Report Synopsis of Study: KP-Niacin-2010

EudraCT-Nr.: 2010-019954-42

Vorlage-Nr.: 4036450

1) **Name of Sponsor/Company:**	4) **Individual Study Table Referring to Part of the Dossier:** not applicable[1]	*(For National Authority Use only)*
Klinikum der Ludwig-Maximilians Universität München	Volume: not applicable	
2) **Name of Finished Product:** Tredaptive		
3) **Name of Active Substance:** Niacin/Laropiprant	Page: not applicable	

5) **Title of Study[2]:**

Effect of Niacin/Laropiprant on postprandial lipoprotein and glucose metabolism in patients with severe dyslipoproteinemia

Reason for protocol amendments: Ethics committee required minor changes in informed consent forms

Protocol Amendment 21.09.2010, Protocol Version 2.0: the patient information and consent form was revised to make it easier understandable for laypersons; in addition, the insurance policy number was added

6) **Principal Investigator(s):**

Prof. Klaus G. Parhofer

7) **Study centre(s):**

Klinikum der Universität München, Medizinische Klinik II – Grosshadern, Marchioninistr. 15, 81377 München

8) **Publication (reference):** El Khoury P, Waldmann E, Huby T, Gall J, Couvert P, Lacorte JM, Chapman J, Frisdal E, Lesnik P, Parhofer KG, Le Goff W, Guerin M. Extended-Release Niacin/Laropiprant Improves Overall Efficacy of Postprandial Reverse Cholesterol Transport. Arterioscler Thromb Vasc Biol. 2016 Feb;36(2):285-94. doi: 10.1161/ATVBAHA.115.306834. Epub 2015 Dec 17. PubMed PMID: 26681758.

9) **Studied period (years)[3]:**	10) **Phase of development:** Phase IV
2011-2012 Date of first enrolment: 13.7.2011 Date of last completed: 5.12.2012	

11) **Objectives:**

Primary Objectives:

The primary objective was to evaluate the effect of niacin/laropiprant on postprandial triglyceride metabolism as determined by the incremental area under the plasma triglyceride curve following a standardized oral fat challenge.

Secondary Objectives:

- Postprandial chylomicron metabolism
- Postprandial chylomicron remnant metabolism
- Fasting lipid parameters (cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, VLDL-triglycerides, LDL subtype distribution (small dense LDL), apoB 100, apoE, apoC-III)
- Postprandial glucose metabolism (oral glucose tolerance test, including insulin concentrations)
- Fasting glucose, insulin, C-peptide

[1] This information is only required in connection with filing of a dossier for marketing authorization.

[2] The latest protocol version must be clearly stated, this means including all amendments – the amendments are to be declared and identified.

[3] Here also study suspensions and premature terminations of a trial/premature conclusion of a trial should be listed, including the reasons for that.

Report Synopsis of Study: KP-Niacin-2010

EudraCT-Nr.: 2010-019954-42

Vorlage-Nr.: 4036450

12) **Methodology:** This was a 12 week single centre, study of niacin/laropiprant given as additional therapy in statin treated patients with severe dyslipoproteinemia, not adequately controlled on diet/life style advise and statin therapy. At the end of the intervention period a standardized oral fat challenge was performed to determine primary and secondary objectives.

13) **Number of patients (planned and analyzed):** planned 24 analysed 12

14) **Diagnosis and main criteria for inclusion:**

- Male or female 19-70 years
- High risk patients (PROCAM risk ≥20%) on statins (simvastatin 20-40 mg/d)
- HDL-cholesterol ≤50 mg/dl (women)/≤40 mg/dl (men) and /or triglycerides 150-400 mg/dl and/or LDL-cholesterol >100 mg/dl
- Patients may have normal glucose metabolism (normal HOMA) be insulin resistant (abnormal HOMA), have impaired fasting glucose or impaired glucose tolerance but not diabetes mellitus
- Without niacin therapy for at least 6 months
- Dosage of any concomitant medication has been stable for at least 3 weeks
- If female, postmenopausal for the past 12 months, surgically sterile or using an adequate method of birth control or sterolized partner

