Effect of Mipomersen on LDL-Cholesterol levels in Patients with Severe LDL-Hypercholesterolemia and Atherosclerosis Treated by Regular Lipoprotein-Apheresis (MICA)

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Conflict of interest

**Anja Vogt** has received honoraria for presentations or advisory board activities by Aegerion, Amgen, Fresenius, Genzyme, Kaneka, Merck Sharp & Dohme, and Regeneron/Sanofi and research support by Genzyme, Merck Sharp & Dohme, and BBraun.

**Klaus G. Parhofer** has received honoraria for presentations, advisory board activities or DMC activities by Aegerion, Amgen, Fresenius, Genzyme, Kaneka, Kowa, Merck Sharp & Dohme, Novartis, Regeneron, Roche and Sanofi. KGP has received research support by Genzyme, Merck Sharp & Dohme, Novartis, Regeneron/Sanofi.

**Elisa Waldmann** has nothing to declare

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Mipomersen

- Antisense oligonucleotide inhibiting the production of apoB in the liver

- Decreases LDL-cholesterol by approximately 30% in different populations (heterozygous FH, homozygous FH, high risk patients, etc.)

- Also decreases lipoprotein(a) by approximately 23%

- Relevant side effects include injection site reaction (ISR, 70-100%), flu like symptoms (FLS, 30-50%), elevated liver function tests (LFT, 20%)
Effect of mipomersen in heterozygous FH (n=82, mipomersen 200 mg/week, 26 weeks)

reduces concentrations of plasma apoB, LDL-cholesterol and Lp(a) in addition to statins and other LLT in patients not treated by regular apheresis

Stein et al., Circulation 2012
MICA - Objectives

**Primary goal:**
Efficacy of mipomersen in patients with severe LDL-hypercholesterolemia treated by regular LDL-apheresis

**Main secondary goal:**
Evaluation of the safety and tolerability of mipomersen in patients on regular apheresis
MICA - Study outline

• Phase II, mono-center, prospective, randomized, placebo-controlled trial

• 17 patients on regular apheresis (> 3 months) for elevated LDL-cholesterol

• Randomization 12 : 5 (mipomersen : control), statistically 10% drop out allowed

• Intervention: weekly mipomersen (200 mg/wk sc)
  - phase I: 26 wk + unchanged weekly apheresis
  - phase II: 12 wk + potential change of apheresis schedule

• Follow up: 26 wk

• No placebo injection in control group
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>mipomersen (n=11)</th>
<th>control (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>male</strong></td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td><strong>female</strong></td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td><strong>age</strong></td>
<td>$53.7 \pm 11.6$</td>
<td>$64.5 \pm 7$</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td>$29.0 \pm 5.2$</td>
<td>$24.8 \pm 2.4$</td>
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<tr>
<td><strong>RR syst. (mmHg)</strong></td>
<td>$116.5 \pm 7.4$</td>
<td>$125.5 \pm 12.5$</td>
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<tr>
<td><strong>HR (min^{-1})</strong></td>
<td>$73.3 \pm 10.1$</td>
<td>$68.5 \pm 7.5$</td>
</tr>
<tr>
<td><strong>LDL-c (mg/dl)</strong></td>
<td>$189.3 \pm 47$</td>
<td>$141.0 \pm 20$</td>
</tr>
<tr>
<td><strong>Lp(a) (mg/dl)</strong></td>
<td>$76.2 \pm 67$</td>
<td>$88.1 \pm 88$</td>
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</table>
Results: reduction of LDL-c, n = 15
Results: reduction of LDL-c

→ LDL-cholesterol reduction 19.2 ± 15%, significant
Results: reduction of Lp(a), n = 15
Results: reduction of Lp(a)

\[ \text{Lp(a) reduction} \approx 12.1 \pm 16\%, \text{ n. s.} \]
Adverse events

- High rate of early drop out and early study termination due to adverse events (57 %)
- 3 patients dropped out very early and were replaced
- 5 patients dropped out later and were not replaced
- Most AE were ISR: 70 %
- Flu like symptoms: 5 %
- Liver enzyme elevation: 25 %
MICA - Conclusion

- Mipomersen reduced LDL-cholesterol significantly when added to regular lipoprotein-apheresis
- Lp(a) also was reduced, but not significantly
- High rate of adverse events limited the use of mipomersen
THANK YOU FOR YOUR ATTENTION