LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN

Medizinische Klinik II
Medizinische Klinik IV

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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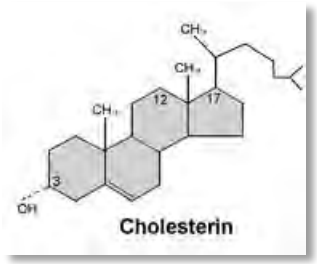

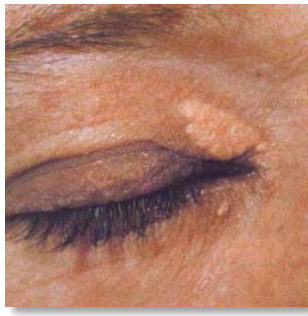

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Conflict of interest

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 acitivities 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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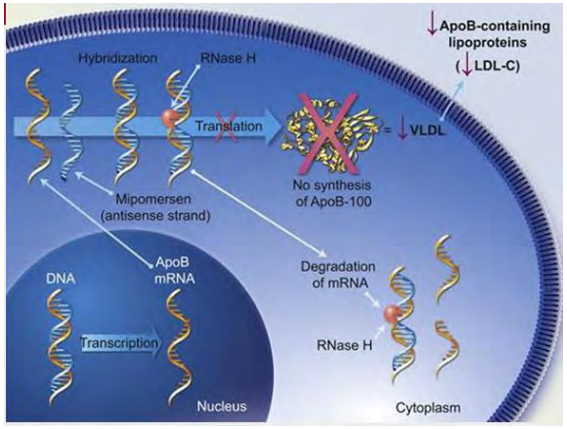
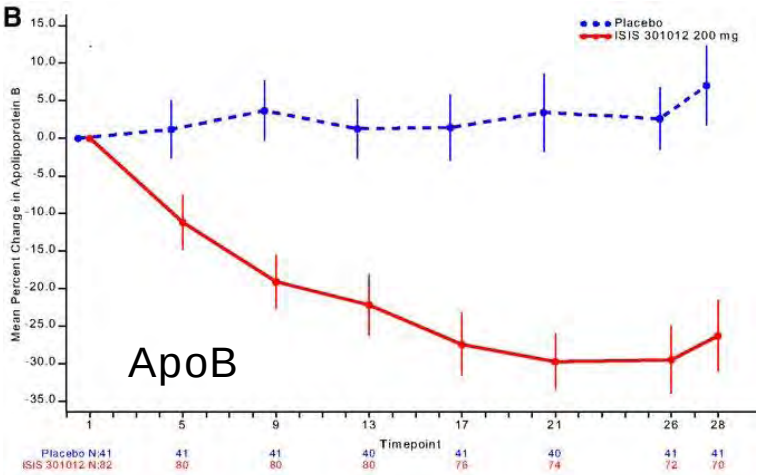
Mipomersen

