Association between improvement in machine learning-assessed steatosis area and magnetic resonance imaging-proton density fat fraction in patients with compensated non-alcoholic steatohepatitis cirrhosis

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Steatosis reduction assessed by MRI-PDFF was consistent with ML evaluation in patients with NASH cirrhosis

Background and Aims

- Liver biopsies evaluated by hepatopathologists are a key method for assessing treatment response in trials of non-alcoholic steatohepatitis (NASH).[1,2]
  - Artificial intelligence has shown promise in supporting liver biopsy assessment.[2]
- Magnetic resonance imaging-proton density fat fraction (MRI-PDFF) is a non-invasive imaging technique that can assess total liver fat content.[3,4]
- This post hoc analysis aimed to compare steatosis assessment by histologic evaluation (pathologist or PathAI's machine learning [ML] models) and by MRI-PDFF.
  - The analysis used data from a randomized, double-blind, placebo-controlled phase 2 trial investigating once-weekly subcutaneous semaglutide 2.4 mg in patients with NASH and compensated cirrhosis.

Methods

- Liver biopsies obtained at baseline and week 48 were assessed by a single pathologist and subsequently digitized for ML evaluation.
- Agreement between baseline pathologist and ML steatosis grade was measured and the percentages of patients with improvement at week 48 were compared. Baseline and changes from baseline at week 48 in ML steatosis proportionate area were also measured and correlated with MRI-PDFF assessment.

Results

Patient characteristics

- Of 71 patients enrolled in the trial, 70 patients had available ML results for analysis.
- In enrolled patients, mean (standard deviation) age and body mass index were 59.5 (8.0) years and 34.9 (5.9) kg/m^2, respectively, and 75% of patients had type 2 diabetes.
- Geometric mean (coefficient of variation) for baseline steatosis measured using MRI-PDFF was 10% (57).

Weight loss at week 48

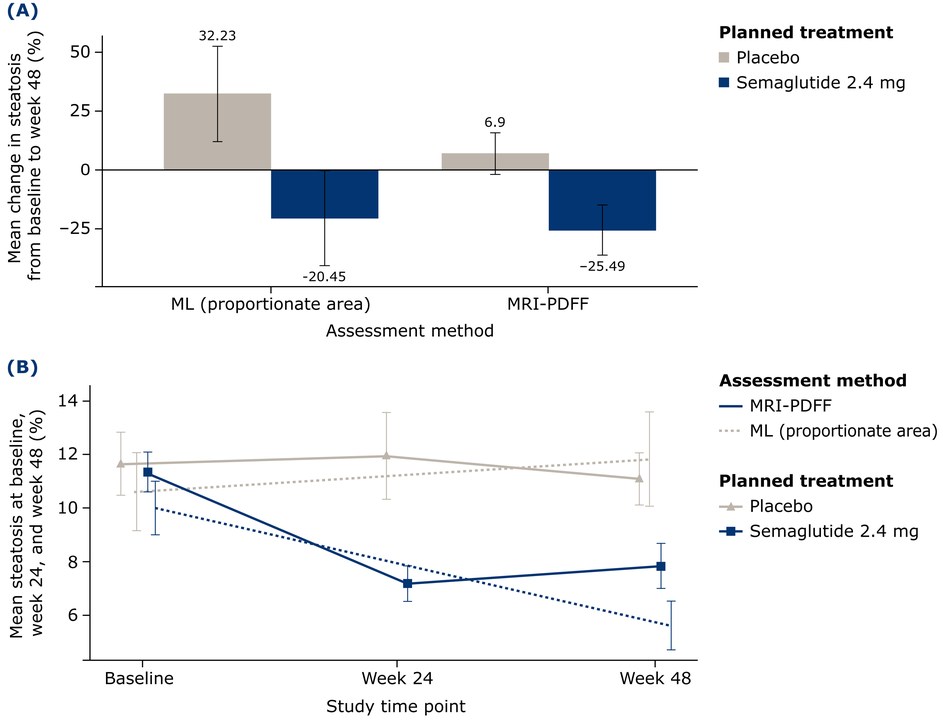
- At week 48, semaglutide led to a mean change in body weight of −8.83% vs −0.09% for placebo (p<0.0001).

Comparison between pathologist and ML assessment of steatosis

- Baseline steatosis by pathologist assessment was grade 1 in 66% of patients, grade 2 in 27% of patients, and grade 3 in 7% of patients.
  - ML assigned the same baseline steatosis grade as the pathologist in 68% of samples (Kappa = 0.48).
- The percentage of patients with an improvement in steatosis grade at week 48 was greater for semaglutide vs placebo by both methods:
  - 45% vs 33% by pathologist assessment
  - 33% vs 4% by ML assessment.

Figure 1: Steatosis measured by ML (proportionate area) and MRI-PDFF by treatment arm for (A) change from baseline to week 48, (B) baseline, week 24, and week 48

Key result



Plot shows mean ± standard error of the mean. Biopsies were not performed at week 24.
ML, machine learning; MRI-PDFF, magnetic resonance imaging-proton density fat fraction.

Comparison between ML and MRI-PDFF assessment of steatosis

- At baseline, there was a moderate positive correlation between ML steatosis proportionate area and MRI-PDFF assessment (Pearson R = 0.49; p<0.001).
- For change from baseline at week 48 in steatosis, ML steatosis proportionate area and MRI-PDFF assessment both showed a treatment benefit for semaglutide vs placebo (**Figure 1A**).
  - This treatment benefit was evident with MRI-PDFF by week 24 (**Figure 1B**)
  - There was a moderate positive correlation for change from baseline at week 48 between ML steatosis proportionate area and MRI-PDFF assessment (Pearson R = 0.48; p<0.001).

Conclusion

- In patients with compensated NASH cirrhosis, once-weekly subcutaneous semaglutide 2.4 mg reduced liver steatosis relative to placebo across pathologist and ML assessment.
- Steatosis reduction assessed by MRI-PDFF was consistent with ML steatosis proportionate area evaluation; MRI-PDFF detected a meaningful change in steatosis at week 24.

References:
(**1**) Gawrieh S et al. Ann Diagn Pathol 2011:15;19–24;
(**2**) Taylor-Weiner A et al. Hepatology 2021:74;133–47;
(**3**) Loomba R et al. Hepatology 2020:72;1219–29;
(**4**) Noureddin M et al. Hepatology 2013:58;1930–40

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