3-pt MACE[b] (adjudicated)	**1 (0.3)**	**1 (0.3)**	**1 (0.3)**
Other cardiovascular events (adjudicated)	**0**	**1 (0.3)**	**3 (0.9)**

[a]Events considered by the investigator to be related to resmetirom or placebo.
[b]Nonfatal stroke, nonfatal myocardial infarction, and cardiovascular death.
MACE, major adverse cardiovascular event; TEAE, treatment-emergent adverse event.
AE, adverse event; GI, gastrointestinal; MACE, major adverse cardiovascular event; TEAE, treatment-emergent adverse event.
Harrison SA et al. *N Engl J Med*. 2024;390:497-509.

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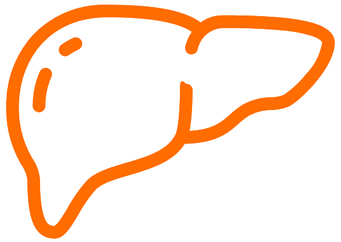
Resmetirom: First Approved Therapy in MASH with Exceptional Profile



Liver directed MOA

THR-β agonist targets underlying causes of MASH

Highly effective

Halts/improves liver stiffness in 91% of patients

Once daily oral pill

Differentiated ease of administration

Well tolerated

Positive real-world results

- Resmetirom was approved by accelerated approval pathway in March 2024: in conjunction with diet and exercise for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis consistent with stages F2 and F3
  - Based on improvement in MASH and liver fibrosis
  - Approved by EMA and EC in 2025

USPI FDA 2024

External Benchmark : Month 48 Regenerate Outcome Events

	Placebo N=728	OCA 10 mg N=729	OCA 25 mg N=730
Any event	137	115	107
Event rate (95% CI)	18.8 (16.0 – 21.9)	15.8 (13.2 – 18.6)	14.7 (12.2 – 17.4)
Mean rate difference (95%CI)		-3.0 (-6.9 to 0.8)	-4.2 (-8.0 to -0.4)
Stratified log-rank test P value vs pbo		0.103	0.044
Stratified hazard ratio vs placebo (95%Ci)		0.814 (0.635 – 1.043)	0.772 (0.600 – 0.994)
Death	9 (1.2%)	7 (1.0%)	11 (1.5%)
Liver transplant	0	1 (0.1%)	1 (0.1%)
MELD progression	2 (0.3%)	4 (0.5%)	2 (0.3%)
Hospitalization for complications of hepatic decompensation	0	1 (0.1%)	2 (0.3%)
Ascites secondary to cirrhosis requiring medical intervention	0	3 (0.4%)	4 (0.5%)
Progression to cirrhosis	**126 (17.3%)**	**99 (13.6%)**	**87 (11.9%)**

- In Regenerate, 87% of events were histologic conversion to cirrhosis
- Progression to cirrhosis in placebo was 17% (any outcome event, 19%)
  - Dependent on mix of F2 and F3 as they have different rates of progression to cirrhosis
- Meta-analyses have shown that progression to cirrhosis is ~3.5x faster in F3 than in F2

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Serial Biomarkers in M-NASH: Opportunity to Link to Fibrosis Progression and Clinical Outcomes

- Target specific serial biomarkers that show relationship to resmetirom mediated reduction in both MASH resolution and fibrosis improvement, liver and CV outcomes
  - MRI-PDFF
  - CAP
  - SHBG
  - Lipids

- Target-agnostic MASH imaging and fibrosis biomarkers
  - Liver Stiffness (MRE, VCTE)
  - Fibrosis synthesis biomarkers (ELF and components, PRO-C3)
  - Liver enzymes, adiponectin, CK-18 components
  - Genetic tests
  - Novel biomarkers

Summary/Next Steps

- MAESTRO-NASH will continue to the 54 month timepoint to confirm benefit of resmetirom on clinical outcomes
- M-NASH is well-powered to achieve the primary endpoint using reasonable assumptions for placebo rate and efficacy of resmetirom
- A positive MAESTRO-NASH trial will enable full approval of Rezdiffra in F2/F3