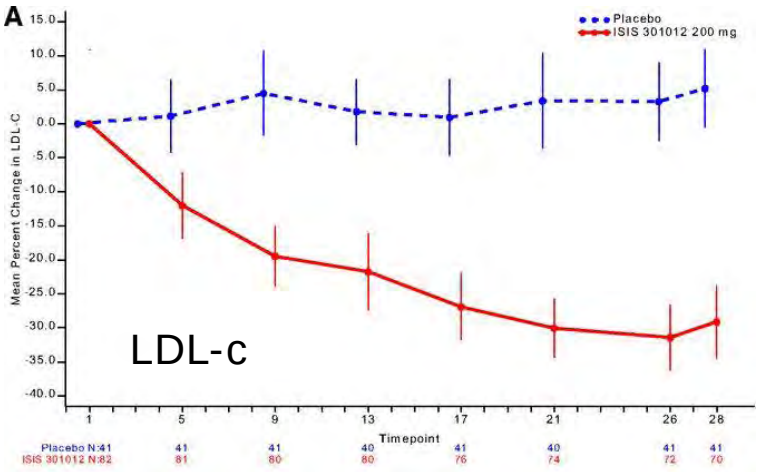


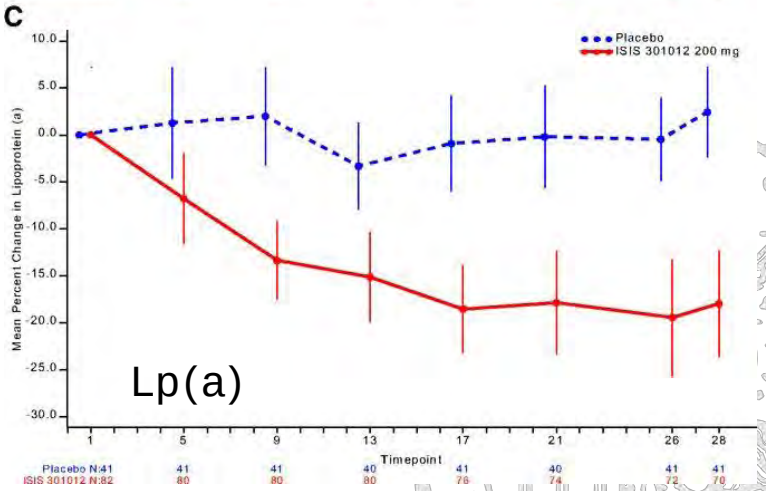
- Antisense oligonucleotide inhibiting the production of apoB in the liver
- Decreases LDL-cholesterol by approximately 30% in different populations (heterzygous FH, homozygous FH, high risk patients, etc.)
- Also decreases lipoprotein(a) by approximately 23 %
- Relevant side effects include
  injection 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

