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See Drug Details page of this website for approved drug label.

Proprietary Drug Name	INN	Therapeutic area and FDA approved indications
Celebrex	Celecoxib	Relief of signs and symptoms of osteoarthritis Relief of signs and symptoms of rheumatoid arthritis in adults Management of acute pain in adults Treatment of primary dysmenorrhea Reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis as an adjunct to usual care

Name of Sponsor/Company: Pfizer Inc.

Title of Study: Protocol Number I49-98-02-107

A Multi-Centre, Double-Blind, Parallel Group Study Comparing the Efficacy and Incidence of Gastroduodenal Ulcer Associated With SC-58635 100 mg BID With That of Diclofenac 50 mg BID Taken for 12 Weeks in Patients With Osteoarthritis or Rheumatoid Arthritis in Hong Kong

Study centre(s): There were 4 study centers in Hong Kong

Publication (reference, if applicable): See attached bibliography.

Studied period:	Phase of development:
02 August 1999 to 28 April 2000	Phase 3

Objectives:

- Compare the arthritis efficacy of SC-58635 100 mg BID with that of diclofenac 50 mg BID in patients with OA or RA
- Compare the incidence of gastroduodenal ulcer over 12 weeks associated with SC-58635 100 mg BID with that of diclofenac 50 mg BID in patients with OA and RA combined (these results are presented in a different study report, document #I49-00-07-849).
- Compare the safety and tolerability of SC-58635 100 mg BID with that of diclofenac 50 mg BID in patients with OA and RA combined.

Methodology: This was a double-blind, randomized, multicenter, active comparator (diclofenac) controlled, parallel group study comparing the efficacy, safety, and incidence of gastroduodenal ulcer in OA or RA patients receiving SC-56835 with those receiving diclofenac. Patients were randomly assigned to receive either SC-58635 100 mg BID or diclofenac 50 mg BID. Those patients who received SC-58635 also received diclofenac matched placebo and those patients who received diclofenac also received SC-58635 matched placebo to maintain double-blind study design (double-dummy design). The duration of treatment was 12 weeks, with visits occurring at screening/baseline, Weeks 4, 8 and 12. Scheduled endoscopies were performed prior to and 12 weeks after the first dose of study medication (or at early termination).

Number of patients (planned and analyzed): Eighty-nine patients were enrolled and randomized (SC-58635: 45 patients; Diclofenac: 44 patients) to receive double-blind study medication. Sixteen of the 89 randomized patients were withdrawn during the course of the study with 73 patients completing the study. Seventy-three patients were female and 16 patients were male. The mean age was 53.0 years for the SC-58635 treatment group (range: 25 to 84 years) and 52.6 years for the diclofenac treatment group (range: 24 to 88 years). Eighty-eight patients (SC-58635: 44 patients; Diclofenac: 44 patients) were included in the safety population and the ITT population.

Diagnosis and main criteria for inclusion: Patients were included in the study if they had a documented clinical diagnosis of OA or RA with a Functional Capacity Classification of I-III, required chronic nonsteroidal anti-inflammatory drugs (NSAIDs), and met the inclusion/exclusion criteria.

Duration of treatment: 12 weeks

Test product, dose and mode of administration: Celecoxib 100 mg BID (SC-58635) capsules, one capsule orally BID

Reference therapy, dose and mode of administration: Diclofenac 50 mg BID film-coated tablets, one tablet orally BID
Placebo for diclofenac, one tablet orally BID
Placebo for celecoxib, one capsule orally BID

Criteria for evaluation: Efficacy: Efficacy was assessed by comparing the patient's and physician's global assessment of OA or RA, the patient's assessment of arthritis pain measured by Visual Analogue Scale, and incidence of and time to withdrawal due to treatment failure.
Safety: Safety and tolerability were assessed by comparing physical examinations (including weight and vital signs), clinical laboratory test results (biochemistry, hematology and urinalysis), and adverse events.

Statistical methods: All analyses were applied to the intent-to-treat patient population.
Efficacy: Observed means were summarized for each efficacy variable, while the categorical change analysis was done with a Cochran-Mantel-Haenszel test stratified by center. Mean value analysis for the efficacy variables was done through an analysis of covariance (ANCOVA) with treatment and center as factors and baseline value as covariate. Additional analyses were performed using an ANCOVA model to investigate various interaction terms. Incidence of withdrawal due to lack of arthritis efficacy was analyzed using Fisher's Exact Test, while time to withdrawal was analyzed using survival analysis (Kaplan-Meier method and log-rank test).
Safety: Adverse events were classified into body system categories, and summarized by the number and percentage of patients recording an event. The individual laboratory values were examined in three ways: a scatter diagram depicting baseline and Week 12 values for each variable; a shift table with Stuart-Maxwell chi-square analysis of the change in the normal range from baseline to Week 12; a display of descriptive statistics for baseline and Week 12 values. The incidence of clinically significant laboratory results was listed for each treatment. Vital signs and weight changes from baseline as well as the compliance to study medication were listed for each treatment group. The treatment groups were compared using an ANOVA.