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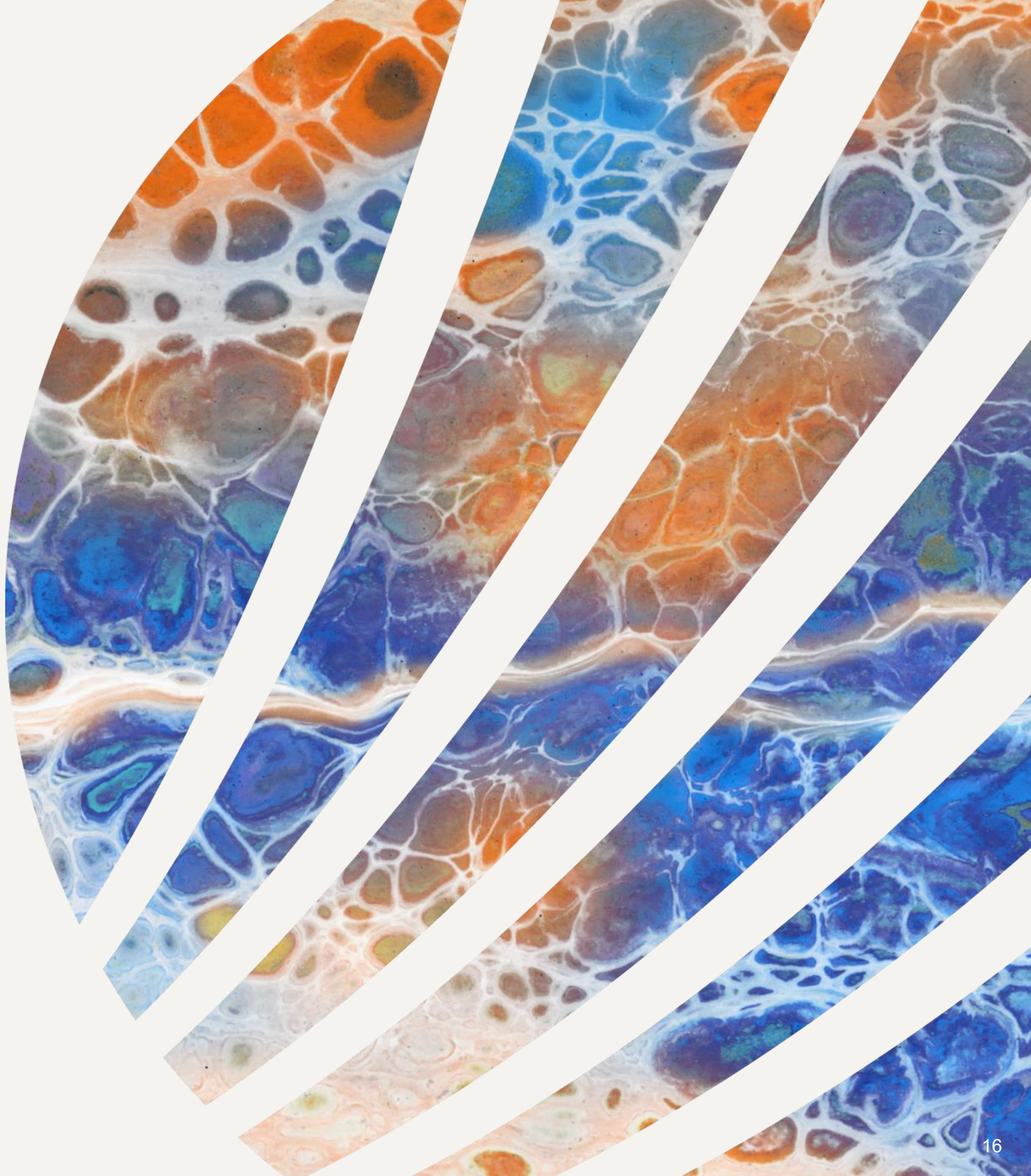
M-NASH-OUTCOMES in F4c



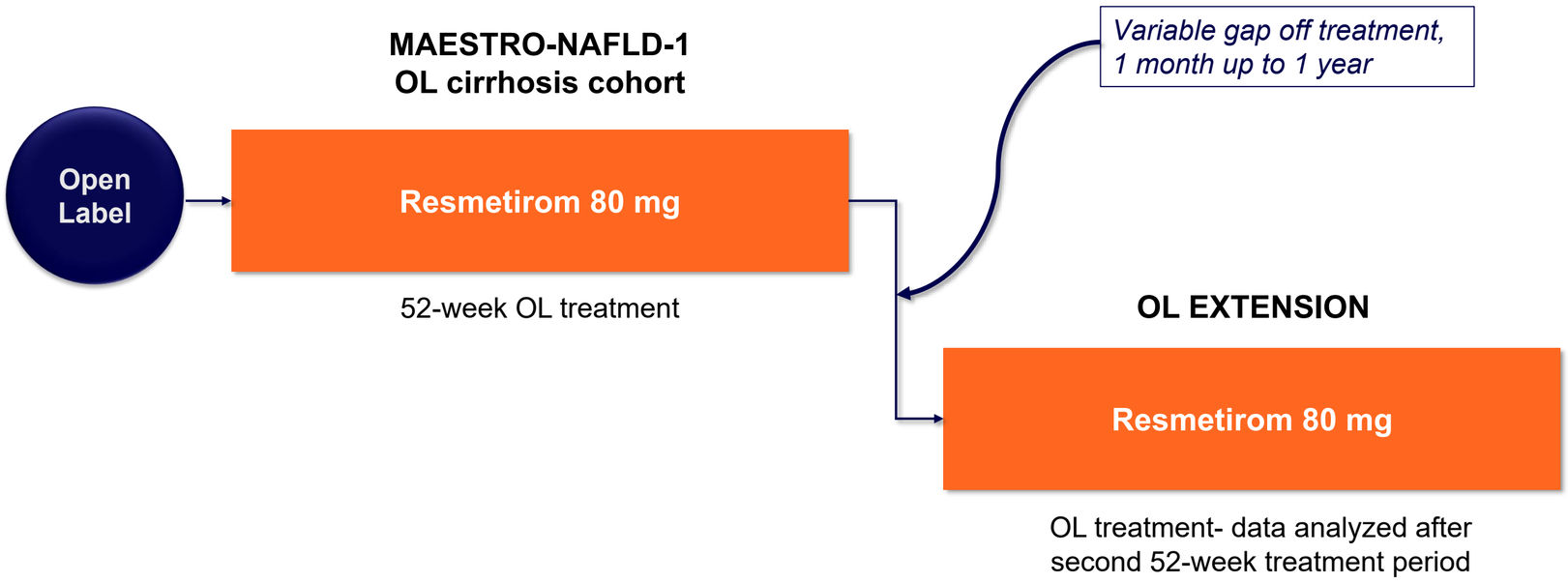
MAESTRO-NAFLD-1 Open-Label (OL) Trial in F4c

Inclusion Criteria

≥3 metabolic risk factors

Well-compensated MASH cirrhosis - Child Pugh A:

- F4 fibrosis[1] OR
- Non-invasive clinical assessment (LSM [VCTE, MRE], ELF, platelets)
- Allowed platelet count ≥70,000
- No history of decompensation

