Conclusion This independent-confirmatory study demonstrated that glucosamine sulfate can be postulated as the first osteoarthritis structure modifying agent. Glucosamine sulfate also improved the disease symptoms in the long-term treatment of the disease, with a safety profile similar to placebo. The action of glucosamine sulfate on both the structure and the symptoms evolution of the disease postulate it as the first osteoarthritis modifying agent.

REFERENCE

1 Lancet 2001;357:251–6

OP0053 SUCCESS-1 IN OSTEOARTHRITIS (OA) TRIAL: CELECOXIB SIGNIFICANTLY REDUCES RISK OF SERIOUS UPPER GI COMPLICATIONS COMPARED TO NSAIDS WHILE PROVIDING SIMILAR EFFICACY IN 13,274 RANDOMISED PATIENTS

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Background SUCCESS-1, the largest double-blind, randomised study in rheumatology, compared 2 therapeutic doses of celecoxib to conventional doses of NSAIDs in a trial designed to closely parallel clinical practice in various worldwide settings.

Objectives To compare the efficacy, safety, and tolerability of celecoxib 200 or 400 mg/d and NSAIDs in OA of the knee, hip, and hand.

Methods SUCCESS-1 enrolled 13,274 patients with OA from 1142 centres in 39 countries. Patients were randomised to: celecoxib 200 mg/d, celecoxib 400 mg/d, or NSAID (naproxen 1000 mg/d in US/Canada, diclofenac 100 mg/d in other 37 countries). Efficacy assessments, stratified by country/subregion, included patient and physician global assessments, pain scale, night pain, and WOMAC. An independent Gastrointestinal Events Committee (GEC) categorised potential clinically significant upper GI (UGI) events in a blinded fashion as ulcer complications (perforations, gastric outlet obstruction, bleeding) or symptomatic ulcerations.

Results Of 13,194 patients treated, 4393 and 4407 received 200 or 400 mg/d of celecoxib, respectively, 905 received naproxen 1000 mg/d, and 3489 received diclofenac 100 mg/d. Most patients were female (67%); mean age was 62 years. Baseline aspirin use and UGI bleeding history were comparable. Efficacy results between the 2 celecoxib doses and naproxen or diclofenac were comparable for most countries/subregions. UGI events (dyspepsia, abdominal pain, and nausea) were significantly reduced in celecoxib- compared to naproxen- or diclofenac-treated patients. Of 144 possible serious UGI GEC-referred events, 9 met strict ulcer complication definition and 36 patients had confirmed ulcer complications and/or symptomatic ulcers.

Abstract OP0053 Table 1

	Celecoxib (n = 8800)	NSAIDs (n = 4394)	OR, 95% CI
UGI Tol, n (%)			
Dyspepsia	422 (4.8)*	259 (5.9)	1.2 (1.1–1.5)

Abdominal pain	423 (4.8)*	274 (6.2)	1.3 (1.1–1.5)
Nausea	207 (2.4)*	151 (3.4)	1.5 (1.2–1.8)
Serious GI events, n (inc/100 pt yrs)			
Possible events?	83 (4.8)	61 (7.1)	1.5 (1.1–2.1)
Ulcer complics?	2 (0.1)*	7 (0.8)	7.0 (1.5–33.8)
Symptomatic ulcer/complics?	18 (1.0)*	18 (2.1)	2.0 (1.0–3.8)

?investigator-determined; ?confirmed; *p < 0.05.

Conclusion Compared to conventional NSAIDs, celecoxib reduced the risk of ulcer complications by almost 87.5%, while providing equivalent efficacy and better tolerability. Sponsored by Pharmacia Corporation and Pfizer Inc.

OP0133 CARDIOVASCULAR SAFETY PROFILE OF ROFECOXIB: A META-ANALYSIS

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Background COX-1 inhibition compromises GI homeostasis; however, by inhibiting platelet aggregation, COX-1 blockade is cardioprotective. COX-2 inhibitor therapy results in marked reductions in GI events relative to non-selective NSAID (COX-1/COX-2 inhibitor) therapy. Because COX-2 inhibitors do not have antiplatelet properties, chronic use of COX-2 inhibitors or non-selective NSAIDs may result in differential risks of platelet-mediated vascular events. Evaluation of the impact of these agents on vascular events is complicated by the variable effects of NSAIDs on platelet aggregation. NSAIDs that mediate near complete inhibition of platelet function throughout their entire dosing cycle may be similar to aspirin and reduce the risk of vascular events; other compounds with less substantial platelet inhibition may have no impact on vascular events.

Objectives To evaluate the cardiovascular (CV) safety profile of rofecoxib, a selective COX-2 inhibitor.

Methods A meta-analysis of all Phase IIb-V clinical trials was conducted using individual patient data and focusing on the relative risk of CV thrombotic serious adverse experiences in patients taking rofecoxib as compared to placebo, naproxen (an NSAID with near complete inhibition of platelet function throughout its dosing interval), and non-selective NSAIDs that lack potent sustained inhibition of platelet function (diclofenac, ibuprofen, and nabumetone). The primary metric utilised was the Antiplatelet Trialists' Collaboration (APTC) combined endpoint of cardiovascular or unknown death, stroke, or myocardial infarction.

Results Over 28,000 patients in 19 studies (Osteoarthritis, Rheumatoid Arthritis, Alzheimer's, and Chronic Low Back Pain trials) representing over 14,000 patient-years at risk were included in the meta-analysis. The relative risk (95% CI) for an APTC combined endpoint was: 0.59 (0.37, 0.94) when comparing naproxen (n = 7870) vs. rofecoxib (n = 9083); 1.27 (0.64, 2.50) when comparing non-naproxen NSAIDs (n = 2755) vs. rofecoxib (n = 4549); 1.19 (0.73, 1.96) when comparing placebo (n