Background and Aims: MAESTRO-NASH (NCT03900429) is an ongoing 54-month, randomized, double-blind, placebo-controlled Phase 3 trial evaluating efficacy of resmetirom in patients with biopsy-confirmed non-alcoholic steatohepatitis (NASH/MASH) and fibrosis. 966 patients with biopsy-confirmed NASH were randomized 1:1:1 to resmetirom 80 mg, resmetirom 100 mg, or placebo once daily. Dual primary endpoints at Week 52 were achieved with both resmetirom 80 mg and 100 mg: NASH resolution with no worsening of fibrosis (NR) or ≥1-stage improvement in fibrosis with no worsening of NAS (FI). The benefit of resmetirom in patients with and without indicators of increased alcohol consumption above protocol-allowed limits for NASH/MASH was assessed on biopsy endpoints and MRI-PDFF (liver fat reduction).

Method: Carbohydrate Deficient Transferrin (CDT) was collected longitudinally in all patients over 52 weeks. Post-randomization, a PEth test was performed in patients suspected of increased alcohol consumption. Patients with baseline or post-baseline CDT >2.5% (ULN 2.47) and/or a PEth >20ng/ml (ULN 20ng/ml) were assigned to a possible “MetALD” subgroup. Analyses were performed on 782 patients who had both a baseline and Week 52 biopsy.

Results: Of the 782 patients, 75 patients (9.6%) were included in the MetALD subgroup and 707 were not. Baseline characteristics, mean (SD), for the MetALD and non-alcohol subgroups included Age=57.7 (10.5), 60.1 (10.7); percent male=59%, 42%; Presence of diabetes=50.7%, 67.9%; CDT%=2.2 (1.0), 1.6 (0.3); BMI 33.0 (5.5), 35.8 (6.6); MRI-PDFF=21.7% (7.4), 17.4 (6.5), Fibroscan VCTE=13.4 (6.7), 13.2 (6.6); Fibroscan CAP=348.5 (38.5), 347.0 (38.7); FIB-4=1.67 (0.69), 1.37 (0.66); AST=45.6 (21.8), 40.3 (22.9); ALT=55.2 (24.8), 55.5 (32.2); GGT=117.9 (170.8), 75.3 (85.6); Bilirubin=0.69 (0.31), 0.65 (0.29); MCV=92.3 (5.8), 90.3 (5.6); Platelets=200, 229; NAS (median)=5 (5,6), 5 (5,6); and %F3=66.7, 62.5.

For the group of patients with low or no alcoholic consumption:
Patients treated with 80 mg and 100 mg resmetirom doses (n=224 and 228, respectively): 29.9% and 36% had NR, 29% and 33.3% had FI, 59.2% and 71.2% showed a ≥30% reduction from baseline in MRI-PDFF. For patients treated with placebo (n=255), the corresponding results were 10.3%, 13.7%, and 24.5%.

For the possible MetALD group: Patients treated with 80 mg and 100 mg resmetirom doses (n=34 and 20, respectively): 29% and 35% had NR, 35% and 30% had FI, and 88% and 81% showed a ≥30% reduction from baseline in MRI-PDFF. For patients treated with placebo (n=21), the corresponding results were 10%, 19%, and 14%.
Conclusion: A total of 75 (9.6%) of patients had possible MetALD during the first 52 weeks of MAESTRO-NASH. Baseline characteristics showed a higher mean GGT and FIB-4 in the MetALD versus low alcohol group. Response rates to resmetirom in patients with suspected MetALD were similar to those without MetALD.