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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00648453
		Study Code:	L_8564
Generic drug name:	Clopidogrel	**Date:**	10/Apr/2008

Title of the study:	The change of laser Doppler flowmetric parameters characteristic of endothelial dysfunction at clopidogrel treatment. Study number: L 8564		
Investigator(s):	Katalin Farkas MD.		
Study center(s):	Saint Imre Hospital Medical Department No.I. 1115 Budapest, Tétényi str. 12-16., Hungary		
Publications (reference):	NA		
Study period: Date first patient enrolled: 23-Sep-2002 Date last patient completed: 21-May-2004		**Phase of development:** Ph. IV clinical study	
Objectives:	**Primary endpoint:** change of the laser Doppler parameters measured after three months clopidogrel treatment compared to the pre-treatment values. **Secondary endpoint:** safety of clopidogrel treatment		
Methodology:	Open, prospective, self-controlled**.**		
Number of patients:	Planned: 40	Randomized: NA	Treated: 39
Evaluated:	Efficacy: 39	Safety: 39	
Diagnosis and criteria for inclusion:	Proven peripheral arterial disease in Fontaine II-III stage • Doppler index < 0,8 • sex: man, woman • age: 30-70 years • patient submitted to secondary prophylactic treatment with a platelet aggregation inhibitor • Signed informed consent		
Investigational product: Dose: Administration:	clopidogrel 75 mg once daily oral		
Duration of treatment: 3 months		**Duration of observation:** 3 months	

Reference therapy: Dose: Administration:	NA
Criteria for evaluation:	
Efficacy:	Microvascular reactivity (measurements done by laser-Doppler flowmetry, of the endothel-dependent vasodilatation induced by acetylcholine and sodium nitroprusside administered into the skin of the forearm by iontoforesis).
Safety:	Evaluation of safety and of the patient's compliance The unwanted events - depending on their severity - should be scored 1-3 as follows: 1 = mild 2 = moderate 3 = severe Severe unwanted event: it is of fatal outcome, or life dangering, or invalidating, or requiring hospital care, or hospital treatment.
Statistical methods:	The data of the extents of the laser Doppler flow were compared to the Paired Samples Test. We prepared descriptive statistics for demographic parameters, complaints and adverse events.

Summary:	39 PAD /Fontaine II-III stage/ patients have completed the study (27 males, 12 females; mean age 60,2 years). The study examined the dysfunction of endothelial and vascular cells by a simple, clinically applicable method in the population suffering from peripheral arterial vascular disease. Evaluation of the study results renders the follo wing statements possible: In case of peripheral arterial disease both endothelial and vascular damage was demonstrable. The endothelium independent vasodilatation increased upon the effect of 12 weeks clopidogrel /75 mg/day/ treatment. Significant difference was demonstrated between the CVPAD and PAD patient group at rather high risk in the endothelium-dependent vasodilatation. The results of the study allow to get an inside view of the finer possible mechanism of effect of clopidogrel. In the examined patient population consisting of a small number of cases daily 75 mg clopidogrel could be safely administered during the 12 weeks of the study.
Efficacy results:	**Evaluation of primary endpoint:** 1. Compared to healthy individuals, at the patients suffering from peripheral arterial vascular disease both the ACh elicited endothelium-dependent and endothelium-independent vasodilatation decreased measured at SNP by LD. This indicates endothelial and vascular damage. 2. After 12 weeks clopidogrel treatment, the vasodilatation did not significantly change measured with Ach iontophoresis 3. The endothelium independent vasodilatation significantly increased. /p=0,004/ measured at SNP after 12 weeks clopidogrel treatment **Other important statements** Significant difference could be proven in the endothelium-dependent vasodilatation of the patients who have already suffered /CVPAD/ or have not suffered /PAD/ another cardiovascular event /AMI, TIA stroke/ at the second measurement /p=0,052/. In the CVPAD group also the endothelium-independent vasodilatation was lower, but the difference was not significant /p=0,052/.
Safety results:	3 undesirable events were registered at 2 patients, during the three months study period which were the followings: diarrhoea, epigastric pain, allergic cutaneous reaction. Their development is with great probability in connection with the administration the study drug. The diagnosed two gastrointestinal undesirable events ceased without intervention, spontaneously. Three patients were hospitalized during the period of the study, but all three events were in correlation with the basic disease and not with the taking of the study drug, thus they were not considered as serious undesirable events to be reported.
Date of report:	28-February- 2008