P529 / #1375, Poster Topic: *AS04 CLINICAL VASCULAR DISEASE / AS04.09 Lipid-lowering therapies*

EVINACUMAB IN HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA CAUSED BY LDLRAP 1 – FIRST DATA OF 2 UNRELATED CASES

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Background and Aims: Evinacumab is a monoclonal antibody inhibiting the enzyme angiopoietin-like protein 3 (ANGPTL3) and thus lowering low density lipoprotein cholesterol (LDL-C), tryglycerides (TG), and high density lipoprotein cholesterol (HDL-C). LDL-c is lowered independently of LDL-C-receptors. This is relevant for patients with homozygous familial hypercholesterolemia (hoFH) making Evinacumab a new treatment option for these patients. Evinacumab (15 mg per kilogram infusion body weight over 1 hour monthly) was recently approved in Germany for patients with hoFH.
Methods: Two unrelated patients with proven hoFH due to very rare low density lipoprotein receptor adaptor protein 1 (LDLRAP) mutations undergoing regular lipoprotein-apheresis received Evinacumab additionally to Rosuvastatin 40 mg and Ezetimibe 10 mg. Effects on LDL-C and other lipoproteins are compared.
Results: Both patients received the first dose of Evinacumab after a LA session. Lipid levels (non fasting) before this session and after one week (pre LA) are compared. No short term adverse events or safety concerns arose. Patient 1: LDL-C was lowered from 180mg/dl to 46mg/dl (-74%), TG from 182mg/dl to 59mg/dl (-68%), and HDL-C from 41mg/dl to 26mg/dl (-40%). After LA LDL-C was reduced to 20mg/dl. Patient 2: LDL-C was reduced from 448mg/dl to 199mg/dl (-56%), TG from 119mg/dl to 47mg/dl (-61%), and HDL-C from 48mg/dl to 27mg/dl (-44%).
Conclusions: Evinacumab reduced LDL-C in both cases markedly after just one week. After LA the goal for LDL-C (<55mg/dl) was reached in patient 1 and was just slighty exceeded in patient 2. The reductions of TG and HDL-C are as expected; early data don't indicate a negative effect. Reducing the frequency of LA or even discontinuation will be discussed depending on further levels of LDL-C. Data regarding long term safety, differences according to the genetic mutations, and reduction of cardiovascular events remain to be seen.

P530 / #1372, Poster Topic: *AS04 CLINICAL VASCULAR DISEASE / AS04.09 Lipid-lowering therapies*

THE PROTECTIVE EFFECTS OF PCSK9 INHIBITORS ON DNA DAMAGE IN PERIPHERAL BLOOD MONONUCLEAR CELLS IN FAMILIAL HYPERCHOLESTEROLEMIC PATIENTS

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Background and Aims: Familial hypercholesterolaemia (FH) is characterized by a genetic defect in the low-density lipoprotein cholesterol (LDL-C) metabolism pathway that increases the risk of cardiovascular disease. Patients with familial hypercholesterolaemia constitute a special group of patients in whom it is not possible to achieve the desired LDL-C values using standard treatment regimens. PCSK9 (iPCSK9) inhibitors are therefore a new alternative in intensifying lipid-lowering treatment. The aim of the study was to determine the level of DNA damage in peripheral blood mononuclear cells of patients with familial hypercholesterolaemia, as well as the potential impact of iPCSK9 on reducing the resulting damage.
Methods: The study material included peripheral blood mononuclear cells collected from patients with familial hypercholesterolaemia (n=36) who were qualified for the iPCSK9 treatment program. The level of single- and double-strand DNA damage was determined using the alkaline version of the comet test, before treatment and after 6 months of therapy with iPCSK9. The control group included patients with normolipidemia (n=21) who did not undergo lipid-lowering therapy.
Results: In patients before iPCSK9 treatment, the average percentage of DNA damage in the comet's tail was approximately 11.17±1.42%, in patients after 6 months of iPCSK9 treatment, the average percentage of DNA damage in the comet's tail was significantly lower and amounted to approximately 7.53±1.34%.
Conclusions: Patients with familial hypercholesterolemia are characterized by DNA damage. The obtained results suggest that the use of iPCSK9 in this group of patients reduces the level of DNA damage compared to the level of DNA damage before the initiation of lipid-lowering therapy, but not to the level of DNA damage observed in normolipidemia. The research was founded in whole by the National Science Center in Poland as a part of the Preludium-21 scientific project (2022/45/N/NZ7/01622).

