SBP and DBP compared to celecoxib despite providing superior efficacy as determined by PGART and WOMAC.

SAT0096 GASTROINTESTINAL TOLERABILITY IN PRIMARY CARE PATIENTS TREATED WITH NAPROXEN OR ROFECOXIB FOR OSTEOARTHRITIS (OA): THE ADVANTAGE TRIAL

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Background Chronic treatment with dual cyclo-oxygenase (Cox-1/Cox-2) inhibitors is known to increase the risk of serious gastrointestinal (GI) adverse events (AE). Rofecoxib, a selective inhibitor of Cox-2 (coxib) exhibits an efficacy profile comparable to dual Cox-1/Cox-2 inhibitors. In a meta-analysis of several OA trials and in a large prospective study of RA patients, rofecoxib resulted in a markedly lower incidence of serious GI outcomes (i.e. perforation, ulcer and GI bleeding) versus comparator NSAIDs.

Objectives To assess the GI tolerability of rofecoxib compared to naproxen in the treatment of patients with OA in the primary care setting.

Methods 5597 patients with OA were treated for 3-months in a randomised, controlled trial conducted in the U. S. and Sweden. Patients with clinically defined OA of the knee, hip, hand or spine previously treated with an NSAID, coxibs, or acetaminophen were randomised to receive either naproxen (500 BID) or rofecoxib (25 mg QD). Patients using low dose aspirin for cardiovascular prophylaxis were allowed to enter the trial. The primary endpoint was GI tolerability as defined by the incidence of discontinuations due to any GI AEs. The secondary endpoint was usage of concomitant GI medication to treat GI symptoms initiated during the study. Efficacy and overall safety and tolerability were assessed at office visits at baseline, 6 and 12 weeks and by telephone at weeks 3 and 9.

Results The majority of patients were female (71%). The mean age was 63 + 11 years. The racial composition was White (87%), African American (9%), and other racial origin (4%). 12% used low dose aspirin during the trial. The primary study joints were: knee (50%), spine (24%), hand (16%) and hip (10%). In 90% of patients, joints other than their primary joint were involved by OA. 92% had OA symptoms for more than one year. For prior OA therapy, 62% of patients used single therapy with NSAIDs, 7% used acetaminophen alone, and 30% used both. The most common cardiovascular and GI secondary diagnoses at study entry were hypertension (45%) and heartburn (13%). Treatment groups were similar in baseline characteristics. The primary hypothesis, that there would be lower incidence of discontinuations due to GI AEs in patients treated with rofecoxib, was confirmed (rofecoxib: 5.9%; naproxen: 8.1%; $p = 0.005$). The secondary hypothesis, that rofecoxib patients would require less GI concomitant medication than naproxen patients, also was confirmed (rofecoxib: 9.1%; naproxen: 11.2%, $p = 0.014$). The incidences of lower extremity oedema (rofecoxib: 3.5%, naproxen: 3.8%) and hypertension (rofecoxib: 2.9%, naproxen: 2.5%) were similar. Concomitant use of low dose aspirin, did not significantly affect relative rates of discontinuation due to AEs, serious AEs or drug related AEs. No significant difference in OA efficacy was noted between treatments for Patient

Global Assessment of Disease Status [Wk 6: 11.6 mm and 10.8 mm; Wk 12: 10.4 mm and 9.6 mm; for rofecoxib and naproxen, respectively), the AUSCAN OA Hand Index or incidence of discontinuation due to lack of efficacy.

Conclusion In patients with OA of the knee, hip, hand or spine, which included patients concomitantly treated with low dose aspirin, rofecoxib 25 mg QD demonstrated superior GI tolerability and resulted in significantly less use of concomitant GI medications while demonstrating similar efficacy compared to naproxen 500 mg BID.

SAT0097 SUCCESS IN OSTEOARTHRITIS (OA) TRIAL: CELECOXIB SIGNIFICANTLY REDUCES THE RISK OF UPPER GASTROINTESTINAL (UGI) HOSPITALIZATIONS COMPARED TO DICLOFENAC AND NAPROXEN IN 13,274 RANDOMISED PATIENTS WITH OA

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Background NSAIDs increase the risk of serious GI hospitalizations, with studies demonstrating 5–7x increases in risk (1%? 1.5% NSAID vs 0.1%–0.2% background rates). Additionally, GI-related hospitalizations impose higher cost on payers.

Objectives To compare the incidence of upper GI (UGI) hospitalizations in OA patients exposed to celecoxib, a COX-2 specific inhibitor, or conventional NSAIDs (diclofenac or naproxen).

Methods SUCCESS-1 in OA was a 12-week, multinational, double-blind, randomised trial in 13,274 patients, designed to reflect standard clinical practice. 6547 patients from Europe and Africa; 2756 from North America; 2889 from Latin America and 1082 from Australasia were enrolled. Patients were treated with celecoxib (200 mg/d [n = 4421] or 400 mg/d [n = 4429]) or conventional NSAIDs (naproxen 1000 mg/d [n = 914] or diclofenac 100 mg/d [n = 3510]). An independent Gastrointestinal Events Committee (GEC) categorised potential clinically significant UGI events in a blinded fashion as UGI ulcer complications (perforations, gastric outlet obstruction, bleeding) or symptomatic UGI ulcerations. UGI hospitalizations are reported as GI body system code events, investigator-determined potential UGI events, and GEC-confirmed ulcers/ulcer complications.

Results

Abstract SAT0097 Table 1

	Treatment	Hospitalised, n	Rate*	RR(95% CI)	p-value
All GI Hospitalizations	Celecoxib	22	1.17	0.50 (0.28, 0.90)	0.022
	NSAIDs	22	2.34	–	–
Investigator UGI Ulcers + Ulcer Complications	Celecoxib	20	1.06	0.48 (0.26, 0.88)	0.018
	NSAIDs	21	2.23	–	..

