2. SYNOPSIS

Name of sponsor/company: Cardoz AB		
Name of active ingredient: pemirolast		
Title of study: An open pilot study to assess the effects of pemirolast on C-reactive protein levels in subjects with coronary artery disease and in overweight/obese subjects. (Version 1.0) An open study to assess the effects of pemirolast on C-reactive protein levels in subjects with coronary artery disease (Version 1.1)		
Principal Investigators: Centre 01: Ingemar Bylesjö MD, Ph.D Centre 02: Jan Nilsson MD, Ph.D., Professor		
Study centre: Centre 01: Berzelius Clinical Research Center AB Berzelius Science Park, Linköping, Sweden Centre 02: Klinisk Forskningsavdelning, Akutcentrum Malmö University Hospital, Sweden		
Publication (reference): Not applicable		
Studied period (years): 2010-03-02 (date of first enrolment) 2011-03-21 (date of early study termination)	**Phase of development:** Phase IIa- a pilot study in subjects	
Objectives: *Primary:* To determine the effects of pemirolast on C-reactive protein levels. *Secondary:* To determine the safety and tolerability of pemirolast administration.		
Methodology: A two-centre, open-label, non-randomized study		
Number of subjects (planned and analysed):	Test drug	Placebo/Comparator drug
No. planned:	24	Not applicable
No. enrolled and treated:	2	
Males/females:	1/1	
Mean age (range)	63.5 years (63 – 64)	
No. analysed for efficacy:	2	
No. analysed for safety:	2	
No. completed:	2	
Diagnosis and main criteria for inclusion: **Subjects with coronary artery disease (CAD):** *Inclusion criteria:* a) CAD (diagnosed on the basis of a previous myocardial perfusion study or cardiac catheterisation, or a history of myocardial infarction or coronary angioplasty or coronary artery bypass surgery.		

b) Male or female subjects aged 40 – 70 years. Body Mass Index between 19 and 29 kg/m^3
c) Stable statin therapy since one month.
d) High sensitivity CRP (hs-CRP) >2.0 and < 10.0 mg/L.
e) No change in cardiac medications since one months
f) Female subjects have to be non-fertile, i.e. postmenopausal or surgically sterile.

g) In the opinion of the Investigator, the subject will be able to comply with the requirements of the protocol
h) Subjects will have given their written informed consent to participate in the study

Exclusion criteria:

a) Acute illness within the last two weeks
b) Pharmacologically treated type 1 or type 2 diabetes mellitus
c) Recent coronary events (within 3 months)
d) Clinical heart failure
e) Subjects with, or with a history of, any clinically significant neurological, gastrointestinal, renal, hepatic, cardiovascular, psychological, pulmonary, metabolic, endocrine, haematological or other major disorder other than CAD as judged by the Investigator
f) Pregnancy or breast feeding
g) Subjects who previously have demonstrated hypersensitivity to the investigational medicinal product
h) Subjects atopic or with history of allergy as judged by the Investigator
i) Subjects who have used any prescribed systemic, except prescribed statin and cardiovascular medications (beta blockers, calcium inhibitors, ACE-inhibitors, diuretics, clopidogrel (Plavix) and low dose trombyl), or topical medication within14 days before the first dose administration
j) Subjects who have used any OTC systemic or topical medication within 7 days before the first dose administration (with the exception of vitamin/mineral supplements, paracetamol, NSAIDs or nasal decongestants at the discretion of the Investigator)
k) Subjects who have participated in a clinical study involving administration of an investigational drug or a marketed drug within the past 3 months
l) Subjects who have donated blood during the last 3 months or plasma the last month
m) Subjects who have had a clinically significant illness within 4 weeks of the start of the study as judged by the Investigator
n) Subjects who are known to have serum hepatitis or who are carriers of the hepatitis B surface antigen (HBsAg), or hepatitis C antibody, or have a positive result to the test for HIV antigens and/or antibodies
o) Heavy smokers and/or excessive use of alcohol, as judged by the Investigator.

