

Comparison of the effects of semaglutide on liver histology in patients with non-alcoholic steatohepatitis cirrhosis between machine learning model assessment and pathologist evaluation

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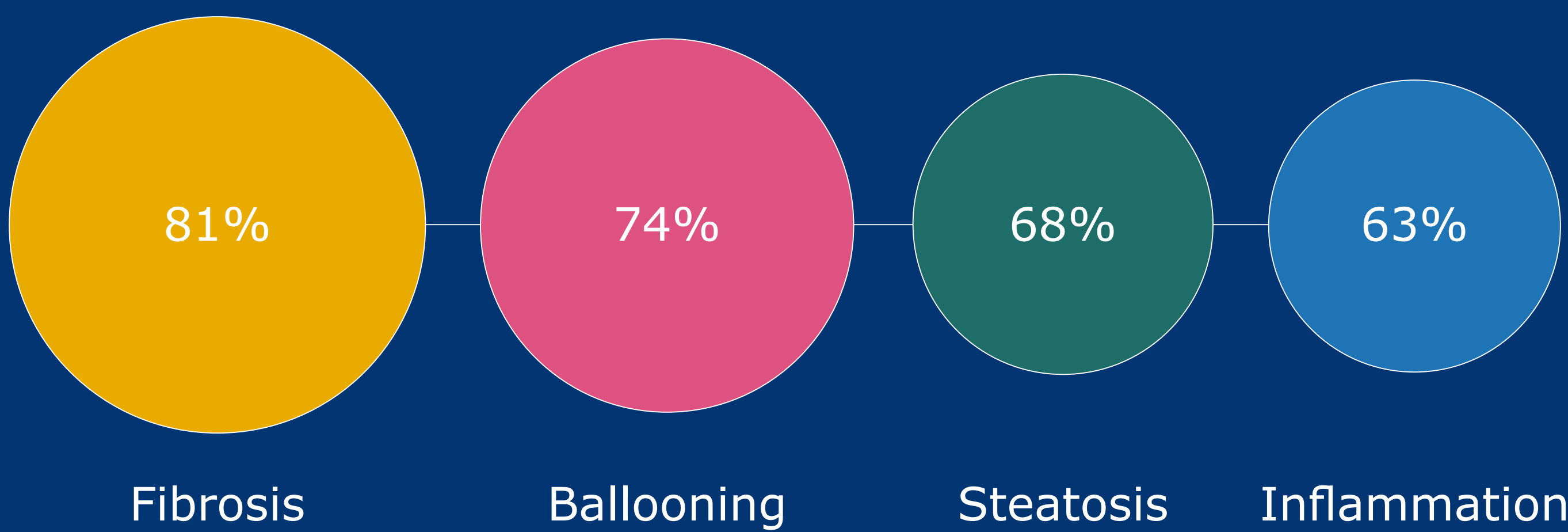
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In patients with NASH cirrhosis, evaluation of liver histology was generally consistent between pathologist and machine learning assessment

Alignment between pathologist and ML assessment for baseline categorical histology



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 also shown promise in liver biopsy assessment.²
- Identification and assessment of NASH components can be subject to inter- and intra-observer variability, especially for hepatocyte ballooning.³
- This post hoc analysis aimed to assess the effect of semaglutide vs placebo on histological components of NASH as assessed by a pathologist and PathAI's machine learning (ML) models.
 - 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.