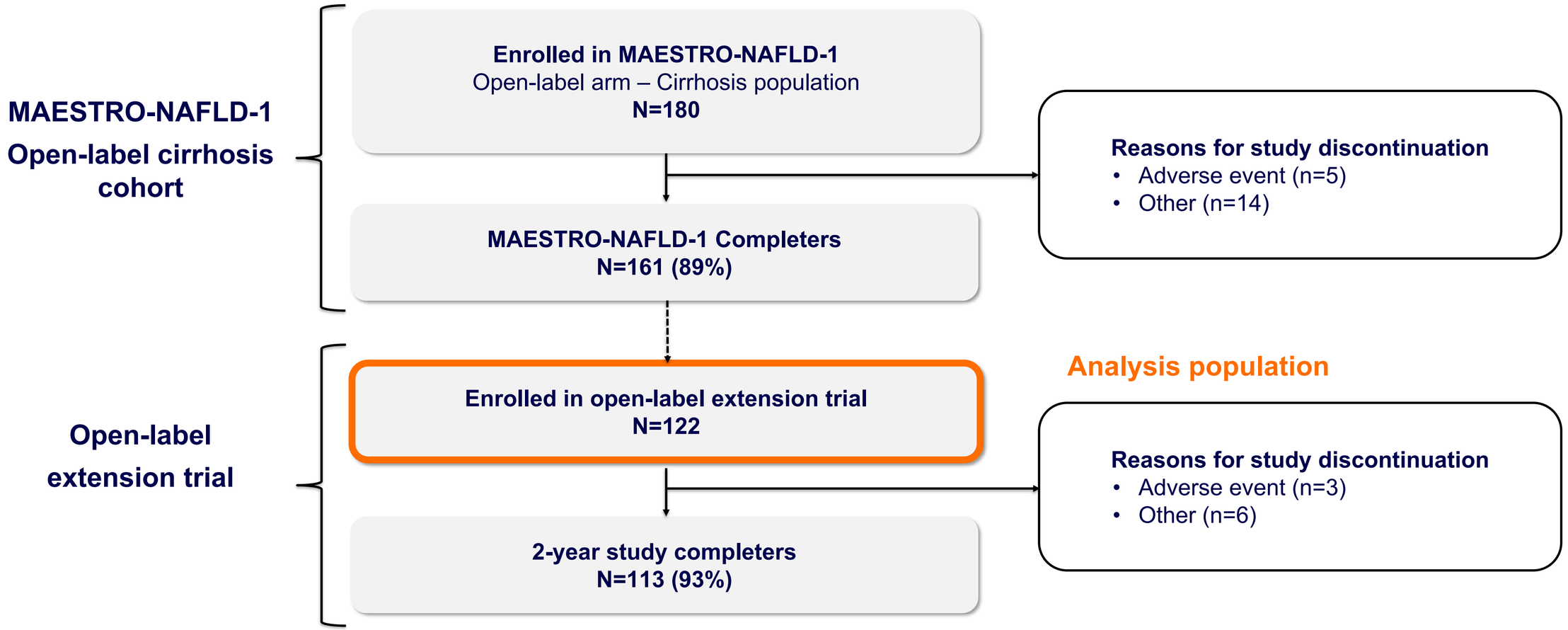


Primary endpoint: Safety and tolerability of resmetirom in patients with cirrhosis
Secondary/Exploratory endpoints: VCTE, MRE, MRI-PDFF, liver enzymes, biomarkers, lipids, liver and spleen volume

Resmetirom is not approved by the United States FDA to treat cirrhosis. The safety and effectiveness of resmetirom for the treatment of cirrhosis has not been established.

Liver biopsy was obtained in 66% of patients. For patients with clinical progression from F3 on biopsy to F4, F4 was confirmed by platelets <LLN (most) or MRE >4.2.
ELF, enhanced liver fibrosis; F4c, fibrosis stage 4 (compensated cirrhosis); LLN, lower limit of normal; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging derived proton density fat fraction; NAFLD, nonalcoholic fatty liver disease; OL, open-label; VCTE, vibration-controlled transient elastography.
Alkhouri N et al. Treatment with resmetirom for up to two years led to improvement in liver stiffness, fibrosis biomarkers, fibrosis scores, and portal hypertension in 122 patients with compensated MASH cirrhosis. Presented at the 2025 EASL Congress. May 7-10, 2025. Amsterdam, the Netherlands.

MAESTRO-NAFLD-1 OL Trial Flow



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NAFLD, nonalcoholic fatty liver disease.
Alkhouri N et al. Treatment with resmetirom for up to two years led to improvement in liver stiffness, fibrosis biomarkers, fibrosis scores, and portal hypertension in 122 patients with compensated MASH cirrhosis. Presented at the 2025 EASL Congress. May 7-10, 2025. Amsterdam, the Netherlands.

