Improvement In Health-Related Quality of Life After Treatment with Resmetirom in Patients with Cirrhotic and Non-Cirrhotic MASLD: Data from MAESTRO-NAFLD-1

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Background

- MASLD and MASH significantly impair HRQL, particularly in domains of physical functioning, fatigue, and emotional well-being.
- Patients with cirrhosis typically report the lowest HRQL scores, reflecting high symptom burden and stigma.
- Resmetirom, a thyroid hormone receptor-β agonist, is approved for treatment of F2-F3 MASH in the U.S. and Europe.
- Resmetirom improves liver histology and metabolic parameters.
- Less is known about its impact on HRQL.

Aim

To assess HRQL in patients with MASLD with and without cirrhosis treated with resmetirom in MAESTRO-NAFLD clinical trial.

Methods

- Patients with MASLD cirrhosis (CP-A) or MASLD without cirrhosis (early MASH) were enrolled in a 52-week, Phase 3 double-blind placebo-controlled study of resmetirom (MAESTRO-NAFLD).

Early MASH

VCTE 5.5 to <8.5 kPa or MRE 2.0 to <4.0 kPa

- Double-blind
  - Resmetirom 100 mg
  - Resmetirom 80 mg
  - Placebo
- Open-label – Resmetirom 100 mg

Compensated cirrhosis

(CP-A: well-compensated MASH cirrhosis by biopsy or clinical; no history of decompensation)

- Open-label – Resmetirom 80 mg

Randomization stratified by T2D and ASCVD

MAESTRO-NAFLD Phase 3 clinical trial registered as #NCT04197479
The study results published in : Harrison et al. Nat Med. 2023 Nov;29(11):2919-2928.

Methods

- The HRQL was assessed using LDQOL (17 domains) and CLDQ-NAFLD (6 domains) instruments *(higher scores = better HRQL, positive change = improvement)*.
- For early MASH, the PDFF response was defined as a decrease in MRI-PDFF ≥30% from baseline.
- For MASH cirrhosis, PDFF response was defined as ≥20% decrease in MRI-PDFF (if baseline MRI-PDFF >5%).
- For comparison, we also included similarly collected and previously published HRQL data from patients with biopsy-proven MASH F2-F3 (MAESTRO-NASH study)

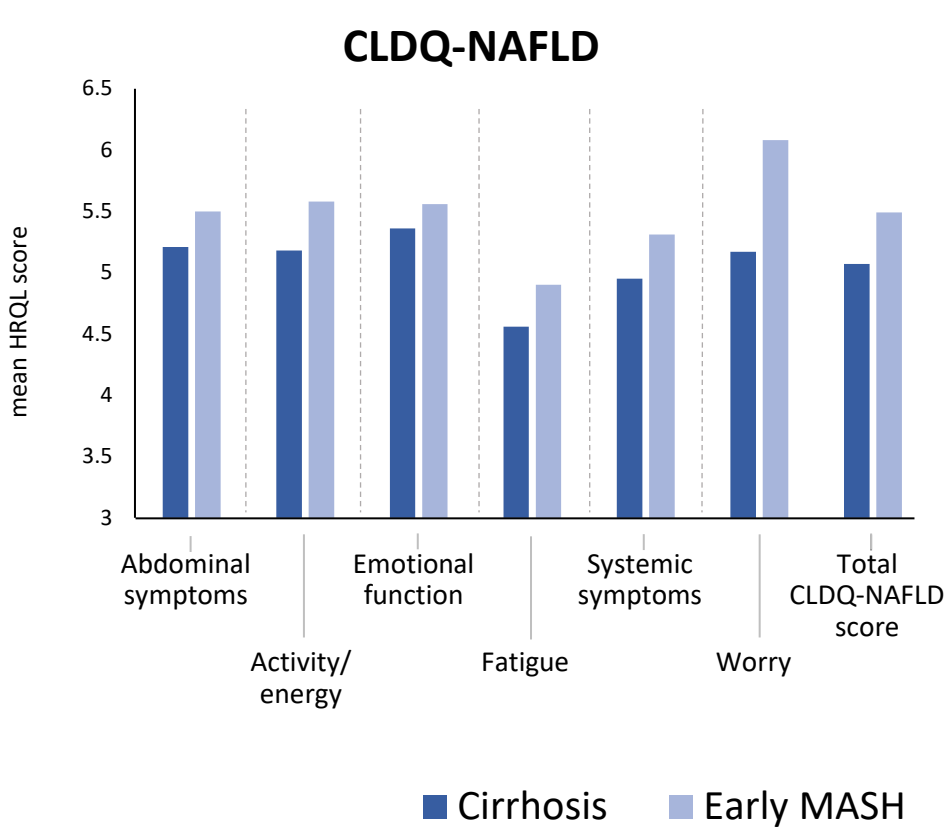
Younossi ZM et al, Hepatology. 2025 Apr 1;81(4):1318-1327.

