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# Synopsis of the original article ***Phase 3 Trial of Semaglutide in Metabolic Dysfunction-Associated Steatohepatitis***

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Synopsis created and reviewed by Novo Nordisk

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# Introduction



Semaglutide, a glucagon-like peptide-1 receptor agonist,
is a candidate for the treatment of metabolic dysfunction-associated steatohepatitis (MASH)

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# Methods

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In this ongoing phase 3, multicenter, randomized, double-blind, placebo-controlled trial, we assigned 1197 patients with biopsy-defined MASH and fibrosis stage 2 or 3 in a 2:1 ratio to receive once-weekly subcutaneous semaglutide at a dose of 2.4 mg or placebo for 240 weeks



The results of a planned interim analysis conducted at week 72 involving the first 800 randomized patients are reported (part 1). The primary end points for part 1 were the resolution of steatohepatitis without worsening of liver fibrosis and improvement in liver fibrosis without worsening of steatohepatitis.

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*MASH, metabolic dysfunction-associated steatohepatitis.*

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# Results

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**Resolution of steatohepatitis without worsening of fibrosis** occurred in **62.9%** of the 534 patients in the **semaglutide** group and in **34.3%** of the 266 patients in the **placebo** group

(Estimated difference, 28.7 percentage points; 95% CI, 21.1 to 36.2; P<0.001)

**Improvement in liver fibrosis without worsening of steatohepatitis** was reported in **36.8%** of the patients in the **semaglutide** group and in **22.4%** of those in the **placebo** group

(Estimated difference, 14.4 percentage points; 95% CI, 7.5 to 21.3; P<0.001)

Results for the three secondary outcomes that were included in the plan to adjust for multiple testing were:

**Combined resolution of steatohepatitis and improvement** in liver fibrosis was reported in **32.7%** of the patients in the **semaglutide** group and in **16.1%** of those in the **placebo** group (difference, 16.5 percentage points; 95% CI, 10.2 to 22.8; P<0.001)

Mean **change in body weight** was **−10.5%** with **semaglutide** and **−2.0%** with **placebo** (difference, −8.5 percentage points; 95% CI, −9.6 to −7.4; P<0.001)

Mean changes in bodily pain scores did not differ significantly between the two groups

Gastrointestinal adverse events were more common in the semaglutide group

*CI, confidence interval.*

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# Conclusions



In patients with MASH and moderate or advanced liver fibrosis, once-weekly semaglutide at a dose of 2.4 mg improved liver histologic results

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