MAESTRO-NAFLD-1: Baseline Characteristics

- In MASH cirrhosis, lower hepatic fat was associated with more advanced disease

	BL MRI-PDFF >5%[a] n=93	BL MRI-PDFF ≤5% n=21
Age, years	61 (56, 68)	63 (61, 67)
Sex, Female	51 (55%)	11 (52%)
Ethnicity, Hispanic	28 (30%)	4 (19%)
BMI, kg/m^2	34.4 (30.6, 39.1)	33.5 (29.8, 37.9)
Type 2 Diabetes	63 (68%)	18 (86%)
VCTE, kPa	19.5 (17.1, 29.5)	24.6 (17.1, 39.4)
CAP, dB/m	331 (302, 372)	291 (249, 329)
MRE, kPa	5.2 (4.0, 6.1)	5.6 (4.9, 7.0)
MRI-PDFF, %	9.5 (7.3, 12.6)	3.9 (3.1, 4.4)
Liver Volume, mL	2291 (1903, 2737)	2093 (1649, 2473)
Spleen Volume, mL	476 (325, 721)	667 (414, 998)

	BL MRI-PDFF >5%[a] n=93	BL MRI-PDFF ≤5% n=21
ALT, U/L	37 (29, 50)	28 (25, 39)
GGT, U/L	66 (43, 126)	106 (45, 146)
Platelets, 10^9/L	139 (112, 193)	110 (90, 141)
Albumin, g/dL	4.2 (4.0, 4.4)	4.2 (4.0, 4.5)
LDL-C, mg/dL	95 (76, 123)	73 (62, 94)
Triglycerides, mg/dL	140 (103, 181)	114 (87, 122)
FIB-4	2.3 (1.6, 3.6)	3.5 (2.2, 4.0)
ELF Score	10.6 (9.9, 11.4)	11.0 (10.7, 11.7)

Resmetirom is not approved by the United States FDA to treat cirrhosis. The safety and effectiveness of resmetirom for the treatment of cirrhosis has not been established.

[a]Only 114/122 patients had baseline MRI-PDFF. Data are median (Q1, Q3) or %.
ALT, alanine aminotransferase; BL, baseline; BMI, body mass index; CAP, controlled attenuation parameter; ELF, enhanced liver fibrosis; FIB-4, Fibrosis-4; GGT, gamma-glutamyl transferase; LDL-C; low-density lipoprotein cholesterol; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging derived proton density fat fraction; NAFLD, nonalcoholic fatty liver disease; VCTE, vibration-controlled transient elastography.
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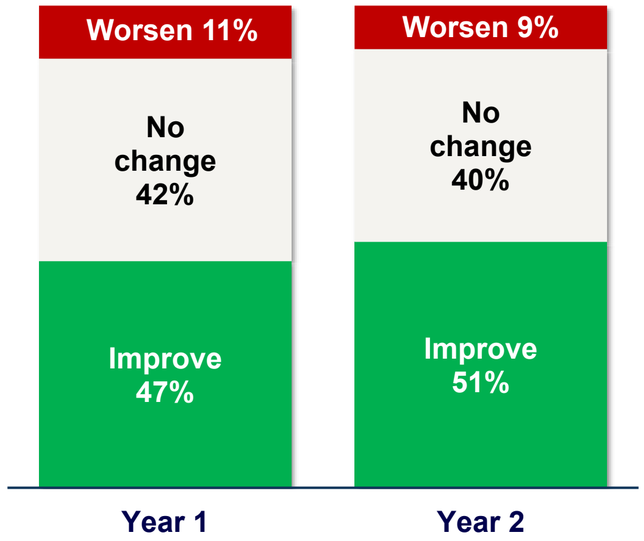
M-NAFLD-1 OL Cirrhosis

Liver Stiffness Measure (LSM) After 2-Year Treatment with Resmetirom

Mean Change from Baseline in VCTE[a]

Percent with 25% Change from Baseline in VCTE



~50% of patients achieved sustained ≥25% reduction in LSM by VCTE at Year 2

Resmetirom is not approved by the United States FDA to treat cirrhosis. The safety and effectiveness of resmetirom for the treatment of cirrhosis has not been established.

[a]Year 1: -6.4 (-9.2, -3.7) kPa; Year 2: -6.7 (-9.4, -4.1) kPa (95% CI).
LSM, liver stiffness measure; MRE, magnetic resonance elastography; VCTE, vibration-controlled transient elastography.
Alkhouri N et al. Treatment with resmetirom for up to two years led to improvement in liver stiffness, fibrosis biomarkers, fibrosis scores and portal hypertension in 122 patients with compensated MASH cirrhosis. Presented at the 2025 EASL Congress. May 7-10, 2025. Amsterdam, the Netherlands.