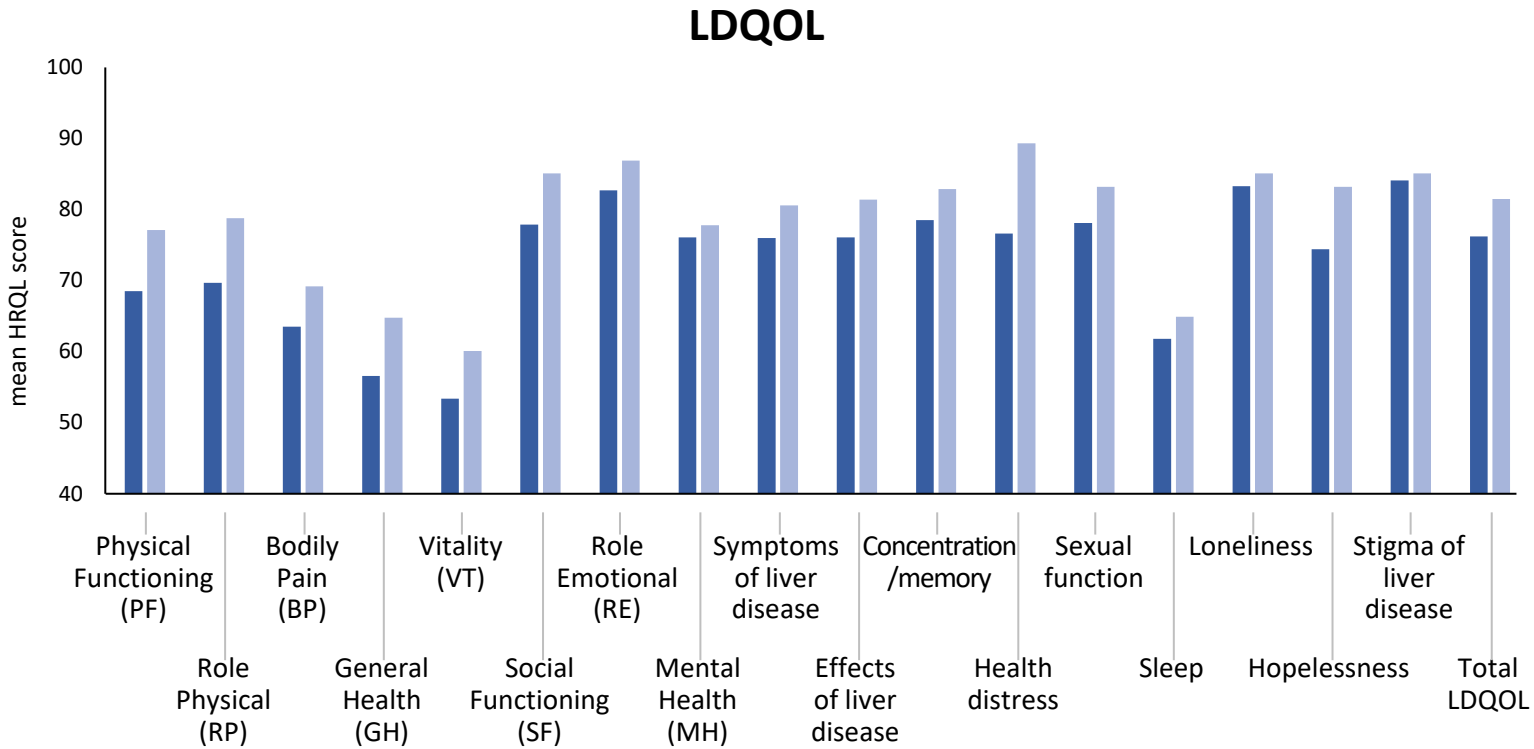
Results

- **1143 early MASH patients:**
  - Double-blind resmetirom 100 mg: 325
  - Double-blind resmetirom 80 mg: 327
  - Double-blind placebo: 320
  - Open-label resmetirom 100 mg: 171
  - Age: 56±12 years
  - Male: 43%
  - Type 2 diabetes: 53%
  - MRI-PDFF: 18±7%
  - MRI-PDFF ≥8%: 100%
- **180 MASH cirrhosis patients:**
  - Age: 61±9 years
  - Male: 38%
  - Type 2 diabetes: 73%
  - MRI-PDFF: 9±6%
  - MRI-PDFF >5%: 75%
  - Open-label resmetirom 80 mg: 180

Results

- In MAESTRO-NAFLD, baseline HRQL scores of patients with MASH cirrhosis were significantly **lower** than those of patients with early MASH.