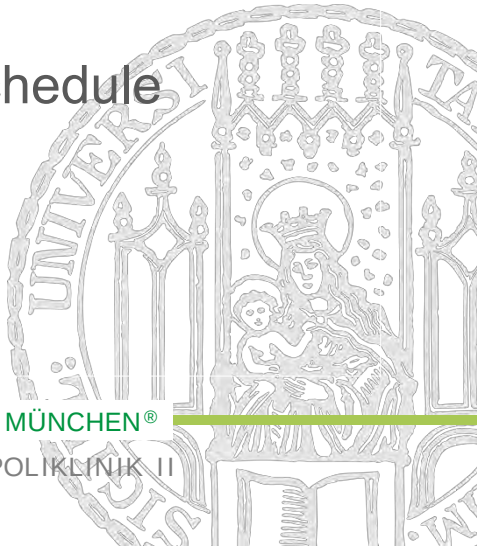
MICA - Objectives

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

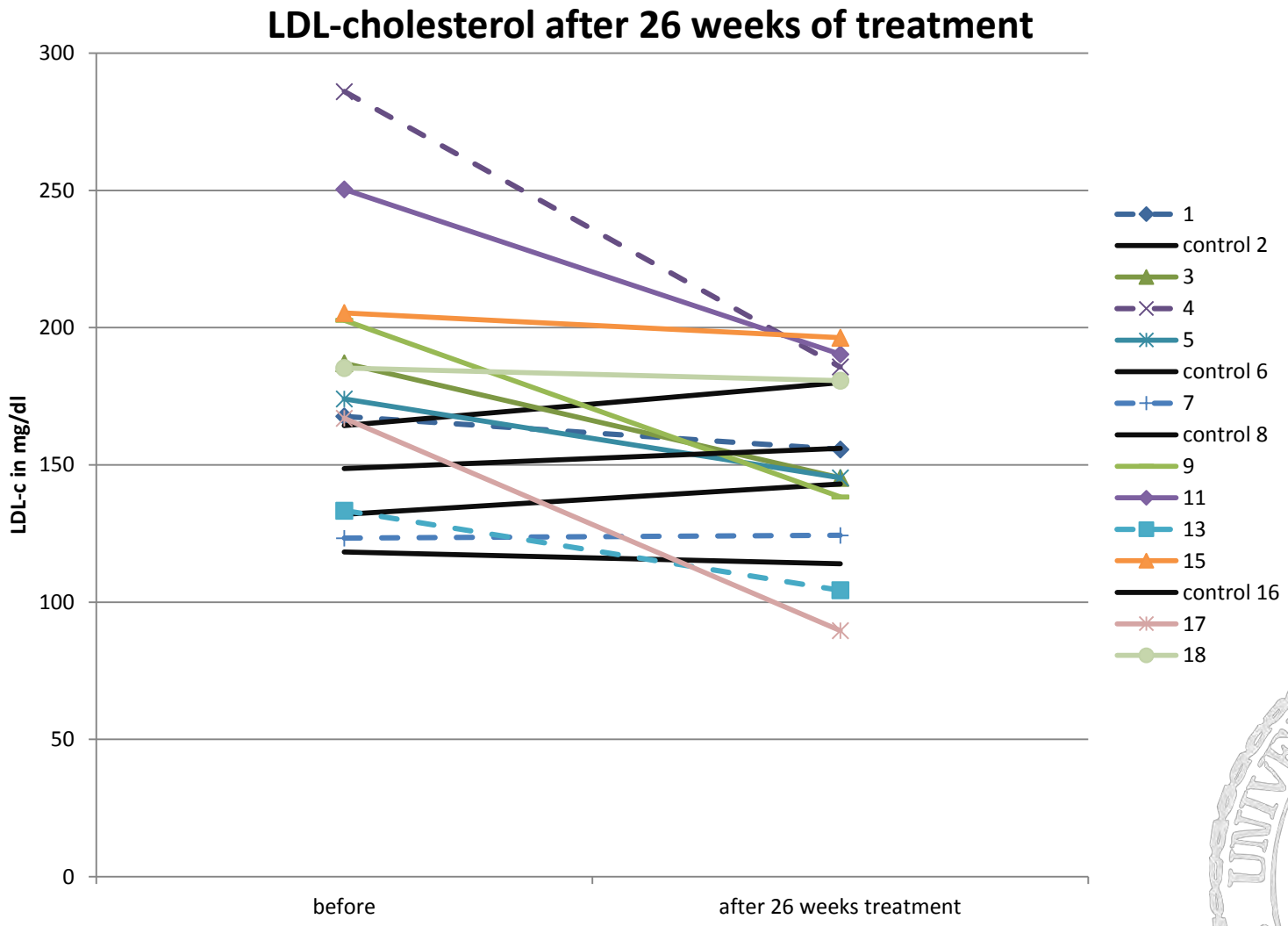
- Phase II, mono-center, prospective, randomized, placebo-controlled trial
- 17 patients on regular apheresis (> 3 months) for elevated LDL-cholesterol
- Randomization 12 : 5 (mipomersen : control), statistically 10% drop out allowed
- Intervention: weekly mipomersen (200 mg/wk sc)
  phase I: 26 wk + unchanged weekly apheresis
  phase II: 12 wk + potential change of apheresis schedule
- Follow up: 26 wk
- No placebo injection in control group



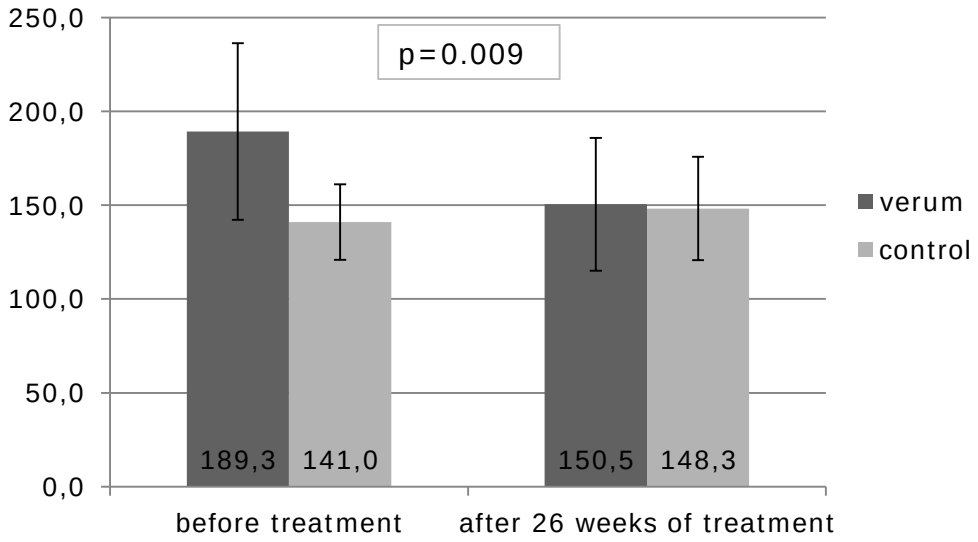
Baseline characteristics

	mipomersen (n=11)	control (n=4)
male	6	3
female	5	1
age	53.7 ± 11.6	64.5 ± 7
BMI (kg/m^2)	29.0 ± 5.2	24.8 ± 2.4
RR syst. (mmHg)	116.5 ± 7.4	125.5 ± 12.5
HR (min^{-1})	73.3 ± 10.1	68.5 ± 7.5
LDL-c (mg/dl)	189.3 ± 47	141.0 ± 20
Lp(a) (mg/dl)	76.2 ± 67	88.1 ± 88