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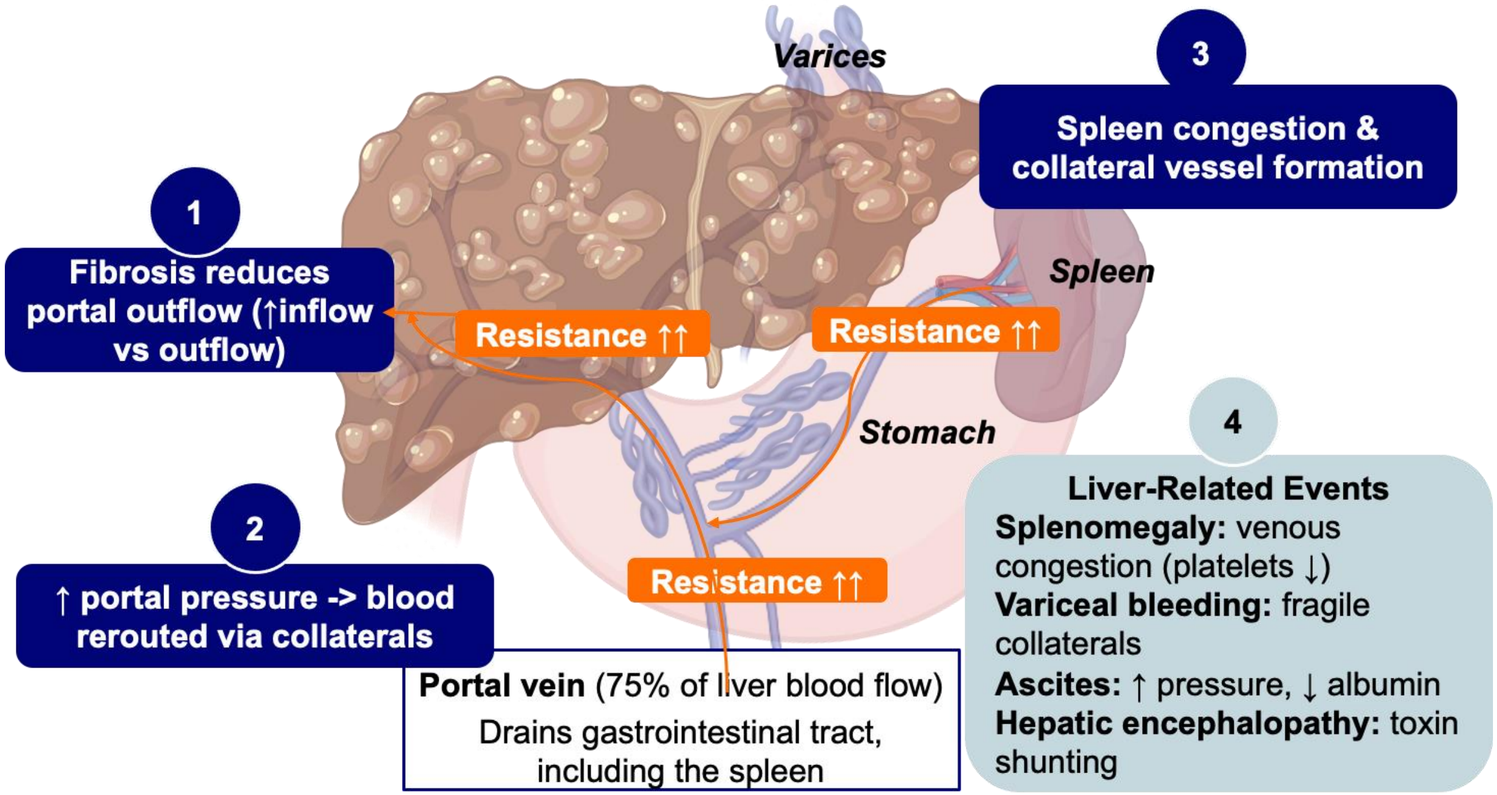
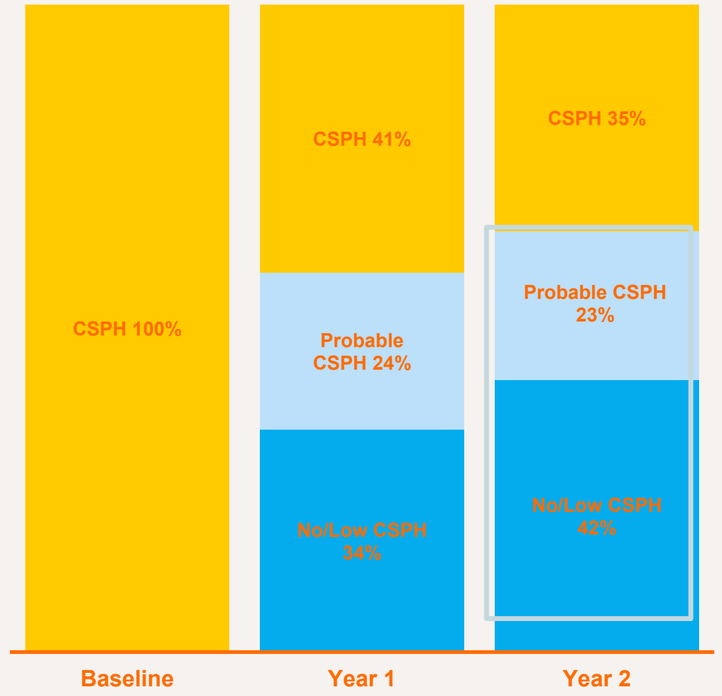
Reduction in Clinically Significant Portal Hypertension (CSPH) Risk

CSPH is Responsible for the Most Severe and Fatal Complications of Cirrhosis[1]