15) **Test product, dose and mode of administration, batch number:** Niacin/Laropiprant; 1000mg/20mg; oral once daily for 4 weeks, then twice daily for 8 weeks; LOT-Nr: DL0017259; the lot consisted of 100 boxes each containing 35 tablets; each included patient received 3 boxes;

Patients: Tred01: 3 boxes à 35 tablets; Tred02: 3 boxes à 35 tablets; Tred03: 3 boxes à 35 tablets; Tred04: 3 boxes à 35 tablets; Tred05: 3 boxes à 35 tablets; Tred06: 3 boxes à 35 tablets; Tred07: 3 boxes à 35 tablets; Tred08: 3 boxes à 35 tablets; Tred09: 3 boxes à 35 tablets; Tred10: 3 boxes à 35 tablets; Tred11: 3 boxes à 35 tablets; Tred12: 3 boxes à 35 tablets.

16) **Duration of treatment:**

12 weeks

17) **Reference therapy, dose and mode of administration, batch number:**

NA

18) **Criteria for evaluation:**

The primary endpoint of the study is the incremental area under the plasma triglyceride curve over 8 hours following a standardized oral fat tolerance test. Incremental AUC will be determined from the baseline (fasting), 2 hours, 4 hours, 6 hours and 8 hours plasma triglyceride concentrations.

Secondary objectives

- •Postprandial chylomicron and chylomicron remnant metabolism
- •Fasting lipid parameters (cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, VLDL-triglycerides, LDL subtype distribution (small dense LDL), apoB 100, apoE, apoC-III)
- •Postprandial glucose metabolism (oral glucose tolerance test, including insulin concentrations)
- •Endogenous CETP activity

Assessment of Safety:

Adverse experiences, physical examination including vital signs, clinical laboratory safety studies.

19) **Statistical methods:**

For the primary end point (comparison of the changes in triglyceride-AUC induced by niacin/laropiprant) a t-test was used, if the values were normally distributed, while a Wicoxon sum ranking, if the values were not normally distributed. Other parameters were compared by t-test/Wilcoxon test after Bonferroni adjustment.

20) **Summary – Conclusions:**

Efficacy results: Compared with baseline, ERN/LRPT significantly reduced postprandial hypertriglyceridemia (incremental area under the curve-triglyceride: -53%; P=0.02).

Report Synopsis of Study: KP-Niacin-2010

EudraCT-Nr.: 2010-019954-42

Vorlage-Nr.: 4036450

Secondary EP:

AUC of chylomicrons (-62%; p=0.008) and AUC of chylomicron remnants (-33%; p<0.001) were significantly reduced.

Fasting lipid parameters: cholesterol -9%; ns; LDL-C -20%; p=0.041); HDL-C +17%, 0.028; VLDL-C -25%; p=0.04; VLDL-TG-28%; p=0.04; small dense LDL qualitatively reduced; apoB 100, apoE, apoC-III qualitatively reduced)

Postprandial glucose metabolism: glucose +5%, p=0.173; insulin +87%, p=0.028

CETP activity: postprandial increase (+24%; p<0.004 and +30%; p<0.04, 4h and 6h after fat load, respectively) attenuated with Niacin/laropiprant (+7%, ns and +6% ns 4h and 6h after fat load, respectively)

Safety results:

No adverse experiences, changes in physical examination including vital signs, clinical laboratory safety studies were observed.

Conclusion:

ERN/LRPT treatment efficiently attenuates atherogenic postprandial lipemia and stimulates HDL-mediated cholesterol return to the liver and elimination into feces during postprandial phase, thus maintaining an efficient removal of cholesterol from the body.

21) **Date of the report:** **27.2.2020**