Results: reduction of LDL-c, n = 15

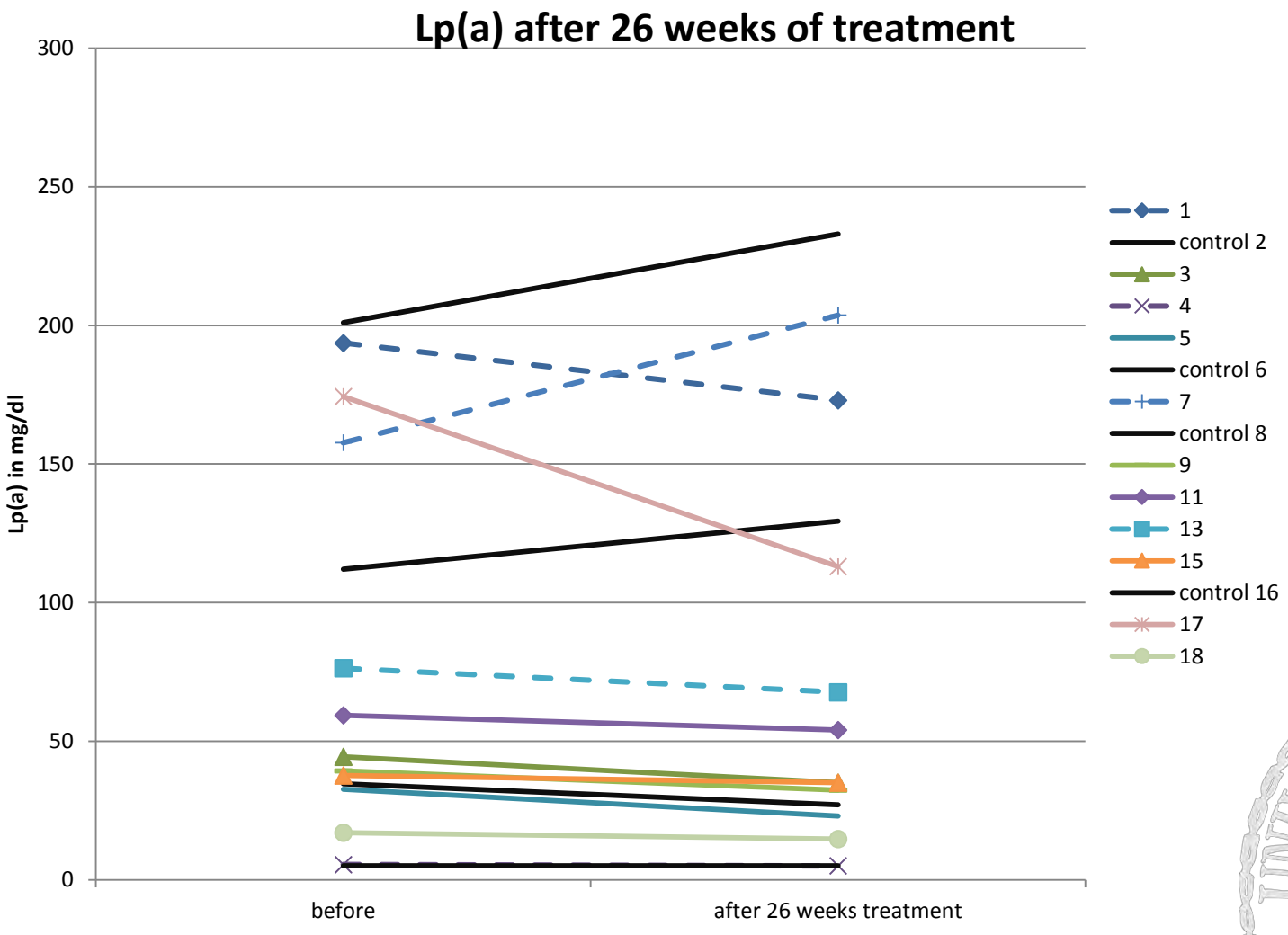


Results: reduction of LDL-c

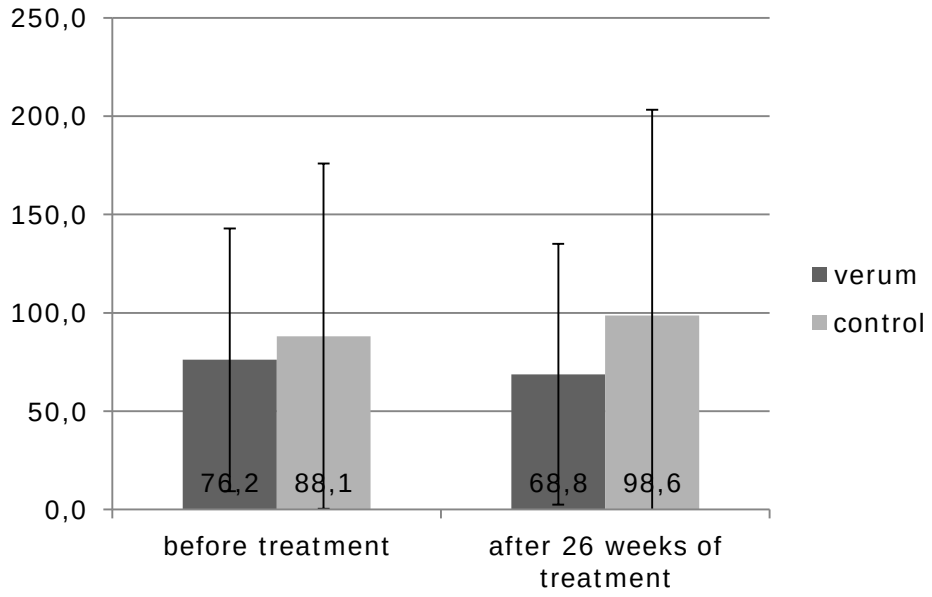


→ LDL-cholesterol reduction 19.2 ± 15%, significant

Results: reduction of Lp(a), n = 15