65% of Patients with CSPH at Baseline Moved into Lower Risk Categories at Year 2

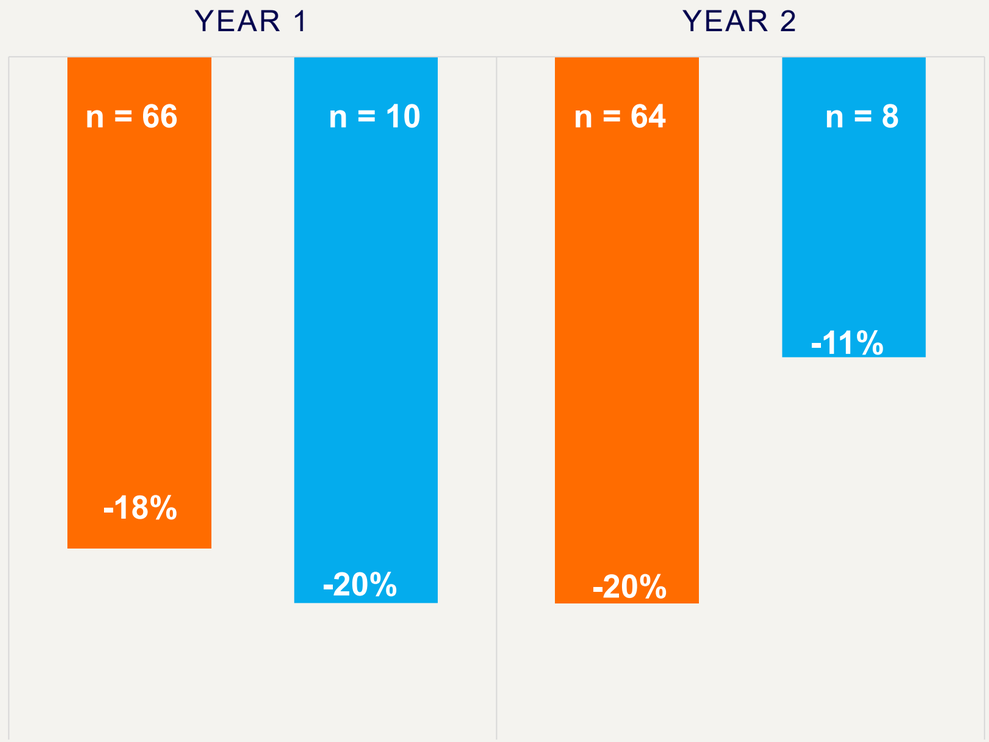


Alkhouri, N et al EASL 2025

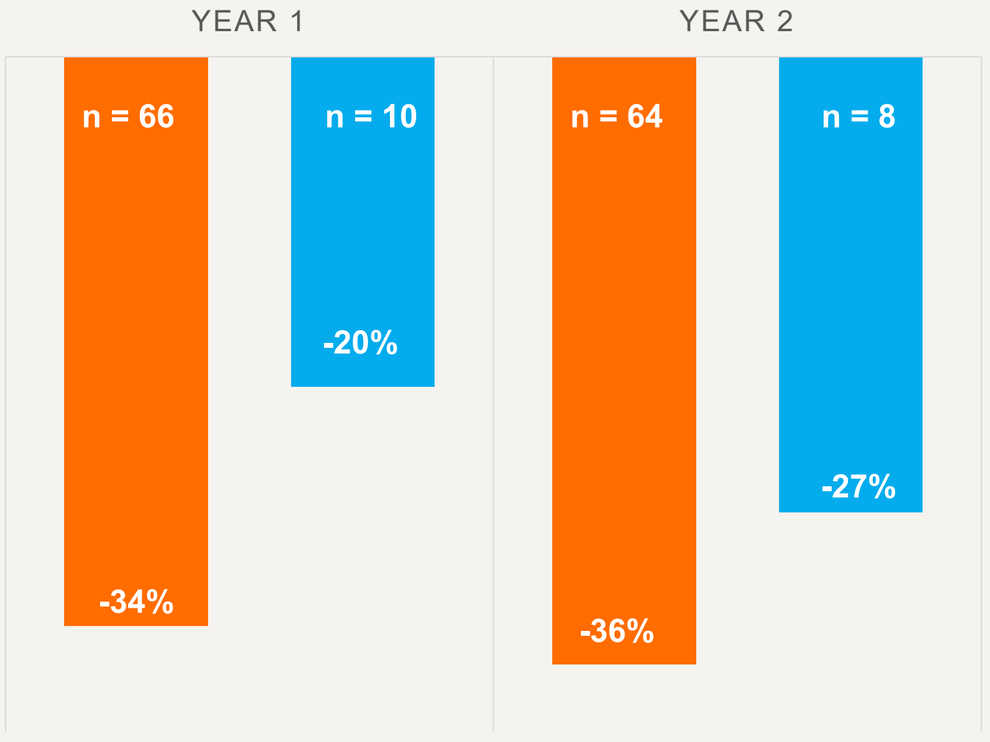
1. de Franchis R, et al. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022;76(4):959-974; image adapted from Mayo Clinic: Esophageal varices - Symptoms and causes - Mayo Clinic.

Effect of Resmetirom on ALT and GGT

Mean percent change from baseline in ALT (Patients with ALT ≥30 IU at baseline)[a]



Percent change from baseline in GGT[b]



Baseline MRI-PDFF >5% Baseline MRI-PDFF ≤5%

Resmetirom is not approved by the United States FDA to treat cirrhosis. The safety and effectiveness of resmetirom for the treatment of cirrhosis has not been established.

Based on observed data.
[a]Overall ALT, Year 1 Week 48, -18% (95% CI: -26%,-11%); Year 2 Week 104, -19% (95% CI: -27%,-11%).
[b]Overall GGT Year 1, Week 48, -32% (95% CI: -38%,-27%); Year 2 Week 104, -35% (95% CI: -44%, -27%).
ALT, alanine aminotransferase; GGT, gamma-glutamyltransferase; MRI-PDFF, magnetic resonance imaging proton density fat fraction.
Figures adapted from Alkhouri et al. 2025.
Alkhouri N et al. Presented at EASL International Liver Congress: May 7-10 2025; Amsterdam, the Netherlands.