Overweight/obese subjects:

Inclusion criteria:

a) Overweight or obese subjects with BMI 27.0 – 34.9 kg/m^2.
b) Male or female subjects, aged 30 – 65 years.
c) hs-CRP >2.0 and <10.0 mg/L.
d) Subjects must be in good health, as determined by a medical history, physical examination, 12-lead ECG and clinical laboratory evaluations as judged by the Investigator.
e) No change in prescribed medical therapy since one month.
f) Female subjects have to be non-fertile, i.e. postmenopausal or surgically sterile.
g) In the opinion of the Investigator, the subject will be able to comply with the requirements of the protocol.
h) Subjects will have given their written informed consent to participate in the study.

Exclusion criteria:

a) Acute illness within the last two weeks.
b) Pharmacologically treated type 1 or type 2 diabetes mellitus.
c) Subjects with, or with a history of, any clinically significant neurological, gastrointestinal, renal, hepatic, cardiac, pulmonary, metabolic, endocrine, haematological, psychological or other major disorder as judged by the Investigator.
d) Pregnancy or breast feeding.
e) Subjects who previously have demonstrated hypersensitivity to the investigational medicinal product.
f) Subjects atopic or with history of allergy as judged by the Investigator.
g) Subjects who have used any prescribed systemic, except prescribed statin and cardiovascular medications (beta blockers, calcium inhibitors, ACE-inhibitors, diuretics and low dose trombyl), or topical medication

within 14 days before the first dose administration.

h) Subjects who have used any OTC systemic or topical medication within 7 days before the first dose administration (with the exception of vitamin/mineral supplements, paracetamol, NSAIDs or nasal decongestants at the discretion of the Investigator).
i) Subjects who have participated in a clinical study involving administration of an investigational drug or a marketed drug within the past 3 months.
j) Subjects who have donated blood during the last 3 months or plasma the last month.
k) Subjects who have had a clinically significant illness within 4 weeks of the start of the study as judged by the Investigator.
l) Subjects who are known to have serum hepatitis or who are carriers of the hepatitis B surface antigen (HBsAg), or hepatitis C antibody, or have a positive result to the test for HIV antigens and/or antibodies.
m) Heavy smoker and/or excessive intake of alcohol as judged by the Investigator.

Additionally, subjects are to be excluded from the study for the following reasons:

- Positive urine drug screen result.
- Clinically significant pathological vital signs or 12-lead ECG finding.
- Intercurrent illnesses or clinically significant adverse events.
- Violation of study restrictions, unless in the opinion of the Investigator these violations would not have interfered with the study procedures, compromised the safety of subjects, or affected the study results.

Test product, dose and mode of administration, batch number:
Pemirolast tablets 10 mg (Ulgixal™, Batch No. 751061); oral administration 3 x 10 mg b.i.d.

Duration of treatment:
14 days

Reference therapy, dose and mode of administration, batch number:
None.

Criteria for evaluation:
The Full Analysis Set (FAS) for the analysis of hs-CRP was to include all subjects who had received the IMP according to the protocol and with available results on hs-CRP at baseline and at least once thereafter. Subjects who acquired an acute infection during the study were to be excluded from the FAS.

Efficacy evaluation:

Blood samples for assessment of hs-CRP were collected at the Screening , Day1, day 8 and Day 15 visits.

Safety evaluation :

Medical history information was to be obtained at the Screening visit. A physical examination including vital signs, 12-lead ECG, weight and height was to be performed at the Screening and Day 15 visits. Samples for haematology and chemistry panels and urinalysis were to be collected at the Screening and Day 15 visits. Subjects were evaluated for adverse events at each visit.

Statistical methods:
Sample size assessment: No formal statistical assessment of sample size was conducted. Twenty-four (24) subjects were to be included in the study, 12 subjects with CAD and 12 overweight/obese subjects.

There were no statistical analyses performed as only two subjects were included in the study at the termination. The

study was terminated due to the expiry of the shelf life of the study drug.

SUMMARY – CONCLUSIONS

SAFETY RESULTS:

- No SAEs were reported.
- Mouth dryness and gastritis of mild intensity were the two reported AEs.
- The two AEs reported were considered as possibly related to the study medication.
- No subject discontinued from the study, due to AE or any other reason.
- There were no clinically important findings in laboratory values, vital signs or ECG.
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CONCLUSION:

No conclusion can be drawn from the study as this study was prematurely stopped due to the expiry of the study drug's shelf life and there were only two subjects included in the study.