GEC UGI Ulcers + Ulcer Complications	Celecoxib	6	0.32	0.25 (0.09, 0.67)	0.006
	NSAIDs	12	1.27	–	–

*Per 100 pt yr exposure (duration from first dose to hospitalisation, or to last contact); celecoxib: 1883 pt-yrs, NSAIDs: 942 pt-yrs.

Conclusion UGI hospitalisation rates were 2–4x lower, and less UGI-related healthcare resources were utilised for celecoxib- vs NSAID-treated patients. The incidence of serious clinical UGI safety endpoints was significantly lower in the celecoxib-treated patients. Sponsored by Pharmacia Corporation and Pfizer, Inc.

SAT0098 COX-2 SPECIFIC INHIBITORS – IS THERE ANY BENEFIT OF USING THESE AGENTS IN PATIENTS ON LOW DOSE ASPIRIN (ASA)?

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Background COX-2 specific inhibitors have been shown to significantly reduce the risk of gastrointestinal complications compared to conventional NSAIDs, while providing equivalent efficacy. However, there is significant controversy regarding the UGI safety and tolerability benefits of COX-2 specific inhibitors, such as celecoxib, in patients on concomitant low-dose ASA (<325 mg/day) for cardiovascular protection.

Objectives To evaluate the UGI tolerability and safety of celecoxib 200 or 400 mg per day and the commonly prescribed conventional NSAIDs (diclofenac or naproxen) in patients taking ASA in SUCCESS-1, a large multinational double-blind, randomised study.

Methods SUCCESS-1 enrolled 13,274 patients from 1,142 centres in 39 countries 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 NSAIDs (naproxen 1000 mg/d in US and Canada and diclofenac 100 mg/d in all other countries). Adverse events were captured at week 6 and week 12 using standard adverse assessment ascertainment. In addition, all investigator-identified potentially clinically significant UGI events were referred to an independent Gastrointestinal Events Committee (GEC), which reviewed all data in a blinded fashion. Events were categorised as UGI ulcer complications (perforations, gastric outlet obstruction, bleeding), symptomatic UGI ulcerations or other GI events.

Results Of the 13,194 patients randomised in the SUCCESS-1 trial, 4421 and 4429 patients received 200 or 400 mg per day of celecoxib respectively, 914 patients received 1000 mg per day of naproxen, and 3510 patients received 100 mg per day of diclofenac. Patients were mostly female (67%), and 42% were 65 years or older (mean age: 62 years). Patients in each group had comparable baseline aspirin use and past history of upper GI (UGI) bleeding. A total of 697 patients took celecoxib and ASA. In the NSAID arm, 348 patients took concomitant ASA.

Abstract SAT0098 Table 1

	UGI SAFETY	Celecoxib and ASA (n = 697)	NSAIDs and ASA (n = 348)	Celecoxib without ASA (n = 8103)	NSAIDs without ASA (n = 4046)
Serious UGI events/100 pt yrs (n)					
Possible UGI events (investigator determined)		10 (13)	17.4 (11)	4.4 (70)	6.3 (50)
Confirmed Ulcer complications		0.8 (1)	1.6 (1)	0.1 (1)	0.8 (6)
Confirmed Ulcer complications/symptomatic ulcers		2.3 (3)	6.3 (4)	0.9 (15)	1.8 (14)

In the non-ASA groups, patients on celecoxib experienced risk reduction of 30–88% in serious UGI events compared to conventional NSAIDs. In ASA groups, patients on celecoxib experienced risk reduction of approximately 43–63%.

Conclusion Risk reduction with celecoxib and ASA is lower than risk reduction in patients not taking ASA. However, the magnitude of this risk reduction is clinically significant. Therefore, celecoxib continues to have a role in reducing risk of UGI complications even in patients on low dose ASA.

Metabolic and crystal arthropathies

AB0152 THE DIFFERENTIAL DIAGNOSTIC SPECIFICITIES OF PURINE ENZYMES ACTIVITY IN RHEUMATOID ARTHRITIS AND GOUT

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Background The clinical picture of gouty arthritis (GA) and rheumatoid arthritis (RA) can be quite often much alike, and the differential diagnosis of these diseases is rather difficult. The GA and RA patients often have hyperuricemia, which is indicative of purine metabolism breaches in patients with these diseases.

Objectives To study differential diagnostic specificity of Purine enzymes activity in Rheumatoid arthritis and Gout.

Methods We observed 71 RA patients. The mean age of the patients $\pm$ 43.2 $\pm$ 3.6 years. The mean duration of the disease – 11.9 $\pm$ 3.6 years. I degree of RA activity was determined in 17 (23.94%), II $\pm$ in 44 (61.97%), III $\pm$ in 10 (14.09%) observations. 34 Gout patients were examined. The mean age of the patients $\pm$ 48.2 $\pm$ 2.2 years. The mean duration of the disease 8.8 $\pm$ 1.3 years. The intermittent form of Gout was determined in 21 (61.8%), the chronic form $\pm$ in 13 (38.2%) observations. Adenosin deaminase (ADA), AMP-desaminase (AMPDA), Xanthine dehydrogenase (XDG), Xanthine oxidase (XO) activities were measured with spectrophotometer, ADA, XDG isoenzymes were examined with method of electrophoresis in agarose gel and obtained enzymograms were evaluated at densitometry.

Results XDG activity was more high, XO/XDG activities ratio was less in Gout patients in comparison with RA patients (I