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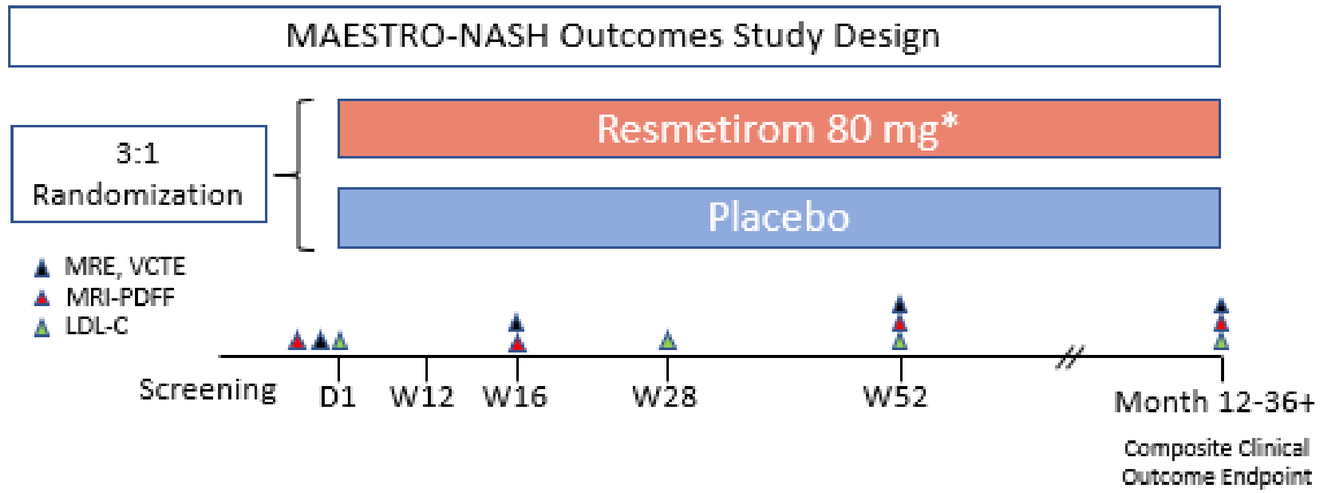
MAESTRO-NASH Outcomes (Study 19) Design

Comparator/Arms

- 3:1 Resmetirom 80 mg vs placebo
- 845 patients total enrollment
- >100 centers, North America, and Europe



*Dose adjustment Week 12 based on change in SHBG and FT4, expected ~20% to increase to 100mg and <5% to decrease to 60mg

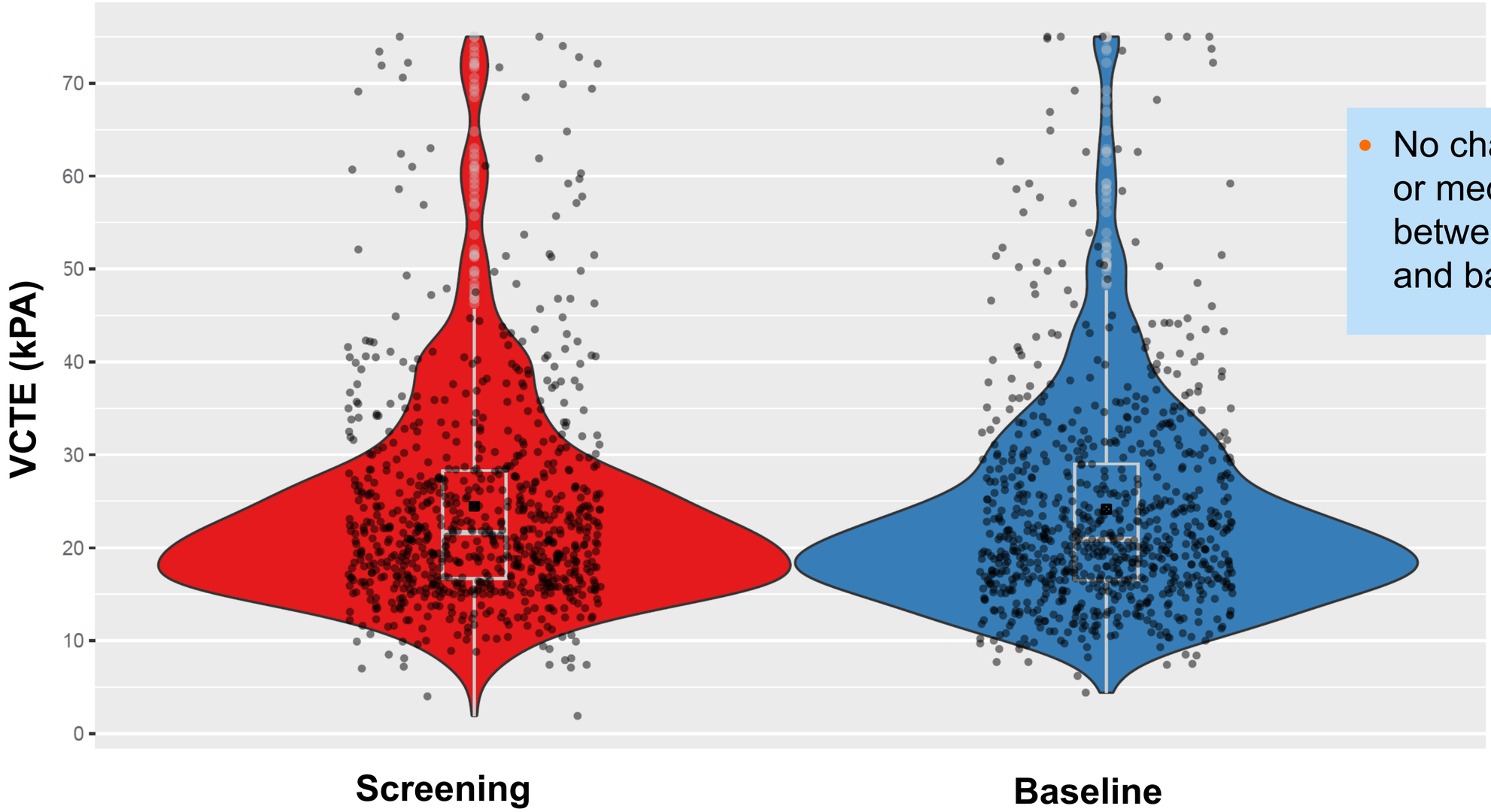
Key Inclusion/Exclusion Criteria

- Requires 3 metabolic risk factors (Metabolic Syndrome)
- No history of decompensation
- Compensated NASH cirrhosis (Child-Pugh A, score 5-6)
  - Historical biopsy confirming cirrhosis/F4
  - Historical biopsy confirming NASH with proof of progression to cirrhosis based on noninvasive tests
  - No biopsy: At least two: MRE ≥4.2 kPa, FS>=15 kPa, ELF>=10.25, Fib-4>=3, Platelets <140K

