The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No: CUC111342

Title : An open label, 7-day repeat dose study to evaluate the pharmacodynamics of SB-656933-AAA in patients with Ulcerative Colitis

Rationale: 99m-Tc-HMPAO scintigraphy using SPECT is a quantitative translational imaging technique which allows objective assessment of PMN migration to inflamed tissue. PMN migration to inflamed colonic tissue is a predominant feature of active Ulcerative Colitis (UC). SB-656933-AAA significantly reduces PMN accumulation in pre-clinical models of colitis. Therefore, 99m-Tc-HMPAO scintigraphy is an appropriate technique to observe the PD effects of SB-656933-AAA in this UC proof of mechanism study. The method is relatively simple, safe, minimally invasive and not limited by the inherent subjectivity of clinical disease activity indices.

Phase: II

Study Period: Initiation Date: 22 JAN 2009, Completion Date: 12 DEC 2009, Early Termination Date: 17 FEB 2010

Study Design: The primary objective of this study was to assess the effect of 20mg or 100mg SB656933-AAA on leukocyte migration to the inflamed colon as measured by 99mTc-HMPAO labelled leukocyte scintigraphy in subjects with moderately active ulcerative colitis. This study was a single centre, open label, repeat dose study. A sufficient number of subjects were planned be enrolled so that initially 12 evaluable subjects completed the study. However, this study was terminated after 3 subjects completed dosing and critical assessments.

Centres: Academic Medical Centre, Amsterdam, The Netherlands

Indication: Ulcerative Colitis

Treatment: SB656933 tablet strength = 10 mg /Dose = 20 mg or SB656933 tablet strength = 50 mg /Dose = 100 mg

Objectives: The primary objective was to assess the effect of a daily dose of SB-656933-AAA on leukocyte migration to the inflamed colon after 1 and 7 days dosing as measured by 99mTc-HMPAO labeled leukocyte scintigraphy in subjects with moderately active UC.

Statistical Methods: The primary objective was to describe the pharmacodynamics of SB-656933-AAA, and therefore there were no formal hypotheses tested in this study. As the study was terminated early, after only 3 subjects had been dosed with SB-656933 the data was listed only, and no formal statistical analyses were conducted or summaries generated

Study Population: Male or female between 18 and 65 years with a history of UC for at least 3 months with the diagnosis confirmed by radiologic, endoscopic or histological assessment, moderately active UC and a documented Mayo endoscopic score of 2 or 3 within 14 days of dosing

Number of Subjects:	**20mg**	**100mg**
Planned N	4	8
Dosed N	1	2
Completed n (%)	1	2
Total Number Subjects Withdrawn N (%)	0	0
Withdrawn due to Adverse Events n (%)	0	0
Withdrawn due to Lack of Efficacy n (%)	0	0
Withdrawn for Other Reasons n (%)	0	0
Demographics	**Group A**	**Group B**
N (ITT)	1	2
Age in Years, Mean (SD)	59 (0.00)	39 (15.56)
Females: Males	1:0	2:0
Mean Weight in Kg (sd)	NA	NA
White n (%)	1	2

Pharmacokinetics (PK), pharmacodynamics (PD), PK/PD Endpoints: Plasma concentration data were collected from 2 subjects whom received 100 mg and 1 whom received 20 mg. There were not sufficient data to allow calculation of any PK parameters. Given the limited sample size, differences in exposure between subjects and linearity of exposure with dose cannot be estimated. However, exposure to the drug is significantly higher after 100 mg as compared to 20 mg.
It is not possible to draw any meaningful conclusions from the very limited PD data available.

Safety results: Only two adverse events were reported: one subject (receiving 100 mg) reported a brick like sensation in the stomach on day 1 of dosing (which resolved) and a second subject (receiving 20 mg) developed herpes simplex

on day 29.		
Adverse Events:	**20mg**	**100mg**
N (ITT)	1	2
No. subjects with AEs n (%)	1 (100%)	1 (50%)
Serious Adverse Events, n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]: None		