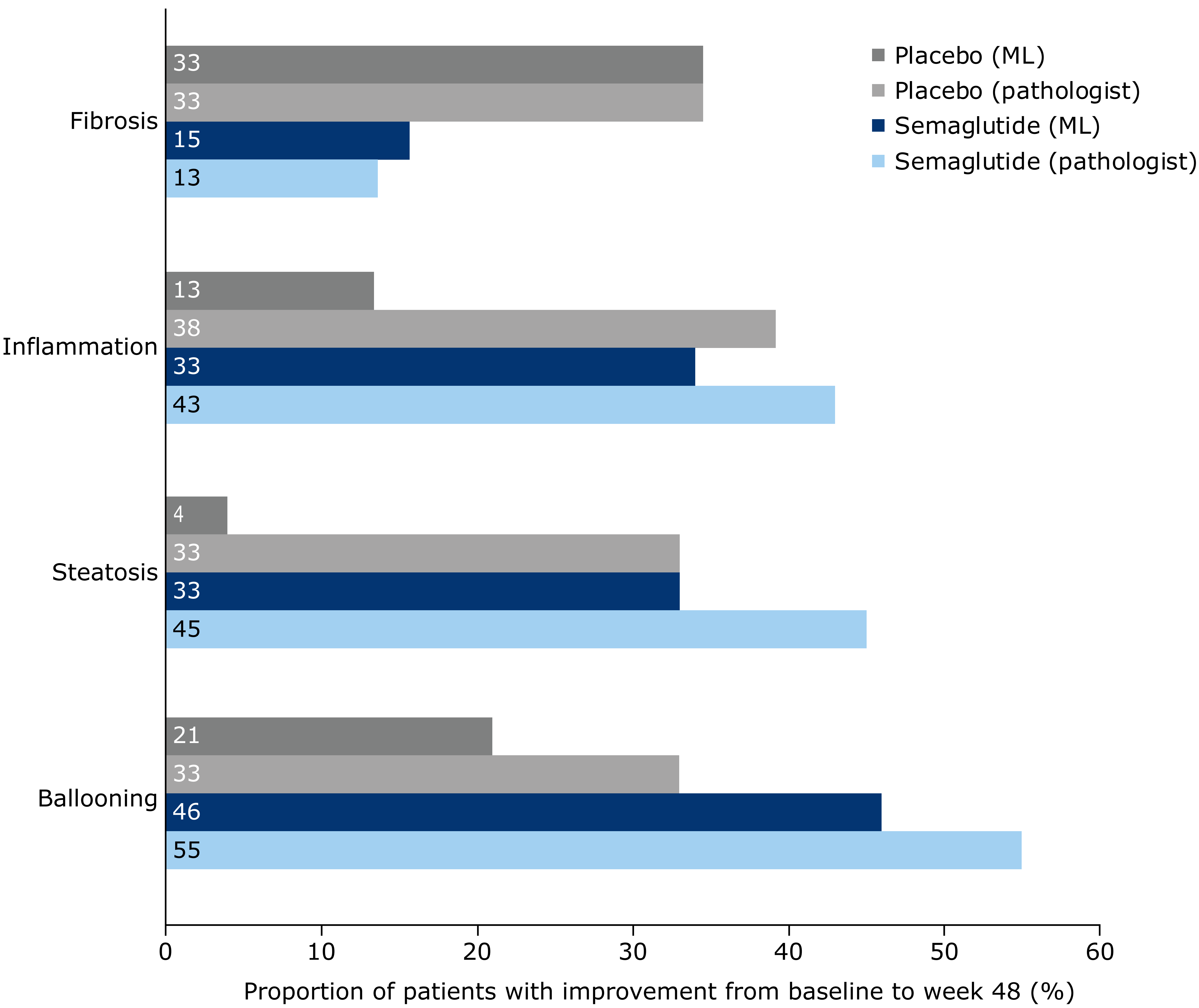
Methods

- Liver biopsies obtained at baseline and week 48 were assessed by a pathologist and subsequently digitized for ML evaluation.
- Evaluations included changes in categorical (pathologist and ML) and continuous (ML only) scores for fibrosis, hepatocyte ballooning, lobular inflammation, and steatosis.

Results

- Of the 71 patients enrolled in the trial, 70 had baseline ML results available for this analysis.
- In enrolled patients, mean (standard deviation) age and body mass index were 59.5 (8.0) years and 34.9 (5.9) kg/m², respectively, and 75% of patients had type 2 diabetes.
- For categorical baseline histology, alignment between pathologist and ML assessment was greatest for fibrosis (81%), followed by ballooning (74%), steatosis (68%), then inflammation (63%).
 - Stage 4 fibrosis assessed by a pathologist was a trial inclusion criterion; 13 patients had stage 3 fibrosis by ML assessment.
- For categorical changes in histology from baseline at week 48, a numerically higher proportion of patients with improvement was seen across both assessment methods for semaglutide vs placebo for inflammation, steatosis, and ballooning, but not fibrosis (**Figure 1**).
- For continuous ML scores, there was a significant estimated treatment difference (ETD) between the semaglutide and placebo groups for steatosis (ETD = -0.50 [95% confidence interval (CI) -0.84, -0.15]; p=0.0047) and ballooning (ETD = -0.51 [95% CI -0.90, -0.11]; p=0.0120).
 - There was no significant difference for fibrosis (ETD = 0.00 [95% CI -0.24, 0.24]; p=0.9884) or inflammation (ETD = -0.22 [95% CI -0.48, 0.04]; p=0.1030).

Figure 1: Proportion of patients with improvement in histological component (categorical) from baseline to week 48 for both evaluation methods



ML, machine learning.

Key result

- Alignment between categorical pathologist and ML assessment for the proportion of patients with improvements in histology at week 48 was 81% for ballooning, 73% for fibrosis, 54% for steatosis, and 51% for inflammation.

Conclusion

- In patients with compensated NASH cirrhosis, the effects of once-weekly subcutaneous semaglutide 2.4 mg vs placebo were generally consistent across pathologist and ML evaluation.
- Consistent with a phase 2 trial in patients with fibrosis stage 1–3 (NCT02970942),⁴ histological improvement was greater for semaglutide vs placebo in the present cohort with cirrhosis.
- A lower placebo response was observed for ML compared with pathologist assessment for categorical inflammation, steatosis, and ballooning.
 - This gives confidence that ML-detected changes in histology in patients treated with semaglutide were treatment-induced, as ML assessment is reproducible.
- ML continuous scoring of histology enabled granular evaluation of treatment-induced histologic change and delivered insights beyond categorical scoring.

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Disclosures:

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