- Primary Endpoint
  - Incidence of adjudicated Composite Clinical Outcome (~36 months); All cause mortality, liver transplant, ascites, hepatic encephalopathy, gastroesophageal variceal hemorrhage, and confirmed increase of MELD score from <12 to ≥15 due to liver disease

DB, double-blind; ELF, enhanced liver fibrosis; FT4, free thyroxine; MELD, model for end-stage liver disease; LDL-C, low-density lipoprotein cholesterol; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging-proton density fat fraction; NASH, nonalcoholic steatohepatitis; SHBG, sex hormone binding globulin.
ClinicalTrials.gov (NCT05500222). https://clinicaltrials.gov/ct2/show/NCT05500222. Accessed 24Aug2022.

MAESTRO-NASH OUTCOMES



- No change in mean or median kPa between screening and baseline VCTEs

MAESTRO-NASH Outcomes- NASH Cirrhosis

	Patients with Biopsy (N=392)	Patients without Biopsy (N=453)
Age, years, mean (SD)	62.6 (8.8)	63.4 (9.4)
Sex, male, n (%)	138 (35)	147 (32)
Ethnicity, Hispanic/Latino, n (%)	70 (18)	107 (24)
Body weight, kg, mean (SD)	94.2 (22.0)	95.0 (21.1)
Body mass index, kg/m^2 , mean (SD)	33.8 (6.7)	34.6 (7.1)
Hypertension, n (%)	311 (79)	316 (70)
Hypothyroid, n (%)	91 (23)	99 (22)
Type 2 diabetes, n (%)	300 (77)	295 (65)
Documented ASCVD, n (%)	20 (5.1)	21 (4.6)
ELF Test, n	391	388
≥11.3, n (%)	102 (26.1)	132 (34.0)
<11.3, n (%)	289 (73.9)	256 (66.0)
MELD, n	379	387
≥12, n (%)	12 (3.2)	26 (6.7)
9-11, n (%)	89 (23.5)	122 (31.5)
<9, n (%)	278 (73.4)	239 (61.8)
MRI-PDFF, n	358	355
<5, n (%)	95 (26.5)	128 (36.1)
≥5, n (%)	263 (73.5)	227 (63.9)
MRI-PDFF, % fat fraction, mean (SD)	8.8 (5.3)	7.6 (5.1)
MRE, kPa, n	324	319
≥6	94 (29.0)	108 (33.9)
<6	230 (71.0)	211 (66.1)
MRE, kPa, mean (SD)	5.5 (1.5)	5.8 (1.7)

	Patients with Biopsy (N=392)	Patients without Biopsy (N=453)
FibroScan VCTE, kPa, mean (SD)	23.0 (11.0)	27.6 (36.6)
Fibroscan TE median (Q1,Q3) (kPa)	20.1 (16.2, 26.1)	22.30 (17.4, 30.0)
Fibroscan TE < 15 (n,%)	60 (15.3%)	46 (10.2%)
Fibroscan TE 15-20 (n,%)	130 (33.2%)	125 (27.7%)
Fibroscan TE 20-25 (n,%)	86 (22.0%)	104 (23.0%)
Fibroscan TE >= 25 (n,%)	115 (29.4%)	177 (39.2%)
FibroScan CAP, dB/m, mean (SD)	303.0 (59.1)	304.1 (52.0)
Statin use, n (%)	221 (56.4)	220 (48.6)
Thyroxine Any, n (%)	98 (25.0)	101 (22.3)
GLP-1 use, n (%)	143 (36.5)	125 (27.6)
SGLT2 use, n (%)	90 (23.0)	69 (15.2)
Other laboratory parameters, mean (SD)		
FIB-4	2.8 (1.4)	3.3 (1.6)
Total bilirubin, mg/dL	0.8 (0.3)	0.9 (0.4)
Direct bilirubin, mg/dL	0.2 (0.1)	0.2 (0.1)
Platelet count, K	161.6 (58.6)	145.7 (61.2)
Albumin, g/dL	4.3 (0.3)	4.2 (0.3)
INR	1.2 (0.2)	1.2 (0.1)
ELF Test	10.7 (0.9)	10.9 (0.9)
ALT, IU/L	42.4 (25.3)	39.1 (23.2)
AST, IU/L	41.4 (19.9)	39.9 (19.9)
GGT, IU/L	105.7 (122.8)	109.1 (101.3)

MAESTRO Outcomes Population is Advanced (845 Patients)
Selected Baseline Characteristics

Baseline Characteristics	
%Male	37%
Mean Age (yrs)	64 years
%T2DM	80%
%GLP1	29%
%Hypertension	83%
Mean ALT (SD)	40.6 (24)
Mean VCTE (SD)	24.2 (12.1)
Mean ELF (SD)	10.8 (0.9)
Mean FIB-4 (SD)	2.8 (1.5)
Mean Platelets (SD) x 1000	155 (60)
%CSPH (CSPH / Probable CSPH)	28% / 28%

Summary/Next steps

- MAESTRO-OUTCOMES is well-powered for the occurrence of liver outcome events in an appropriate study population
  - Data with other first-in-indication treatments support plausibility of this effect being achieved
  - Open-label data are supportive of a positive biological effect in the population

- A positive MAESTRO-OUTCOMES study would enable full approval for both F4c patients and F2/F3

- This event-driven study was initiated in August 2022 and is estimated to completed 2027 (event-driven trial)