P531 / #1238, Poster Topic: *AS04 CLINICAL VASCULAR DISEASE / AS04.10 Anti-thrombotic therapies*

ANALYSIS OF PLATELET HEMOSTASIS IN PATIENTS ON THE BACKGROUND OF DUAL ANTIPLATELET THERAPY FOR 12 MONTHS

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Background and Aims: New approaches to selecting antiplatelet agents attempt to balance time, benefits and risks for patients. After PCI, whether patients have chronic coronary syndrome or acute coronary syndrome, an initial course of dual antiplatelet therapy with aspirin and a P2Y12 inhibitor (usually six months for CCS and 12 months for ACS) is recommended in order to minimize the risk of thrombotic complications. It remains crucial to investigate the residual ability of platelets to aggregate after doses of antiplatelet therapy in order to assess its effectiveness. The aim is to assess the effect of dual antiplatelet therapy (clopidogrel/ticagrelor) in patients with CHD on the state of platelet haemostasis during one year of follow-up.
Methods: Materials and methods: 39 patients with coronary heart disease were examined (men - 20 women - 19, average age - 64.5 ± 6.3).1 group of patients (22 people) took acetylsalicylic acid (ASA) 75 - 100 mg/day and clopidogrel 75 mg/day), 2 group (17 patients) took acetylsalicylic acid (ASA) 75-100 mg/day and ticargelor 180 mg/day.The control group consisted of 19 practically healthy persons.The state of functional activity of thrombocytes was studied using laser aggregometry by light transmission curves with evaluation of spontaneous aggregation and aggregation induced by arachidonic acid (AA), adenosine diphosphate (ADP), collagen, ristocetin and epinephrine in low doses.
Results: Parameters of platelet hemostasis parameters in patients after 12-month DAPT (Me [25%; 75%])

Indicators		Coronary heart disease		Control	p
Light transmission curve		1 group	2 group		
Spontaneous aggregation	Degree, %	2,12** [1,42; 2,99]	0,9 [0,2; 1,79]	0,41 [0,20; 0,81]	p_1-p_2<0,05
Adenosine diphosphate	Degree, %	44,9* [34,4; 62,6]	25,2** [5,14; 46,4]	63,2 [58; 68,1]	p_1-p_2<0,01
Arachidonic acid	Degree, %	48,5* [11,3; 68,4]	5,67** [1,72; 26,7]	64,9 [57,5; 71,2]	p_1-p_2<0,01

Conclusions: In annual follow-up, the combination of ASA + ticagrelor achieves inhibition of both spontaneous and induced platelet aggregation ($p < 0.01$)

P532 / #1425, Poster Topic: *AS04 CLINICAL VASCULAR DISEASE / AS04.10 Anti-thrombotic therapies*

EFFICACY AND SAFETY OF DIFFERENT REGIMENS PROLONGED ANTITHROMBOTIC THERAPY IN REVASCULARIZED PATIENTS WITH STABLE CAD AND MULTIFOCAL ATHEROSCLEROSIS

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Background and Aims: We aimed to assess the efficacy and safety of different regimens of prolonged antithrombotic therapy (dual antithrombotic therapy – DAT (low dose of rivaroxaban 2.5 mg twice per day in addition to acetylsalicylic acid (ASA)) and dual antiplatelet therapy – DAPT (ASA + clopidogrel)) for CAD