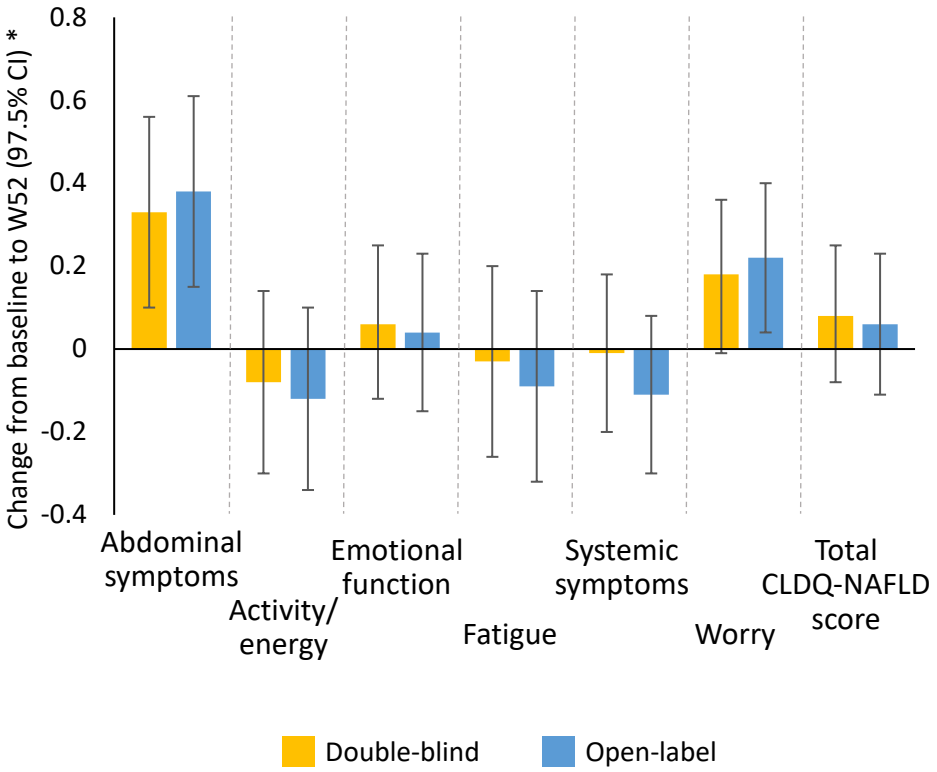




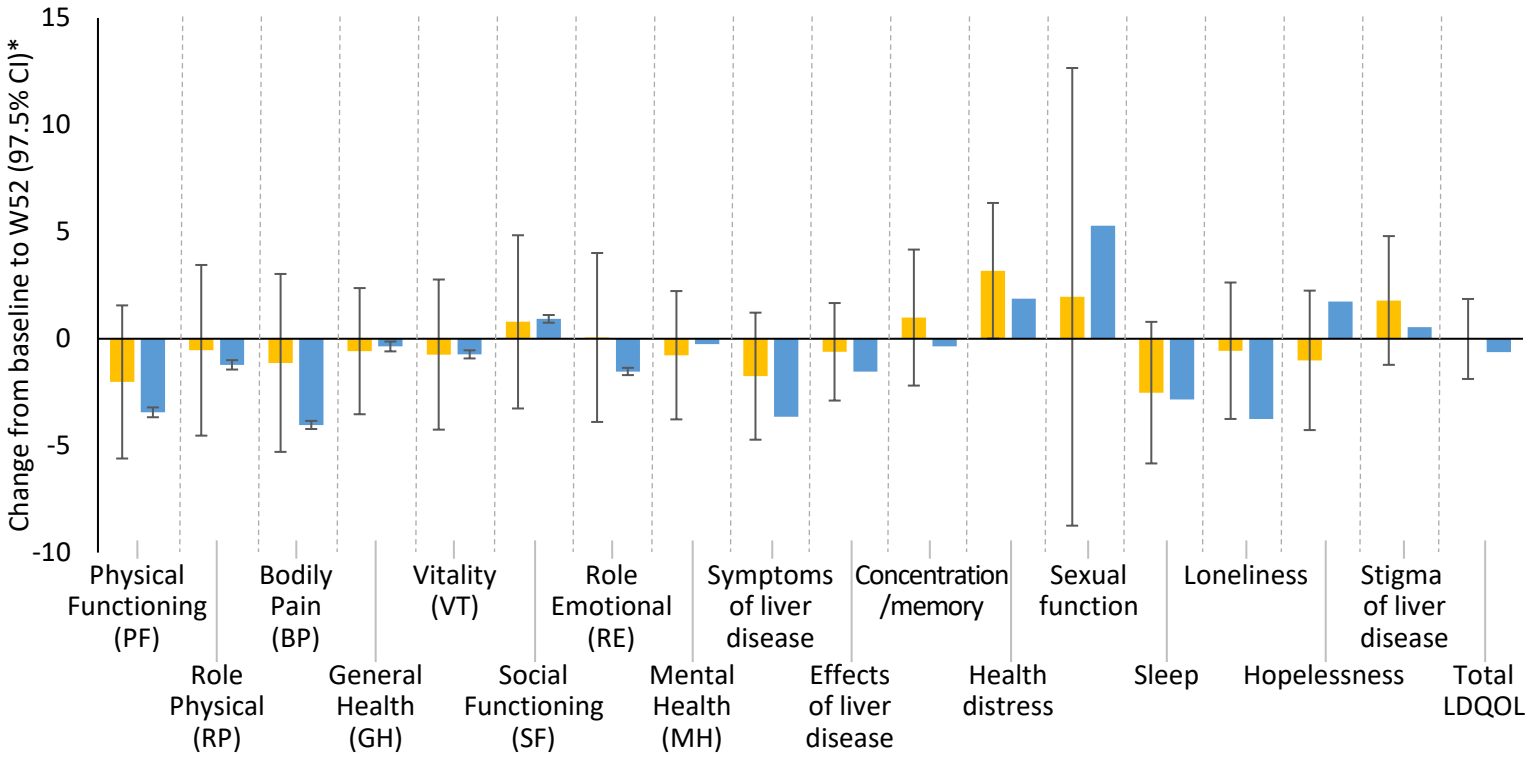
Results

- In early MASH, the HRQL changes from baseline to week 24 or week 52 of double-blind treatment with 100 mg resmetirom were not different from open-label (all DB vs. OL p>0.05).
- Therefore, for all further analyses, the double-blind 100 mg and open-label 100 mg groups were pooled.

