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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 I49-98-02-105. A multicenter, double-blind, parallel group study comparing the efficacy and incidence of gastroduodenal ulcer associated with SC-58635 (celecoxib) 100 mg BID with that of diclofenac 50 mg BID taken for 12 weeks in patients with osteoarthritis (OA) or rheumatoid arthritis (RA) in the People's Republic of China.

Study centre(s): 14 centers in the People's Republic of China.

Publication (reference, if applicable): See attached bibliography

Studied period: 24 Jul 1999 - 26 Apr 2000

Phase of development: Phase 3

Objectives: The objectives of this study were as follow:

1. Compare the arthritis efficacy of SC-58635 100 mg BID with that of diclofenac 50 mg BID in patients with OA or RA.

2. 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.

3. 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): Six hundred and sixty-six patients (SC-58635: 332 patients; diclofenac: 334 patients) were enrolled. Eighty-six patients were withdrawn during the course of the study. Five hundred and eighty patients completed the study. Five hundred and sixty-one patients were female and 105 patients were male. The mean age was 49.6 years (range 17 to 78 years) for the SC-58635 treatment group and 49.1 years (range 18 to 73 years) for the diclofenac treatment group. Six hundred and fifty-seven patients (SC-58635: 327 patients; Diclofenac: 330 patients) were included in 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 (SC-58635) 100 mg capsules, one capsule orally BID. Placebo, one capsule orally BID.

Reference therapy, dose and mode of administration: Diclofenac 50 mg film-coated tablets, one tablet orally BID. Placebo, one tablet 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 the 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: **Disposition of Patients and Baseline Characteristics**: The study was well balanced between treatment groups in terms of patient baseline characteristics (demography, arthritis assessments and endoscopy scores). Of the 666 patients, 561 were female and 105 male. The race/ethnic origin of all patients was Asian. The mean age of the patients was 49.6 years for the SC-58635 treatment group (range: 17 to 78 years) and 49.1 years for the diclofenac treatment group (range: 18 to 73 years).

Efficacy Results:

Efficacy Variables	SC-58635 100 mg BID	Diclofenac 50 mg BID	p-value (a)
Patient's Assessment of Arthritis Pain - VAS			
Baseline Means	64.2	61.8	
Week 4*	-15.9	-15.5	0.710
Week 8*	-24.2	-23.8	0.771
Week 12*	-30.9	-30.9	0.982
Patient's Global Assessment of Arthritis			
Baseline Means	3.4	3.3	
Week 4*	-0.5	-0.6	0.080
Week 8*	-0.7	-0.8	0.460
Week 12*	-0.9	-0.9	0.979
Physician's Global Assessment of Arthritis			
Baseline Means	3.3	3.2	
Week 4*	-0.5	-0.5	0.408
Week 8*	-0.7	-0.7	0.489
Week 12*	-0.9	-0.9	0.745

* 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.

The results that describe and discuss the incidence of gastroduodenal ulcers have been combined with similar results from Protocols I49-98-02-106 and I49-98-02-107 and presented in Clinical Study Report I49-00-07-849.

Safety Results: In the SC-58635 treatment group 127 patients (39%) had at least one adverse event and in the diclofenac treatment group 150 patients (45%) had at least one adverse event. Two hundred patients (61%) had no AEs in the SC-58635 treatment group while 180 patients (55%) had no AEs in the diclofenac treatment group. No deaths occurred during the course of the study. Twelve patients (4%) in the SC-58635 treatment group had at least one adverse event causing withdrawal, while 18 patients (5%) in the diclofenac treatment group had AEs causing withdrawal. Six patients had serious adverse events. Two patients (1%) in the SC-58635 treatment group had serious AEs, namely abdominal pain and hemorrhoids. Four patients (1%) in the diclofenac treatment group had serious AEs, namely collagenosis, appendicitis, cholecystitis and an accidental fracture.

The changes in oral temperature, pulse rate (sitting), respiration rate (sitting), systolic blood pressure (sitting), diastolic blood pressure (sitting), and weight from baseline to Week 12 (or termination visit) were similar for both treatment groups. The safety results suggest that SC-58635 was at least as well tolerated as diclofenac.

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 thereafter a gradual decrease to Week 12. The observed mean changes for patient's and physician's global assessment of arthritis were similar for the SC-58635 treatment group and the diclofenac treatment group over most visits; and no difference was statistically significant. The observed mean changes for patient's assessment of arthritis pain, indicating reduction of arthritis pain, for the SC-58635 treatment group were higher than for the diclofenac treatment groups over all visits, although these differences were not statistically significant.

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 AEs leading to withdrawal than the patients in the SC-58635 treatment group and more patients in the diclofenac group experienced serious AEs than the patients in the SC-58635 treatment group.

The changes in oral temperature, pulse rate (sitting), respiration rate (sitting), systolic blood pressure (sitting), diastolic blood pressure (sitting), and weight from baseline to Week 12 (or termination visit) were similar for both treatment groups.

The safety profile of SC-58635 of patients in the People's Republic of China 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 are generally equivalent to the results observed for diclofenac, although the treatment differences were generally not statistically significant. The safety results suggest that SC-58635 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: 07 August 2000