SAT0092 SUCCESS-1 IN OSTEOARTHRITIS (OA) TRIAL: CELECOXIB DEMONSTRATES SIGNIFICANTLY LOWER HEPATIC TOXICITY THAN DICLOFENAC IN THE TREATMENT OF OSTEOARTHRITIS

¹J Goldstein, ²G Singh, ³J Fort, ³A Bello. ¹Internal Medicine, University of Illinois at Chicago School of Medicine, Chicago, USA; ²Internal Medicine, Stanford University School of Medicine, Palo Alto, USA; ³Internal Medicine, Pharmacia, Peapack, USA

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Background Significant elevations of liver enzymes have been reported in patients taking NSAIDs. Among all NSAIDs, diclofenac and aspirin have been associated with the highest rates of liver toxicity. In previous trials with patients in the US and Canada treated for osteoarthritis (OA), the incidence of hepatic adverse events in patients receiving celecoxib 200 or 400 mg per day was similar to placebo and significantly lower than the incidence for patients receiving diclofenac 100 or 150 mg per day.

Objectives We compared the hepatic tolerability of celecoxib and the most commonly used regimen of diclofenac in the treatment of OA of the knee, hip, or hand in 13,274 patients enrolled in SUCCESS-1, a multinational, double-blind, randomised trial.

Methods In the SUCCESS-1 in OA trial, patients with OA from Europe and South Africa, Asia, Latin America, and the US and Canada were evaluated for 12 weeks using fixed dosages of celecoxib 200 mg per day, celecoxib 400 mg per day, or diclofenac 100 mg per day. Patients with pretreatment ALT or AST $\geq$ 3x ULN were excluded. Laboratory tests were obtained at pretreatment and at the final visits.

Results Overall, patients were mostly female (78%), and had a mean age of 62 ($\pm$ 10.4) years. Previous daily diclofenac use was comparable (p = 0.57). Clinically meaningful elevations ($\geq$ 3x ULN) in ALT and AST were significantly more frequent in the diclofenac- vs celecoxib-treated patients (p < 0.001) at 12 weeks. In parallel, physician-reported hepatic adverse events, including hepatic dysfunction and increases from pretreatment ALT and AST, were significantly more frequent in patients treated with diclofenac (p < 0.01).

Abstract SAT0092 Table 1

	Celecoxib 200 mg/d	Celecoxib 400 mg/d	Diclofenac 100 mg/d
Laboratory value elevation	n = 2988	n = 2948	n = 2998
AST $\geq$ 3x ULN at final visit	1 (<0.1%)	3 (0.1%)	20 (0.7%)*
ALT $\geq$ 3x ULN at final visit	6 (0.2%)	6 (0.2%)	45 (1.5%)*
Adverse events, incidence			
AST increased from pretreatment	11 (0.3%)	13 (0.4%)	31 (0.9%)
ALT increased from pretreatment	20 (0.6%)	15 (0.4%)	58 (1.7%)*

ULN: upper limit of normal; diclofenac vs celecoxib 200 or 400 mg/d: * p < 0.01.

Conclusion Celecoxib, with its greater hepatic tolerability than the most commonly prescribed regimen of diclofenac, offers a clinical advantage over diclofenac in the management of OA patients.

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SAT0093 SUCCESS-1 IN OSTEOARTHRITIS: CELECOXIB DEMONSTRATES SIMILAR EFFICACY TO THE CONVENTIONAL NSAIDS, DICLOFENAC AND NAPROXEN, IN PATIENTS WITH OSTEOARTHRITIS TREATED IN 39 COUNTRIES IN 6 CONTINENTS

¹G Singh, ²J Goldstein, ³J Fort, ³A Bello, ¹S Boots. ¹Department of Medicine, Stanford University, Palo Alto, USA; ²Department of Medicine, University of Illinois at Chicago Medical School, Chicago, USA; ³Department of Medicine, Pharmacia, Peapack, USA

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Background The SUCCESS-1 trial is the largest controlled study comparing celecoxib and NSAIDs. This long-term trial was intended to closely parallel clinical practice in a variety of world-wide settings to assess the overall efficacy, tolerability, and safety of celecoxib and NSAIDs with a large group of diverse physicians.

Objectives This study compared the efficacy, safety, and tolerability of celecoxib 200 and 400 mg per day and the most commonly prescribed NSAIDs in 39 countries in the treatment of the signs and symptoms of osteoarthritis (OA) of the knee, hip, and hand.

Methods The SUCCESS-1 in OA trial is a large double-blind, randomised study conducted in patients from 1,142 centres in Europe and South Africa, Asia, Latin America, and the US and Canada. Patients were treated for 12 weeks using celecoxib (200 or 400 mg/d) and the most common regimens of NSAIDs (naproxen 1000 mg/d in US and Canada and diclofenac 100 mg/d in all other countries). Assessments of arthritis efficacy were performed by country or region. Safety and tolerability were assessed globally.

Results Of the 13,194 intent-to-treat patients, the mean age was 62 years, and the majority were female (76%) and caucasian (80%). Patients in each group had comparable baseline aspirin use and history of upper GI bleeding. Arthritis assessments were based on mean changes in baseline arthritis pain by VAS and night pain at week 12. Data is presented from European countries/regions. No significant differences between celecoxib 200 mg/day and celecoxib 400 mg/day compared to diclofenac 100 mg/day were observed. In addition, celecoxib 200 mg/day and 400 mg/day were similar in efficacy. Comparable efficacy between celecoxib and NSAIDs was also demonstrated in other countries/regions that participated in the study.

Abstract SAT0093 Table 1

	Patient's Assessment of Arthritis Pain VAS, mean change, mm?	Patient's Assessment of Night Pain, mean change?		
EFFICACY	Celecoxib 200 mg/ day*	Diclofenac 100 mg/day	Celecoxib 200 mg/ day*	Diclofenac 100 mg/day
Central	-22.1	-20.4	-0.73	-0.69
Europe				
Germany	-28.3	-25.7	-0.89	-0.67
Italy	-17.6	-20.6	-0.50	-0.54
Nordic	-13.4	-14.2	-0.36	-0.38
regions				
Spain/ Portugal	-18.4	-21.0	-0.68	-0.66
UK/Ireland	-10.9	-11.9	-0.33	-0.38

?Scale: 0 = no pain to 100 = most severe pain; ?5 pt scale: 1 = very good to 5 = very poor; * p > 0.18.