2. STUDY SYNOPSIS

Title of the study:	A 4-week double-blind placebo-controlled pilot study, evaluating niacin-induced flushing and lipid parameter effects of V0002 CA 1g 3 capsules/day associated with Niaspan® (from 375 mg to 1000 mg) in addition to usual care statin, in patients suffering from dyslipidemia with uncontrolled elevated triglycerides
Investigator(s):	General practitioners from the ALTI network. Coordinating investigator: Dr Philippe Igigabel
Study centre(s):	34 centres participated in this study
Publications (references):	None
Period of study:	First patient in: 28/04/2008 – Last patient out: 02/09/2008
Clinical phase:	Phase IIa
Objectives:	The primary objective of this proof-of-concept study is to determine whether V0002 CA co-administered with Niaspan® during 4 weeks of therapy, can help reducing niacin-induced vasodilatation.
Methodology (design of study):	Multicentre, double-blind, randomized, placebo-controlled, parallel group
Number of patients:	V0002 CA / Placebo / Total Planned: 60 / 60 / 120 Enrolled: 61 / 57 / 118 Completed 55 / 53 / 108 Discontinued 6 / 4 / 10
Diagnosis and main criteria for inclusion:	Dyslipidemia with elevated triglycerides uncontrolled by dietary measures and a statin alone, deemed for additional nicotinic acid treatment.
Test product, dose and mode of administration, batch number:	V0002 CA capsule 1 g - 1 capsule during breakfast and 2 capsules before dinner; oral route Batch no: SB0614/22162
Duration of treatment:	4 weeks (28 days)
Reference therapy, dose and mode of administration, batch number:	Matching V0002 CA placebo - 1 capsule during breakfast and 2 capsules before dinner; oral route Batch n° SB0615/22161
Criteria of evaluation:	Efficacy: The primary criterion is the global intensity of flush defined as the third answer of the FSQ at the first day of each dose increase of Niaspan® (D1, D8, D15, D22). Secondary criteria: Mean global intensity of flushes at each weekly period of escalating dose - Mean global intensity of flushes over the 28 days treatment period - Presence or not of daily flushing symptoms - Number of daily flushing symptoms - Duration of the longest daily flushing symptoms - Global flush score - Intensity of daily flushing-related skin redness, warmth, tingling or itching - Lipid parameters. Safety: Vital signs, physical findings and other observations related to

	safety – hematologic- parameters - biochemistry parameters - Clinical adverse events.
Statistical methods:	The primary criterion was the global intensity of flush defined as the third answer of the FSQ at the first day of each dose increase of Niaspan® (D1, D8, D15, D22). Treatment groups were compared on the FAS by using a generalized linear mixed model based on a negative binomial distribution with groups as fixed factor, patient as random factor and dose of Niaspan® as categorical covariate

Summary and conclusions :

Enrolment of patients and populations analysed: All patients randomized to treatment were included in the FAS and the Safety population; 14 patients in the V0002CA group and 8 in the Placebo group were excluded from the per protocol analysis for major protocol deviation.

Summary of efficacy: The expected efficacy of the V0002 CA to prevent flushes in patients needing to be treated with a combination of statin plus Niaspan® was not reached in this study, as patients did not demonstrate hot-flushes due to Niaspan® initiation.

For lipid parameters, a significantly more pronounced decrease of Total cholesterol, LDL-cholesterol and apoliprotein B was observed with V0002CA than with placebo, but paradoxically no effect was observed on HDL cholesterol and related apolipoprotein A.

Summary of safety: The treatment V0002 CA combined to a statin and Niaspan® can be considered as well tolerated either from a biological point of view than from a clinical point of view.

Adverse events (AE): A total of 8 patients in the V0002 CA group and 15 in the Placebo groups presented at least one adverse event

Serious AE and drop-outs due to AE: No serious adverse event was reported in this study.

Two patients discontinued from the study for adverse event:

- Patient 3503 (V0002 CA) discontinued the study due to erysipelas considered as severe, not related to the study drug.
- Patient 0504 (V0002 CA) withdrawn from the study due to nausea and vomiting, not severe, not related to the study drug.

Conclusions:

Due to an unexpected lack of symptoms at Niaspan® initiation, this study failed to demonstrate a beneficial effect of V0002 CA on flushes. This could be due to a methodological bias, by selecting an inappropriate population, and not considering the only ones who presented symptoms.