CLDQ-NAFLD



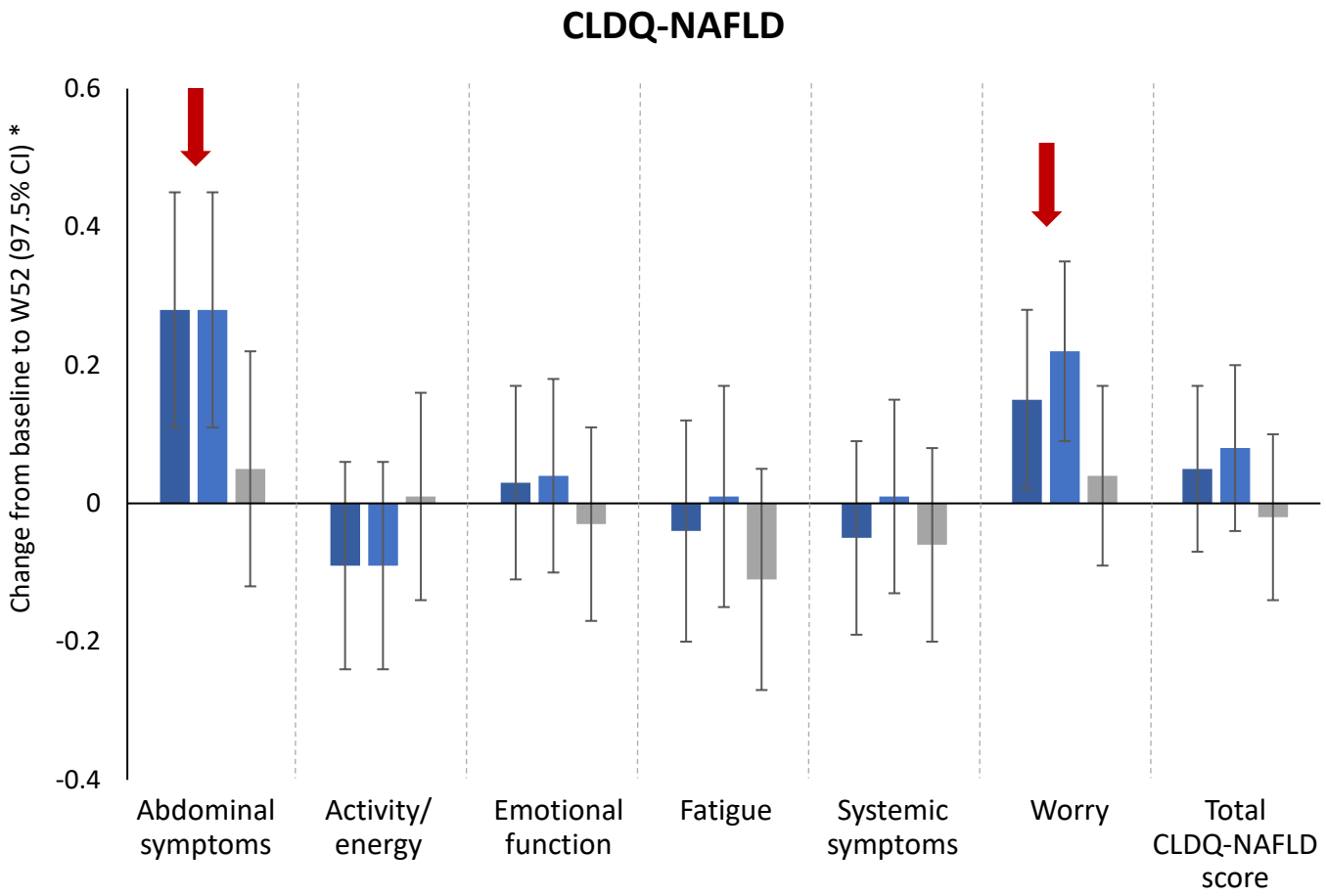
LDQOL

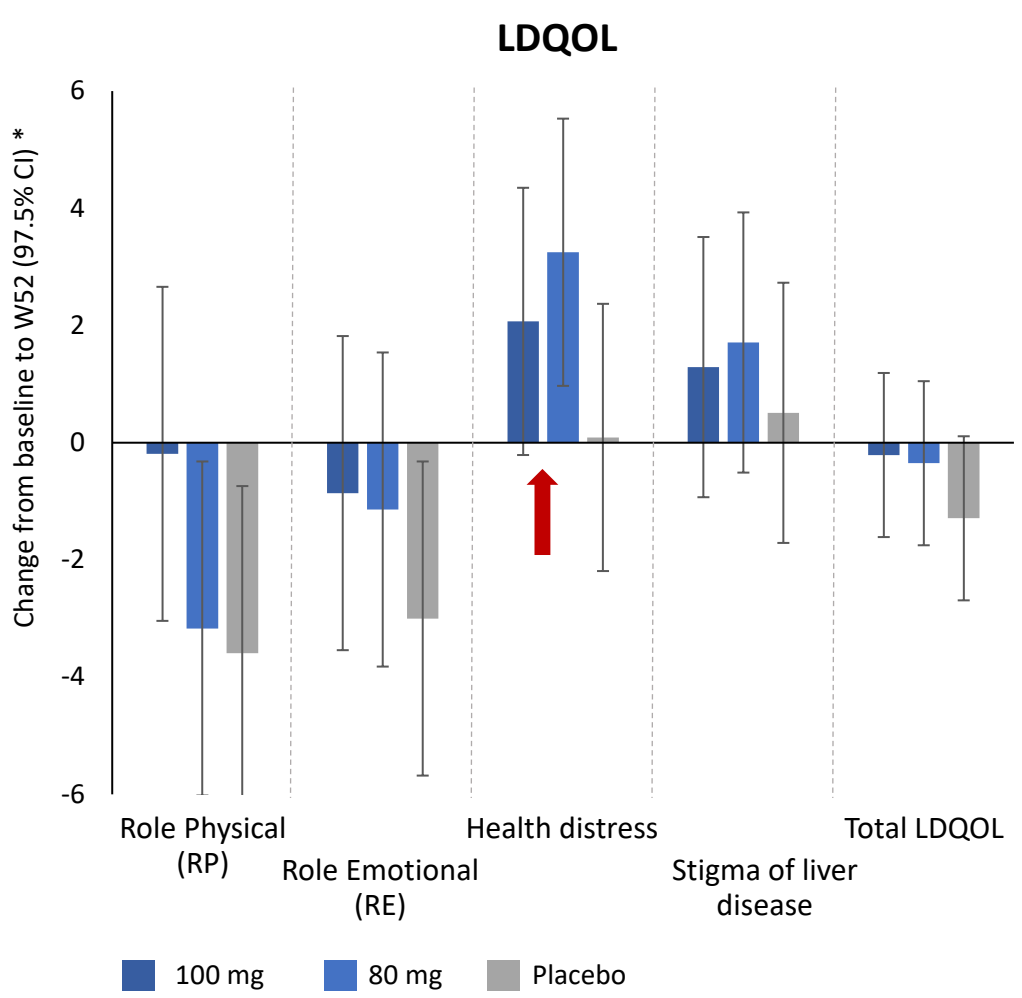


** LSM with 97.5% CI returned by MMRM adjusted for baseline values and stratification factors (T2D and ASCVD)*

Results

- In early MASH, resmetirom compared with placebo significantly **improved** Abdominal symptoms, Worry, and Health distress scores, and attenuated declines in physical and emotional role functioning.

