Health-Related Quality of Life (HRQL) assessments in a 52-Week, double-blind, randomized, placebo-controlled phase 3 study of Resmetirom (MGL-3196) in patients with nonalcoholic steatohepatitis (NASH) and fibrosis (MAESTRO-NASH)

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Background and Aims: NASH, recently renamed as Metabolic Dysfunction-Associated Steatohepatitis (MASH), is highly prevalent liver disease and associated with adverse clinical outcomes and impaired HRQL. Resmetirom is a selective thyroid hormone receptor-β agonist that leads to improvement of fibrosis and resolution of NASH. The aim was to assess HRQL in NASH patients treated with resmetirom.

Method: Non-cirrhotic NASH patients with confirmed or suspected fibrosis were enrolled in a 52-week double-blind randomized placebo-controlled Phase 3 clinical trial with serial biopsy assessments (MAESTRO-NASH, NCT03900429). HRQL was assessed using Chronic Liver Disease Questionnaire-NASH (CLDQ-NASH; 6 domains and score range 1-7) and Liver Disease Quality of Life (LDQOL; 17 domains and score range 0-100) at baseline, week 24, and week 52. Changes in HRQL scores from subjects’ own baseline scores were evaluated in patients receiving resmetirom vs. placebo and compared between subjects with vs. without biopsy response defined as meeting the study histologic endpoint (improvement of histologic fibrosis without worsening of NASH or resolution of NASH without worsening of fibrosis via in-window baseline/week 52 paired biopsies). Minimally clinically important Difference (MCID) in HRQL scores were defined as previously published.

Results: 966 mITT patients were included (57±11 years, 44% male, 67% type 2 diabetes; 60% baseline fibrosis stage F3, 33% F2, 5% F1b, 84% NAS ≥5). Of those, 323 received resmetirom 100 mg, 322 resmetirom 80 mg, and 321 placebo. By weeks 24 and 52, patients receiving both doses of resmetirom experienced improvement of HRQL scores from baseline levels in Worry domain of CLDQ-NASH (mean +0.21 to +0.24, p<0.05). At week 52, subjects who met the histologic endpoint after treatment with resmetirom (100 mg and 80 mg pooled) experienced improvement in several HRQL domains: Worry (WO) of CLDQ-NASH +0.46 (41% met MCID), Role Emotional (RE) of LDQOL +3.0 (28% met MCID), Health Distress (HD) of LDQOL +8.1 (38% MCID), Stigma (ST) of LDQOL +3.5 (39% MCID), and total LDQOL +2.2 (35% MCID) (all p<0.05). Similar improvements in these HRQL domains were observed in biopsy responders from 100 mg and 80 mg resmetirom when groups were studied separately, contrasted by no improvements in both the placebo group and resmetirom biopsy non-responders. In other domains of LDQOL and CLDQ-NASH, MCID was met by 22-41% of resmetirom responders. Biopsy responders with baseline F3 had similar or more pronounced improvements of HRQL (WO +0.57 in F3 vs. +0.32 in F1b/F2, RE +3.6 vs. +1.7, HD +8.8 vs. +7.6, ST +2.9 vs. +5.2, total LDQOL +2.3 vs. +2.5) in comparison to those responders with baseline stage of F2 or F1b.

Conclusion: Patients with NASH who achieve improvement of fibrosis or resolution of NASH with resmetirom experience significant improvements in multiple domains of HRQL by the end of 52-week-long treatment.