Results: reduction of Lp(a)



→ Lp(a) reduction 12.1 ± 16%, n. s.

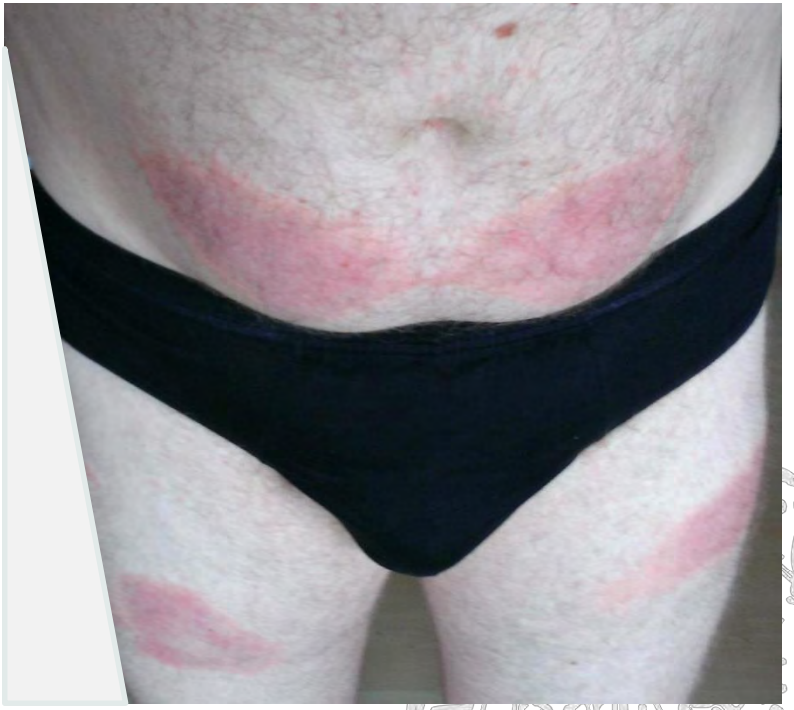
Adverse events

- 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 %

Severe injection side reaction



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