Baseline characteristics in well-compensated MASH cirrhosis patients diagnosed with or without a liver biopsy in MAESTRO-NASH-OUTCOMES, a clinical outcome Phase 3 study assessing the effect of resmetirom in well-compensated MASH cirrhosis

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Background: MAESTRO-NASH-Outcomes (NCT05500222) is a multi-national, multicenter, double-blind, randomized, placebo-controlled study in well-compensated MASH cirrhosis. Patients were randomized 3:1 in a blinded manner to receive resmetirom 80 mg or matching placebo given orally once daily in the morning for the duration of the study (until the required number of Composite Clinical Outcome evens are achieved). Composite Clinical Outcome events are defined as any of the following: mortality, liver transplant, and significant hepatic events, including potential hepatic decompensation events (ascites, hepatic encephalopathy, or gastroesophageal variceal hemorrhage), and confirmed increase of Model for End-stage Liver Disease (MELD) score from < 12 to ≥ 15. The study comprises an up to 60-day screening period and an approximately 3-year treatment period. Baseline factors in patients who were diagnosed with MASH cirrhosis on liver biopsy were compared with those diagnosed with MASH cirrhosis who did not receive a liver biopsy.

Material and Methods: The study enrolls MASH cirrhosis patients with confirmed F4 fibrosis on biopsy with 3 metabolic risk factors, meeting other non-invasive testing and eligibility requirements, or MASH cirrhosis diagnosed non-invasively requiring at least two non-invasive testing requirements for screening: FibroScan vibration-controlled transient elastography (VCTE) ≥ 15 kPa and/or if FibroScan VCTE < 15 kPa; at least two other non-invasive tests (magnetic resonance elastography (MRE) ≥ 4.2 kPa, platelets <140 G/L, ELF ≥ 10.25, FIB-4 ≥ 3). Other screening tests included blood tests, MRE, MRI-PDFF, and assessments for hepatocellular carcinoma and ascites, with MELD < 12 (except for Gilbert).

Results: Based on a current enrollment of 566 patients, baseline factors were generally similar between patients diagnosed as MASH cirrhosis on liver biopsy or diagnosed as MASH cirrhosis without a liver biopsy: mean age 63 years; 34-38% males, mean BMI of 35 kg/m^2, 82% with hypertension, 73-78% with type 2 diabetes. Approximately one third of patients had more advanced disease based on MRE ≥ 6, ELF ≥ 11.3, MRI-PDFF < 5%. A slightly higher percentage of MASH cirrhosis patients diagnosed without a liver biopsy had baseline characteristics suggestive of more advanced portal hypertension (platelets < 140 K, higher MRE, ELF, and Fibroscan VCTE). A slightly higher percentage of MASH cirrhosis patients diagnosed without a liver biopsy met the Baveno VII criteria for clinically significant portal hypertension (CSPH) or high risk of CSPH (83% vs. 68%).

Conclusions: These data support the accuracy of using non-invasive testing to accurately diagnose well-compensated MASH cirrhosis.

	Patients with biopsy N=297	**Patients without biopsy N=269**
Age, years	63 (8.3)	63.3 (9.1)
Male	100 (34%)	103 (38%)
Female	197 (66%)	166 (62%)
Hispanic/Latino	58 (20%)	73 (27%)
Body weight, kg	93.9 (21.5)	96.7 (21.7)
Body mass index, kg/m^2	34.5 (17.0)	35.0 (7.4)
Hypertension	244 (82%)	218 (81%)
Hypothyroid	77 (26%)	71 (26%)
Type 2 diabetes	231 (78%)	196 (73%)
Documented atherosclerotic cardiovascular disease	18 (6.1%)	14 (5.2%)
ELF ≥ 11.3	78 (26.7%)	88 (33.3%)
ELF < 11.3	214 (73.3)	176 (66.7%)
ELF	10.7 (0.9)	11.0 (0.9)
MELD ≥ 12	10 (3.5%)	20 (7.6%)
MELD 9-11	57 (20.1%)	93 (35.5%)
MELD <9	216 (76.3%)	149 (56.9%)
MRI-PDFF < 5%	73 (28.7%)	83 (35.0%)
MRI-PDFF ≥ 5%	181 (71.3%)	154 (65.0%)
MRI-PDFF	8.5 (5.1)	8.0 (5.4)
MRE ≥ 6kPa	76 (31.8%)	87 (37.8%)
MRE < 6 kPa	163 (68.2%)	143 (62.2%)
MRE, kPa	5.6 (1.6)	5.9 (1.7)
VCTE, kPa	23.7 (12.0)	26.8 (13.5)
FibroScan CAP, dB/m	301.9 (59.0)	301.2 (57.3)
Statin	168 (56.6%)	151 (56.1%)
Thyroxine	79 (26.6%)	75 (27.9%)
GLP-1 receptor agonists	108 (36.4%)	85 (31.6%)
SGLT2 inhibitors	66 (22.2%)	51 (19.0%)
FIB-4	2.9 (1.5)	3.4 (1.6)
Total bilirubin, mg/dL	0.8 (0.4)	0.9 (0.4)
Direct bilirubin, mg/dL	0.2 (0.1)	0.2 (0.1)
Platelet, G/L	161.6 (59.9)	141.9 (59.5)
Albumin, g/dL	4.3 (0.3)	4.2 (0.3)
INR	1.1 (0.2)	1.2 (0.1)
ALT, IU/L	41.6 (24.4)	39.9 (24.4)
AST, IU/L	40.8 (18.8)	40.7 (20.8)
GGT, IU/L	105.0 (125.6)	106.4 (102.8)

Data are mean (SD) or n (%)