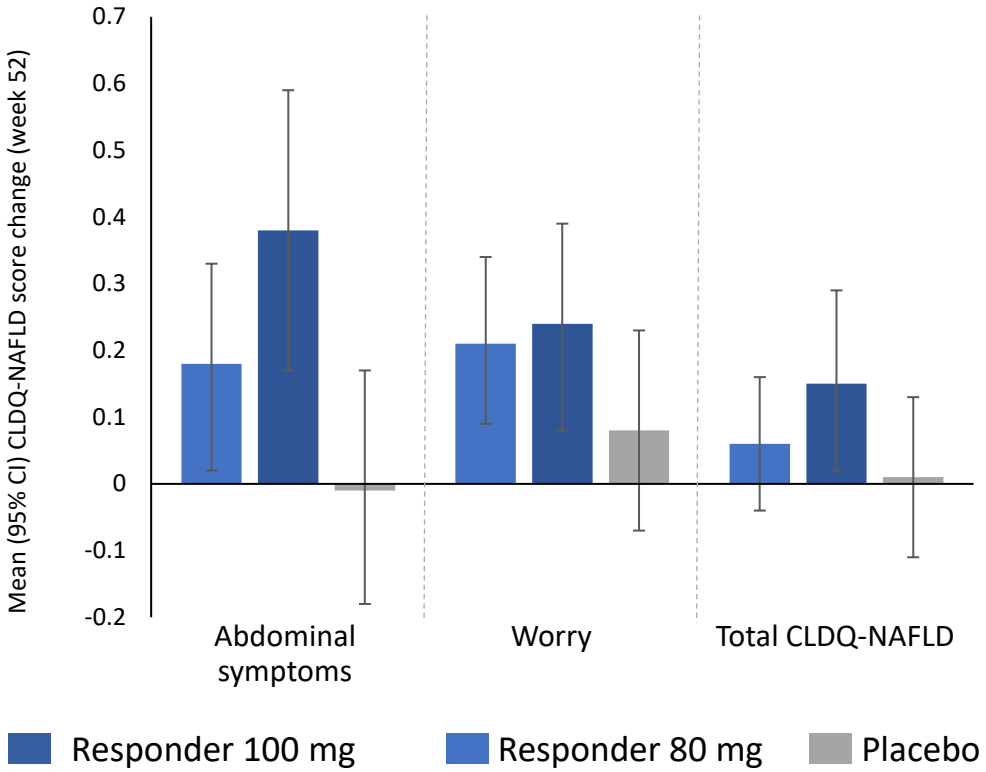


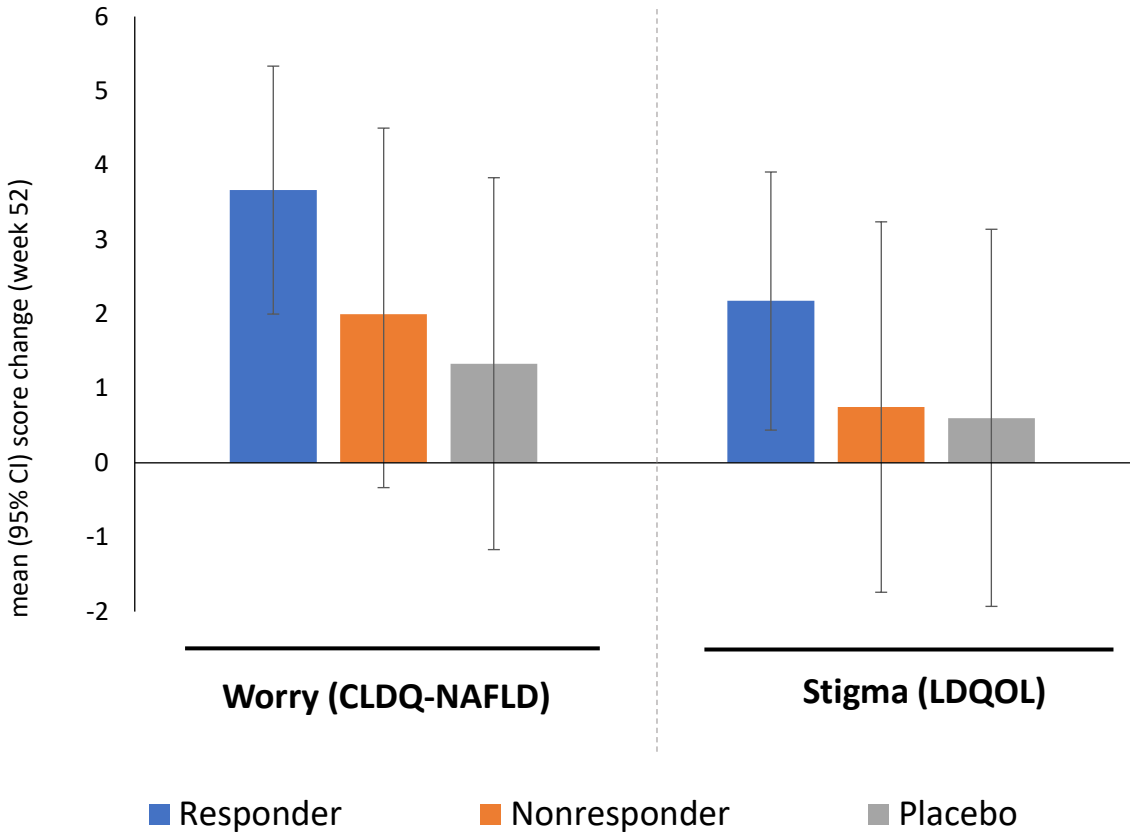


** LSM with 97.5% CI returned by MMRM adjusted for baseline values and stratification factors (T2D and ASCVD)*

Results

- Patients with Early MASH who achieved ≥30% reduction in MRI-PDFF (from baseline by week 52) had greater improvements in select HRQL scores (Worry or Abdominal Symptoms of CLDQ-NAFLD, Stigma from Liver Disease of LDQOL) in comparison to placebo or to nonresponders.

