Health-Related Quality of Life Assessments in a 52-Week, Double-Blind, Randomized, Placebo-Controlled Phase 3 Study of Resmetirom (MGL-3196) in Patients with NASH and Fibrosis (MAESTRO-NASH)

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BACKGROUND

- Nonalcoholic steatohepatitis (NASH), recently renamed as Metabolic Dysfunction-Associated Steatohepatitis (MASH), is highly prevalent liver disease and associated with adverse clinical outcomes and impaired health-related quality of life HRQL.
- Resmetirom is a selective thyroid hormone receptor-β agonist that leads to improvement of fibrosis and resolution of NASH.

AIM

- The aim was to assess HRQL in NASH patients treated with resmetirom.

METHODS

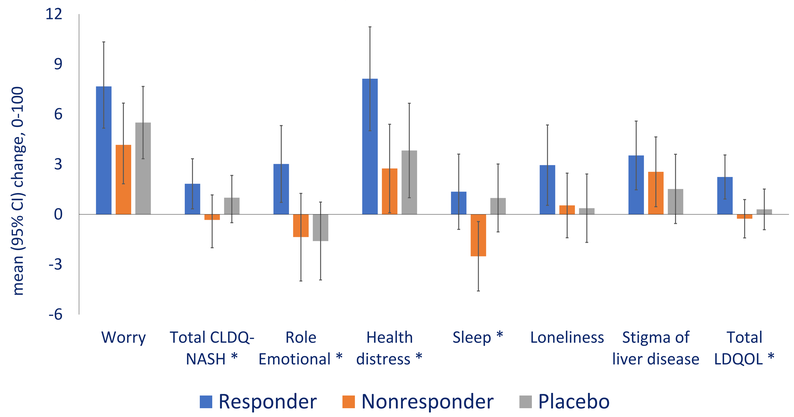
- Non-cirrhotic NASH patients with confirmed or suspected fibrosis were enrolled in a 52-week double-blind randomized placebo-controlled Phase 3 clinical trial with serial biopsy assessments (MAESTRO-NASH, NCT03900429).
- The HRQL was assessed using Chronic Liver Disease Questionnaire-NASH (CLDQ-NASH; 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 histologic response.
- Histologic response was defined as meeting the study histologic endpoint: improvement of histologic fibrosis without worsening of NASH (fibrosis improvement, or FI) or resolution of NASH without worsening of fibrosis (NASH resolution, or NR) 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; 62% 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.
- The full description of the study sample, inclusion/exclusion criteria, safety and efficacy endpoints for MAESTRO-NASH have been published [Harrison et al., N Engl J Med. 2024 Feb 8;390(6):497-509].

RESULTS

Figure 1. Changes in HRQL Scores in Subjects with vs. without Histologic Response (FI or NR) to Treatment with Resmetirom



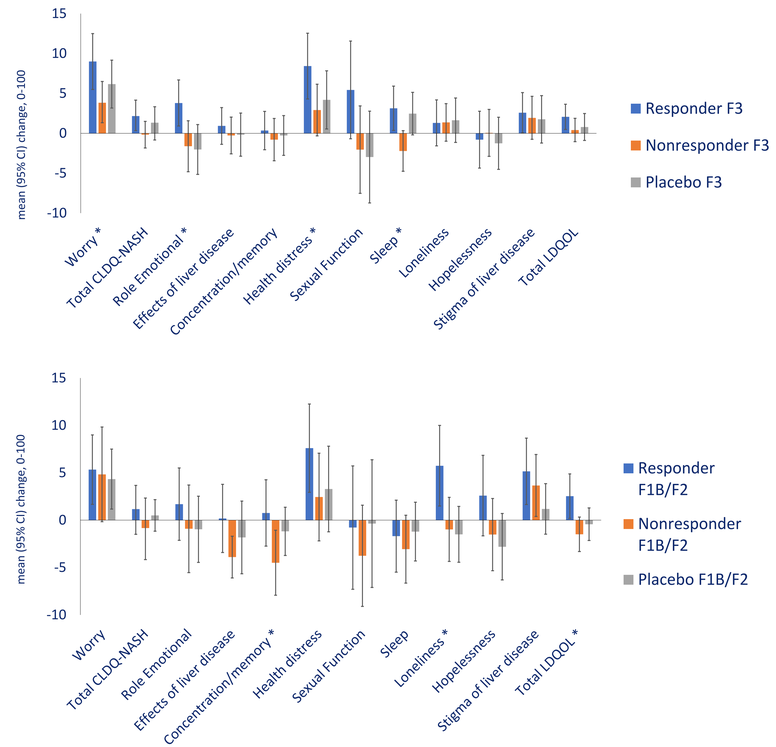
*p<0.05 for comparison of responders to nonresponders;
mean HRQL score change from baseline to week 52 (within-treatment comparison), renormalized from the original scale to 0-100 where applicable, is shown with 95% CI;
only statistically significant changes from baseline to Week 52 (p<0.05 in comparison to zero which would indicate a significant change, or to nonresponders, or to placebo) are shown.

- By treatment week 24, whether or not the patient was a responder on either primary biopsy endpoint, subjects receiving either dose of resmetirom experienced generally similar changes in HRQL scores from baseline levels compared to placebo: all but one parameter, p>0.05
- At week 52, subjects who met the histologic endpoint (Fi or NR) after treatment with resmetirom (100 mg and 80 mg pooled) experienced improvement in several HRQL domains (p<0.05) (**Figure 1**):
  - 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).
- The improvement in HRQL among resmetirom histologic responders with FI or NR was contrasted by no similar improvement in both the placebo group and resmetirom biopsy nonresponders (**Figure 1**).
- Similar improvements in select HRQL domains were observed in histologic responders (FI or NR) from 100 mg and 80 mg resmetirom when groups were studied separately.
- In other domains of LDQOL and CLDQ-NASH, MCID was met by 22-41% of resmetirom responders.

RESULTS

- Histologic responders (FI or NR) with baseline F3 had similar or more pronounced improvements of HRQL (mean WO +0.54 in F3 vs. +0.32 in F1B/F2, RE +3.8 vs. +1.7, HD +8.4 vs. +7.6, ST +2.6 vs. +5.2, total LDQOL +2.1 vs. +2.5) in comparison to those responders with baseline stage F1B/F2 (**Figure 2**).

Figure 2. Changes in HRQL Scores in (A) F3 and (B) F1B/F2 with vs. without Histologic Response (FI or NR) to Resmetirom



*p<0.05 for comparison of responders vs. nonresponders to resmetirom (pooled 100 mg and 80 mg), in F3 and F1B/F2 separately;
mean HRQL score change from baseline to week 52 (within-treatment comparison), renormalized from the original scale to 0-100 where applicable, is shown with 95% CI;
only HRQL scores with statistically significant changes from baseline to Week 52 (p<0.05 in comparison to zero which would indicate a significant change, or to nonresponders, or to placebo) in either F3 or F1B/F2 group are shown.

CONCLUSIONS

- 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.

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