economic status, race, SBP, smoking and alcohol intake [model-2].

Results: Compared with placebo, atorvastatin was associated with improvement in eGFR, regardless of BP-treatment regimen (Figure). Statin and amiodipine-based therapy were associated with the biggest improvement in eGFR from baseline. Randomisation to statin therapy, compared with placebo, was significantly and independently protective, in both model-1 and -2 (p = 0.037 and p = 0.220 0.05–0.44, respectively). The improvement in the eGFR associated with atorvastatin remained, albeit insignificantly, at the end of LLA-extended (+0.22 [-0.02–0.51]); p = 0.07 and +0.23 [-0.03–0.49]; p = 0.09. Blunting of progressive renal deterioration was apparent among the diabetic and chronic kidney disease (eGFR <60 ml/min) patients on statin therapy, compared with placebo, regardless of BP-treatment regimen.

Conclusions: Among hypertensive patients, atorvastatin was associated with no progression of renal dysfunction, and the effect remained 2 years after the trial ended.

[759] Peptide-Based Immunization against PCSK9 Reduces Total Cholesterol in Mice

G. Galabova1, G. Winkler1, B. Wanko, F. Mattner, W. Schmidt, S. Brunner. AFFIBOS AG, Vienna, Austria

Introduction: High levels of Low Density Lipoprotein Cholesterol (LDLc) are a major risk for the development of atherosclerosis. LDLc uptake occurs mainly through the Low Density Lipoprotein Receptor (LDLR), which is found on the cell surface. Proprotein convertase subtilisin kexin type 9 (PCSK9) has the ability to bind LDLR and this complex is internalized. This negatively influences the recycling of the LDLR back to the cell surface and consequently, LDLc uptake from the blood stream is reduced. Compounds that interfere with PCSK9 activity can increase the levels of LDLR and thus result in lower LDLc levels. Therefore, PCSK9 is an attractive therapeutic target.

Objectives: To establish an active immunization with a peptide-based vaccine that induces anti-PCSK9 antibodies which are inhibiting the binding of PCSK9 to the LDLR.

Methods and Results: Peptide-based vaccine candidates have been developed using our proprietary AFFITOME®-technology. Epitopes involved in the LDLR/PCSK9 binding were tested for their ability to induce functional antibodies. Selected peptides were coupled to a carrier protein and administered together with Alhydrogel as adjuvant. The immunogenicity of the peptide vaccines was monitored by anti-peptide-ELISA and by anti-PCSK9 Protein-ELISA. In addition, the ability of the antibodies to interfere with PCSK9/LDLR binding was analyzed. Finally, serum levels of total cholesterol and LDLR levels in livers were quantified. Our vaccines are able to induce antibodies reducing total cholesterol in our mouse model system.

Conclusions: Our PCSK9 vaccine candidates present a new powerful therapy for reducing LDLc.

*authors contributed equally


K.G. Parhofer1, A. Vogt2. 1 Medical Department 2, Grosshadern, Ludwig-Maximilians-University, 2 Medical Department 2, Grosshadern, Ludwig-Maximilians-University, Munich, Germany

Introduction: Weekly lipid-apheresis is a treatment option in patients with CAD and drug-resistant LDL-hypercholesterolemia. Country-specific thresholds for LDL-cholesterol (LDL-C) are used to initiate apheresis (>100 mg/dl, >130 mg/dl, or >160 mg/dl). Mipomersen, an ApoB-synthesis inhibitor, reduces LDL-C significantly when added to maximally tolerated lipid-lowering therapy. We hypothesised that mipomersen may prevent the necessity for apheresis by reducing LDL-C values below thresholds for apheresis eligibility.

Method: Data of a previous study in 123 patients with CAD and heterozygous FH (clinical-trials NCT00706849; maximal statin therapy; mipomersen-82 patients, placebo-41 patients; median age 56years, 63% male; baseline LDL 153 mg/dl, mean reduction 28.0%), were used to evaluate in what percentage of patients the addition of mipomersen resulted in a LDL-C level below the thresholds for apheresis. For this analysis it was assumed that all other apheresis criteria are fulfilled.

Results: Mipomersen reduced the percentage of patients with LDL >160 mg/dl from 39% to 2% (32/2 patients, relative reduction (RR) 95%), with LDL >130 mg/dl from 62% to 16% (51/13 patients, RR 74%), and with LDL >100 mg/dl from 98% to 54% (80/44 patients, RR 45%), while no significant changes were observed with placebo.

Summary: When added to maximally tolerated lipid lowering therapy, mipomersen may reduce the necessity for apheresis in a significant number of patients with heterozygous FH and CAD. In Germany where usually a threshold of 100 mg/dl is applied almost half of aphereses could potentially be avoided with addition of mipomersen to maximally tolerated lipid-therapy. Further studies are warranted to evaluate whether patients who qualify for apheresis could be adequately controlled with mipomersen.

[761] A Randomized Trial of Atorvastatin Plus Etidronate Combination Therapy for Atherosclerotic Aortic Plaques

T. Kawahara1, M. Nishikawa2, T. Furusawa3, T. Inoue4, G. Suzuki5. 1 University of Occupational and Environmental Health, Japan, Kitakyushu, 2 National Institute of Public Health, Wako, 3 Niigata Rosai Hospital, Joetsu, 4 Ritsumeikan University, Ohtsu, 5 International University of Health and Welfare Clinic, Ohtawara, Japan

Background: Bisphosphonates are currently considered the drugs for the prevention and the treatment of osteoporosis and related fractures. However, accumulating evidence suggests that bisphosphonates have the potential to be effective also in reducing atherosclerotic process and vascular calcification.

Methods: We conducted a prospective, randomized, open-label, blind-endpoint trial involving 251 patients with asymptomatic hypercholesterolemia. 123 were assigned to receive 20 mg of atorvastatin, 128 were assigned to receive 20 mg of atorvastatin plus 400 mg of etidronate (combination-therapy). The primary endpoint was the change of maximal wall thickness of atherosclerotic lesions in the thoracic and abdominal aorta, as measured by magnet resonance imaging, after 24 months’ treatment.

Results: In this trial, both groups reduced low-density lipoprotein cholesterol (~44% of the combination-therapy group and ~45% of the atorvastatin group; p <0.001 vs. baseline for both groups). As compared with the atorvastatin group, the combination-therapy group had similar rates of reduction of maximal vessel wall thickness in the thoracic aorta (~13% vs. ~15%, p = 0.587), but higher rates of reduction of that in the abdominal aorta (~1% vs. ~12%, p <0.001) over 24 months. The incidence of major cardiovascular events was lower in the combination-therapy group than in the atorvastatin group (1% vs. 5%, P = 0.049).

Conclusions: 24 months atorvastatin plus etidronate combination therapy significantly reduced both thoracic and abdominal aortic plaques, whereas atorvastatin monotherapy reduced only thoracic ones. In addition, the combination therapy might be superior to atorvastatin monotherapy in decreasing the incidence of cardiovascular events.
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