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Study No.: SB207499/041	
Title: A Multicenter Open-label Extension Study to Evaluate the Safety, Tolerability and Efficacy of Oral Cilomilast (15 mg twice daily) in Patients with Chronic Obstructive Pulmonary Disease (COPD)	
Rationale: This study was conducted in order to further evaluate the long term safety of cilomilast in subjects with COPD.	
Phase: III	
Study Period: 09 June 1999 to 26 June 2002	
Study Design: A multi-centre, open-label extension study	
Centres: 78 centres in the United States, Canada and Mexico.	
Indication: COPD	
Treatment: Study medication was to be taken orally, twice daily, in the morning after breakfast and in the evening after a meal.	
Objectives: To evaluate the long-term safety and tolerability of cilomilast administered at a dosage of 15mg twice daily.	
Primary Outcome/Efficacy Variable: Adverse experiences. No primary efficacy measure was defined.	
Secondary Outcome/Efficacy Variable(s): Not applicable.	
Statistical Methods: No formal power calculations were performed since this was an open-label study with the primary purpose of evaluating subject safety. Summaries include all subjects who had received at least one dose of study medication in study 041.	
Study Population: Males or females with COPD who successfully completed study 039 where subjects received cilomilast 15 mg bd or placebo for 24 weeks without tolerability problems. The study excluded subjects from study 039 who had withdrawn; had a positive faecal occult blood test between Weeks 20 and 24; had a serious adverse event, a gastrointestinal adverse experience or a clinically significant laboratory abnormality that was still present at the end of those studies, which could have been attributed to study medication.	
	Cilomilast
Number of Subjects:	
Enrolled from Placebo:Cilomilast arms of 039	140:215
Enrolled into extension study, N	355
Completed, n (%)	0 (0)
Total Number Subjects Withdrawn, N (%)	355 (100)
Withdrawn due to Adverse Events n (%)	83 (23)
Withdrawn due to Lack of Efficacy n (%)	16 (5)
Withdrawn due to Termination of Study by Sponsor, n (%)	166 (47)
Withdrawn for other reasons n (%)	90 (25)
Demographics	Cilomilast
N (ITT)	355
Females: Males	125:230
Mean Age, years (SD)	65.3 (8.6)
Caucasian, n (%)	332 (94)
Current smoker, n (%)	164 (46)
Primary Outcome Results: Adverse events are displayed in Safety Results.	
Safety Results: An on-therapy adverse event (AE) was defined as an AE with onset on or after the start date of study medication but not later than one day after the last date of study medication. An on-therapy serious adverse event (SAE) was defined as an SAE with onset on or	

after the start date of study medication and up to 30 days after the last dose of medication.	
Extent of Exposure, n(%)	
At least 24 weeks	273 (77)
At least 52 weeks	231 (65)
At least 104 weeks	175 (49)
At least 132 weeks	59 (17)
	Cilomilast
Most Frequent Adverse Events – On-Therapy	n (%)
Subjects with any AE(s), n(%)	333 (94)
Chronic obstructive airways disease	175 (49)
Upper respiratory tract infection	120 (34)
Diarrhoea	82 (23)
Nausea	69 (19)
Abdominal pain	61 (17)
Injury	57 (16)
Dyspepsia	50 (14)
Sinusitis	44 (12)
Rhinitis	44 (12)
Headache	42 (12)
Coughing	42 (12)
Serious Adverse Events - On-Therapy	
n (%) [n considered by the investigator to be related to study medication]	
	Cilomilast
	n (%) [related]
Subjects with any SAEs, n (%)	102 (29) [5]
Chronic obstructive airways disease	37 (10)
Pneumonia	17 (5)
Myocardial infarction	8 (2)
Chest pain	7 (2) [1]
Cardiac failure	6 (2) [1]
Basal cell carcinoma	5 (1)
Injury	5 (1)
Abdominal pain	4 (1) [3]
Fibrillation atrial	4 (1) [1]
Syncope	4 (1)
Angina pectoris	3 (<1)
Coronary artery disorder	3 (<1)
Anemia	2 (<1)
Angina pectoris aggravated	2 (<1)
Bladder carcinoma	2 (<1)
Carcinoma	2 (<1)
Cerebrovascular disorder	2 (<1)
Cholecystitis	2 (<1)
Depression	2 (<1)
Diverticulitis	2 (<1)
Neoplasm malignant	2 (<1)
Pancreas neoplasm malignant	2 (<1)
Pulmonary carcinoma	2 (<1)
Skin neoplasm malignant	2 (<1)
Adenocarcinoma NOS	1 (<1)
Arrhythmia	1 (<1)
Arrhythmia atrial	1 (<1)

Atelectasis	1 (<1)
Breast neoplasm malignant female	1 (<1)
Calcinosis	1 (<1)
Cholelithiasis	1 (<1)
Claudication intermittent	1 (<1)
Coagulation time increased	1 (<1)
Confusion	1 (<1)
Convulsions	1 (<1)
Depression aggravated	1 (<1)
Diarrhoea	1 (<1) [1]
Duodenitis	1 (<1)
Esophagitis	1 (<1)
Fracture pathological	1 (<1)
Gastritis	1 (<1)
Gastroesophageal reflux	1 (<1)
GI Hemorrhage	1 (<1)
Hematoma	1 (<1)
Infection viral	1 (<1)
Intestinal obstruction	1 (<1)
Intestinal perforation	1 (<1)
Melanoma malignant	1 (<1)
Myelomatosis multiple	1 (<1)
Neoplasm NOS	1 (<1)
Nerve root lesion	1 (<1)
Osteomyelitis	1 (<1)
Ovarian cyst	1 (<1)
Peripheral ischemia	1 (<1)
Pneumothorax	1 (<1)
Prostatic disorder	1 (<1)
Renal calculus	1 (<1)
Respiratory disorder	1 (<1)
Tachycardia	1 (<1)
Tachycardia supraventricular	1 (<1)
Tachycardia ventricular	1 (<1)
Therapeutic response increased	1 (<1)
Thrombosis arterial leg	1 (<1)
Urinary retention	1 (<1)
Vascular disorder	1 (<1)
Vertigo	1 (<1)
	Cilomilast
	n (%) [related]
Subjects with fatal SAEs, n (%)	6 (2) [0]
Myocardial infarction	3 (<1)
Cardiac failure	1 (<1)
Intestinal perforation	1 (<1)
Pancreas neoplasm malignant	1 (<1)

Conclusion: Three hundred thirty-three subjects reported adverse events with the most frequently reported being chronic obstructive airways disease and upper respiratory tract infection. One hundred two subjects reported serious adverse events. There were six fatalities reported.

Publications: No Publications

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