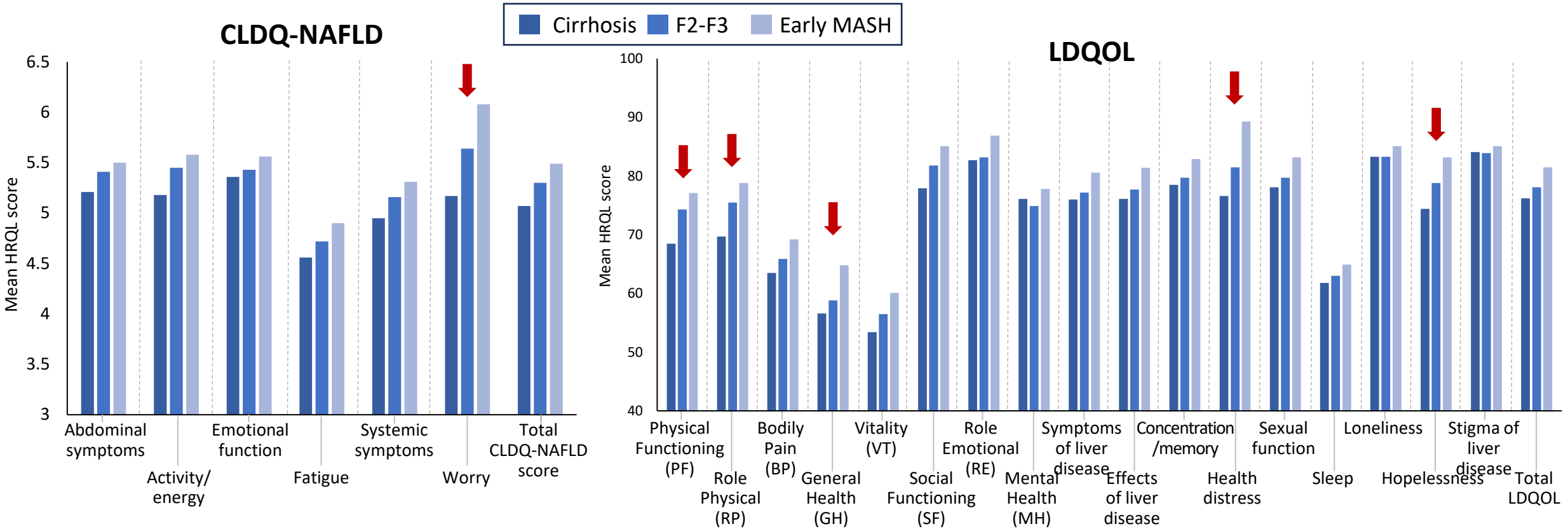




Response to resmetirom (pooled 80 mg and 100 mg)

Results

- Across the spectrum of MASH, HRQL scores of patients with **cirrhosis** were lower than those of patients with **early MASH** as well as patients with biopsy proven **F2-F3 MASH** *(MAESTRO-NASH study, historic data *)*.
- The most significant impairments were noted in the Worry, Health distress, Role Physical, Hopelessness, Physical Functioning, General Health.

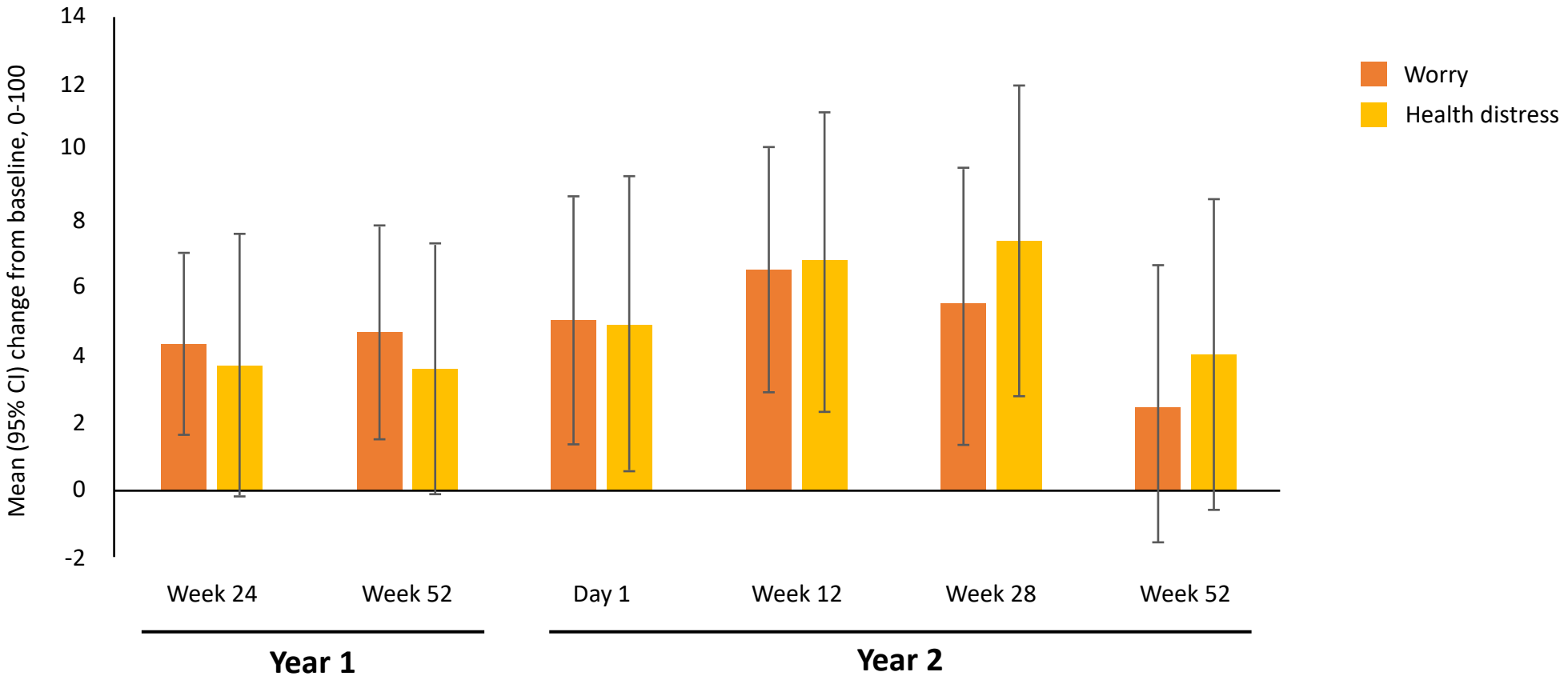


- There was no difference in baseline HRQL between patients with cirrhosis with MRI-PDFF ≤5% vs. >5% (all p>0.05).

