These results are supplied for informational purposes only.

Prescribing decisions should be made based on the approved package insert

Link to 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 I49-98-02-106

A Multi-Centre, 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 Or Rheumatoid Arthritis In Taiwan, IND#48,395

Study centre(s): Six study sites in Taiwan.

Publication (reference, if applicable) See attached bibliography

Studied period: 22 Apr 1999 to 29 Dec 1999 **Phase of development:** 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 or RA combined (these results are presented as the report for Study 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 or RA combined.

Methodology: This was a double-blind, randomized, multicenter, active comparator (diclofenac) controlled, parallel group study comparing the efficacy 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 100 mg also received diclofenac matched placebo and those patients who received diclofenac 50 mg 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): One hundred and twenty-five patients (SC-58635: 63 patients; diclofenac: 62 patients) were enrolled. Nineteen patients were withdrawn during the course of the study. One hundred and six patients completed the study. One hundred and twenty-four patients (SC-58635: 63 patients; Diclofenac: 61 patients) were included in the safety population and ITT population. Twenty-one

patients were female and 104 male patients. The median age was 57 years (range 25 to 80 years) for the SC-58635 treatment group and 56 years (range 18 to 75 years) for the diclofenac treatment group.

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 non-steroidal anti-inflammatory drugs (NSAIDs), and met the inclusion/exclusion criteria.

Duration of treatment: The treatment period was defined as the 12-week interval during which study medication was taken. The Week 4, 8, and 12 visits occurred during this interval. The Week 4 visit had to occur 28 days (± 5 days), the Week 8 visit 56 days (± 5 days), and the Week 12 visit 84 days (± 5 days) after the date of the first dose of medication.

Test product, dose and mode of administration:

- Celecoxib 100 mg BID (SC-58635) capsules, one capsule orally BID Placebo, one capsule orally BID

Reference therapy, dose and mode of administration:

- Diclofenac 50 mg BID 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 arthritis (OA or RA), the patient's assessment of arthritis pain measured by Visual Analogue Scale and incidence of and time to withdrawal 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 Intent-to-treat patients 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 with 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 125 patients, 21 were female and 104 male. The race/ethnic origin of all patients was Asian, except for one patient who was documented as White. The mean age of the subjects was 56.1 years for the SC-58635 treatment group (range: 25 to 80 years) and 52.7 years for the diclofenac treatment group (range: 18 to 75 years).

EFFICACY RESULTS:

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 decreasing gradually to Week 12. The observed mean changes for the SC-58635 treatment group were higher than for the diclofenac treatment group over almost all visits, although these differences were not statistically significant.

More patients improved and fewer patients deteriorated with respect to the global assessments of arthritis (both patient's and physician's) from baseline in the SC-58635 treatment group than in the diclofenac treatment group over all the visits. Again, these differences were not statistically significant.

VAS scores of arthritis pain showed a decrease in observed means from baseline to Week 4 and thereafter gradually declined to Week 12. The observed mean pain reduction for the SC-58635 treatment group was numerically greater than the diclofenac treatment group over all the visits, but the differences were not statistically significant.

One patient (2%) withdrew due to lack of arthritis efficacy in the SC-58635 treatment group, while 4 patients (7%) withdrew in the diclofenac treatment group. Although fewer patients withdrew in the SC-58635 treatment group, but the differences between treatment groups in time to withdrawal was not statistically significant.

Efficacy Variables	SC-58635 100 mg BID	Diclofenac 50mg BID
Patient's Assessment of Arthritis Pain – VAS		
Baseline Means	43.9	44.9
Week 4+	-7.2	-5.3
Week 8+	-10.7	-6.1
Week 12+	-15.1	-9.1
Patient's Global Assessment of Arthritis		
Baseline Means	2.5	2.6
Week 4+	-0.4	-0.2
Week 8+	-0.5	-0.3
Week 12+	-0.5	-0.4
Physician's Global Assessment of Arthritis		
Baseline Means	2.5	2.6
Week 4+	-0.4	-0.2
Week 8+	-0.4	-0.3
Week 12+	-0.6	-0.4

+ Change from Baseline values are least square mean changes.
Negative values signify improvement.

Q-ratios (and 95% confidence intervals) of least square mean changes from Baseline in SC-58635 100 mg BID to diclofenac 50 mg BID treatment groups

	Week 4	Week 8	Week 12
Patient's Assessment of Arthritis Pain-VAS	1.37 (0.64, 3.91)	1.75 (0.84, 6.07)	1.65 (0.95, 3.54)
Patient's Global Assessment of Arthritis	1.85 (0.92, 6.18)	1.55 (0.88, 3.32)	1.40 (0.80, 2.82)
Physician's Global Assessment of Arthritis	1.86 (0.88, 7.31)	1.26 (0.69, 2.56)	1.37 (0.83, 2.49)

SAFETY RESULTS

In the SC-58635 treatment group 29 patients (46%) had at least one adverse event and in the diclofenac treatment group 37 patients (61%) had at least one adverse event. Thirty-three patients (52%) had no AEs in the SC-58635 treatment group while 24 patients (39%) had no AEs in the diclofenac treatment group. One patient (2%) in the SC-58635 treatment group had no AE information. No deaths occurred during the course of the study. One patient (2%) in the SC-58635 treatment group had at least one adverse event (treatment emergent surgery) causing withdrawal, while 4 patients (7%) in the diclofenac treatment group had AEs (dizziness [1], abdominal pain [2], and flatulence [1]) causing withdrawal. Three patients had serious adverse events, which were judged not related to the study medication by the investigators. Two patients (3%) in the SC-58635 treatment group had serious AEs, namely cellulitis and treatment emergent surgery. One patient (2%) in the diclofenac treatment group had a serious AE, namely soft tissue infection.

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.

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. There were no statistically significant changes in the laboratory values from baseline to Week 12, except for SGPT (ALT) where 12 patients in the diclofenac treatment group, showed an increase from normal range (N) during the baseline visit to high range (H) during the week 12 visit.

CONCLUSIONS:

In summary, the observed study results for SC-58635 are generally equivalent to or better than the results observed for diclofenac, although the treatment differences were generally not statistically significant. The safety profile in Asians (Taiwanese) is similar to that seen in the pivotal OA/RA studies conducted in the mixed populations. The safety results suggest that SC-58635 was tolerated at least as well as diclofenac and support the safety in subsets of Asian extraction.

Based on report completed: 22 March 2000