Synopsis of the original article ‘Effect of Semaglutide on Liver Enzymes and Markers of Inflammation in Subjects with Type 2 Diabetes and/or Obesity’


Synopsis created and reviewed by Novo Nordisk
Introduction

Glucagon-like peptide-1 analogues may offer potential for NAFLD treatment
Methods

To evaluate the effect of the glucagon-like peptide-1 analogue, semaglutide, on alanine aminotransferase (ALT) and high-sensitivity C-reactive protein (hsCRP) in subjects at risk of NAFLD.

Data from two trials were analysed:

- **Cardiovascular outcomes in type 2 diabetes trial**
  - Semaglutide 0.5 or 1.0 mg/week
    - 0 weeks of treatment
    - 104 weeks of treatment
    - 104

- **Weight management trial**
  - Semaglutide 0.05-0.4 mg/day
    - 0 weeks of treatment
    - 52 weeks of treatment
    - 52

**Analysis:**

Treatment ratios vs placebo were estimated for ALT (both trials) and hsCRP (weight management trial only).

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*phase 3, randomised, double-blind, multinational, placebo-controlled trial of semaglutide given for the treatment of type 2 diabetes.
†phase 2, randomised, double-blind, multinational, placebo- and active-controlled dose-finding trial of semaglutide in combination with both dietary and exercise counselling.
‡A mixed model for repeated measurements, with or without adjustment for change in body weight was used. NAFLD, non-alcoholic fatty liver disease.
Reduction in ALT and HsCRP at End-of-treatment

**Reduction in ALT or hsCRP from baseline to EOT: Semaglutide vs placebo**

<table>
<thead>
<tr>
<th>% reduction</th>
<th>ALT</th>
<th>ALT</th>
<th>hsCRP</th>
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<tbody>
<tr>
<td>9%</td>
<td>P&lt;0.0024</td>
<td>6-21%</td>
<td>P&lt;0.05</td>
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<tr>
<td>-20%</td>
<td></td>
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<td></td>
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<tr>
<td>-40%</td>
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<tr>
<td>-60%</td>
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- Patients with elevated ALT at baseline (defined as >30 IU/L for men and >19 IU/L for women).
- For dose of 1.0 mg/week.
- For doses ≥0.2 mg/day.
- For doses of 0.2 and 0.4 mg/day.
- Treatment ratios for changes in ALT and hsCRP were not statistically significant after adjustment for weight change.

**Normalisation of elevated ALT at EOT**

<table>
<thead>
<tr>
<th>% of patients with normalisation of elevated ALT</th>
<th>Placebo</th>
<th>Semaglutide</th>
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</thead>
<tbody>
<tr>
<td>18%</td>
<td></td>
<td>25-46%</td>
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</tbody>
</table>

Conclusions

Compared with placebo, semaglutide resulted in:

- Significant reductions in ALT levels in people with obesity and T2D
- A significant reduction in hsCRP levels
- More patients with normalisation of ALT levels

Improvements in markers associated with the development of NAFLD

Treatment effects on ALT and hsCRP were linked to weight loss

ALT, alanine aminotransferase; EOT, end-of-treatment; hsCRP, high-sensitivity C-reactive protein; NAFLD, non-alcoholic fatty liver disease; T2D, type 2 diabetes.

Synopsis of the original article 'Effect of Semaglutide on Liver Enzymes and Markers of Inflammation in Subjects with Type 2 Diabetes and/or Obesity' Newsome P, et al. Aliment Pharmacol Ther, 2019;50(2):193-203 © 2021 Novo Nordisk A/S; Further reproduction and distribution is permitted