Summary

DEMOGRAPHY: The study was well balanced between treatment groups in terms of patient baseline characteristics (demography, arthritis assessments and endoscopy scores). Of the 89 patients, 73 were female and 16 male. The race/ethnic origin of all patients was Asian, except for one patient who was documented as Black. The mean age of the patients was 53.0 years for the SC-58635 treatment group (range: 25 to 84 years) and 52.6 years for the diclofenac treatment group (range: 24 to 88 years).

EFFICACY RESULTS:

Efficacy Variables	SC-58635 100mg BID	Diclofenac 50mg BID	p-value (a)
Patient's Assessment of Arthritis Pain - VAS			
Baseline Means	47.8	40.4	
Week 4*	-10.8	-7.9	0.423
Week 8*	-12.9	-4.4	0.061
Week 12*	-18.0	-6.0	0.021
Patient's Global Assessment of Arthritis			
Baseline Means	3.0	2.9	
Week 4*	-0.6	-0.4	0.119
Week 8*	-0.6	-0.4	0.081
Week 12*	-0.6	-0.4	0.196
Physician's Global Assessment of Arthritis			
Baseline Means	2.5	2.4	
Week 4*	-0.4	-0.2	0.016
Week 8*	-0.5	-0.2	0.062
Week 12*	-0.5	-0.2	0.081

*Change from Baseline values are least square mean changes. Negative values signify improvement.
(a) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate.

SAFETY RESULTS: In the SC-58635 treatment group 28 patients (64%) had at least one adverse event and in the diclofenac treatment group 32 patients (73%) had at least one adverse event. Sixteen patients (36%) had no AEs in the SC-58635 treatment group while 12 patients (27%) had no AEs in the diclofenac treatment group. No deaths occurred during the course of the study. Two patients (5%) in the SC-58635 treatment group had at least one adverse event causing withdrawal, while 5 patients (11%) in the diclofenac treatment group had AEs causing withdrawal. Six patients had serious adverse events. Two patients (5%) in the SC-58635 treatment group had serious AEs. One patient experienced abdominal pain, vomiting and arthritis and one patient experienced hypertension. Four patients (9%) in the diclofenac treatment group had serious AEs. One patient experienced hypotension and syncope, one patient experienced chest wall pain, one patient experienced accidental injury and dizziness and one patient experienced accidental injury. The changes in oral temperature, pulse rate (sitting), respiration rate (sitting), systolic blood pressure (sitting), and diastolic blood pressure (sitting), from baseline to Week 12 (or termination visit) were similar for both treatment groups.

CONCLUSIONS: With respect to both patient's and physician's global assessment of arthritis, and patient's assessment of arthritis pain, the study results show a rapid decrease in observed means from baseline to Week 4, and remain stable thereafter to Week 12 in both treatment groups. These observed mean changes for the SC-58635 treatment group were higher than for the diclofenac treatment group over all visits. A statistically significant difference between the treatment groups was observed at Week 12 for patient's assessment of arthritis pain and at Week 4 for physician's global assessment of arthritis. The results for the safety analysis show that more patients experienced adverse events in the diclofenac treatment group than in the SC-58635 treatment group. More patients in the diclofenac group experienced serious AEs and AEs leading to withdrawal than the patients in the SC-58635 treatment group. The changes in oral temperature, pulse rate (sitting), respiration rate (sitting), systolic blood pressure (sitting), and diastolic blood pressure (sitting), from baseline to Week 12 (or termination visit) were similar for both treatment groups. The safety profile of SC-58635 in patients from Hong Kong is similar to that seen in the pivotal OA/RA studies conducted in the mixed populations suggesting no specific safety concerns in the ethnic subgroups. In summary, the observed study results for SC-58635 100 mg BID are generally equivalent to or better than the results observed for diclofenac 50 mg BID, with statistical significance for the treatment differences in some of the efficacy results. The safety results suggest that SC-58635 100 mg BID was tolerated at least as well as diclofenac and support the safety in the subgroup of patients of Asian extraction.

Based on a report completed on: 7 August 2000