** Younossi et al., Hepatology 2025 (PMID 39250515)*

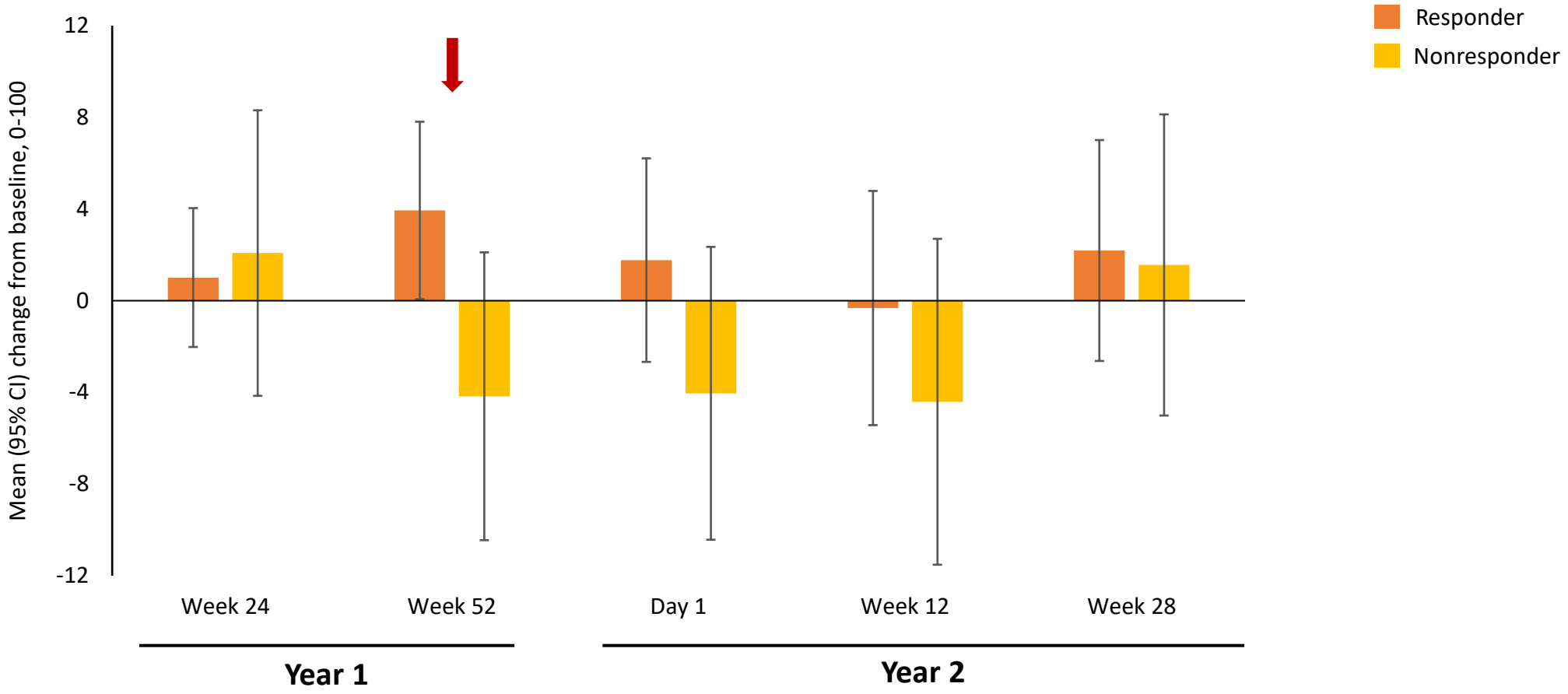
Results

- In patients with MASH cirrhosis, by week 24 of treatment with resmetirom, Worry (CLDQ-NAFLD) and Health Distress (LDQOL) improved.
- The improvements were sustained by week 52 and throughout Year 2 (day 1, week 12, week 28) ($p<0.05$).



Results

In patient with MASH cirrhosis with a PDFF response (week 52), there was improvement in Stigma score ($p<0.05$).



Conclusions

- At baseline, HRQL scores of patients with MASH cirrhosis were worse than patients with Early MASH.
- Resmetirom improved select HRQL scores in patients with both cirrhotic MASH and early MASH, with sustained benefits during long-term treatment.
- The HRQL gains were most pronounced in disease-specific domains (Worry, Abdominal symptoms, Stigma, Health distress).
- Placebo-treated patients with early MASH showed some HRQL decline, underscoring the protective effect of resmetirom.
- Although HRQL scores worsens with more advanced fibrosis (F2 and F3 as well as cirrhosis) in MASH, resmetirom improves some aspects of HRQL across the spectrum of disease severity.
- Resmetirom addresses not only biological endpoints but also patient-reported outcomes (HRQL), supporting its role in comprehensive MASLD care.