ranged from 50 to 82 years, with a mean of 63.9. Twenty (mean age at operation, 62.6 years) of them were administered EHDP, and the rest 20 (mean age at operation, 65.1 years) were not administered the agent. The administration was initiated within 2 weeks postoperatively at a daily dose of 600–1000 mg, and continued for 12 weeks. The patients were clinically evaluated 4, 8, 12, 24, and 96 weeks and 8 years after the start of administration. The Finermann's classification was used for radiological evaluation of ectopic bone formation.

Results The incidences of ectopic bone formation 24, 96 weeks and 8 years after the start of administration in the group administered EHDP (EHDP group) were 15%, 25%, and 30%, respectively, while the corresponding values in the non-administration (control) group were 30%, 40%, and 45%, respectively. Within 12 weeks after operation, the ectopic bone formation occurred in 33% of all patients with the ectopic bone formation and 17% of the patients administered EHDP. According to the Finermann's classification, grade 1 was observed in 67%, grade 2 in 22%, and grade 3 in 11% of all patients with the ectopic bone formation 24 weeks postoperatively, while grade 1 was observed in 73% and grade 2 in 13% grade 3 in 14% 8 years postoperatively.

Conclusion The incidence of ectopic bone formation has been reported to range from 15% to 90% in Western countries. In contrast, the incidence in Japan is 15.7–38.5%, being lower than in Western countries. The severity has also been reported to be mild in Japan, as compared to cases in Western countries. In our data, the incidences were 20% and 30% in the control and EHDP groups, respectively, 24 weeks postoperatively, and the mildest grade 1 accounted for 67%. The ectopic bone formation manifested within 12 weeks after operation in 13% of the patients who had the condition, showing that the occurrence was suppressed during this period. These results suggest that the administration is efficacious for postoperatively early prevention of ectopic bone formation and that the indications for the administration must be taken into much consideration.

SAT0057 A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFECTS OF VALDECOXIB, A NOVEL COX-2 SPECIFIC INHIBITOR, ON PLATELET FUNCTION IN THE ELDERLY

¹PT Leese, ²D Recker, ²ME Kuss. ¹Medical Scientific Services, Quintiles Phase I Services, Lenexa; ²Research and Development, Pharmacia Corporation, Skokie, USA

10.1136/annrheumdis-2001.432

Background Valdecoxib is a novel oral COX-2 specific inhibitor. COX-2 specific inhibitors effectively treat pain and inflammation without causing many of the side effects commonly associated with conventional NSAIDs.

Objectives The purpose of this study was to compare the effects of valdecoxib to ibuprofen on platelet function in healthy subjects, > = 65 years of age.

Methods In this single-centre, double-blind, placebo-controlled, parallel-group study, 65 healthy adults, aged 65–95 years, were randomised to receive valdecoxib 40 mg BID, ibuprofen 800 mg TID, or placebo for 7.5 days. Platelet aggregation in response to arachidonate (AA), adenosine diphosphate (ADP), or collagen; serum thromboxane B₂ (TxB₂) concentrations; and Simplate II bleeding times were assessed at 2, 4, and 8 h after dosing on Days 1 and 8. Vital signs and adverse events were monitored throughout the study.

Results Platelet aggregation responses to AA, collagen, and ADP were not affected by treatment with valdecoxib 40 mg BID. In contrast, ibuprofen resulted in marked decreases in AA-induced platelet aggregation at the 2 h and 4 h assessments on Days 1 and 8. The effects of ibuprofen on platelet aggregation in response to collagen and ADP were not as great as seen with AA. However, for all three stimuli, ibuprofen demonstrated significantly greater decreases in platelet aggregation compared to placebo and valdecoxib at several time points. Valdecoxib 40 mg BID had no effect on bleeding times or serum TxB₂ concentrations compared to placebo. Bleeding times were significantly prolonged ($p < 0.013$) and serum TxB₂ concentrations significantly reduced ($p < 0.026$) in ibuprofen-treated subjects.

Abstract SAT0057 Table 1

	Placebo	Valdecoxib 40 mg BID	Ibuprofen 800 mg TID
Med. change 30 min	-3.0	-2.0	-1.0
Med. change 2 h	-2.0	1.0*	-70.0**
Med. change 4 h	-1.0	0.0*	-60.0**
Med. change 8 h	-2.0	-2.0	-1.0

Platelet Aggregation Response to Arachidonate (%), Median Change From Baseline After Final Dose on Day 8 (* $p \leq 0.05$ vs ibuprofen, ** $p < 0.05$ vs placebo).

Conclusion Valdecoxib 40 mg BID does not affect platelet function, serum TxB₂ levels or bleeding times, and is well tolerated in healthy elderly subjects. However, ibuprofen significantly alters hemostasis. These findings suggest that valdecoxib can provide its previously demonstrated analgesic and anti-inflammatory therapeutic benefits without negatively influencing platelet function in subjects > = 65 years.

Sponsored by Pharmacia Corporation and Pfizer, Inc.

SAT0058 THE NOVEL COX-2 SPECIFIC INHIBITOR, VALDECOXIB, DOES NOT AFFECT PLATELET FUNCTION IN HEALTHY ADULTS

¹PT Leese, ²D Recker, ²ME Kuss. ¹Medical Scientific Services, Quintiles Phase I Services, Lenexa; ²Research and Development, Pharmacia Corporation, Skokie, USA

10.1136/annrheumdis-2001.433

Background Conventional NSAIDs have traditionally been used to manage pain and inflammation; however, as nonspecific inhibitors of cyclooxygenase (COX-1 and COX-2), they are associated with significant adverse events, including impaired platelet function.

Objectives The purpose of this study was to compare the effect of valdecoxib, a new COX-2 specific inhibitor, on platelet aggregation and bleeding time to that of the conventional NSAIDs, naproxen and diclofenac.

Methods This was a single-centre, double-blind, randomised comparison of valdecoxib 40 mg BID, naproxen 500 mg BID, diclofenac 75 mg BID, and placebo in healthy adult subjects. Sixty-two subjects received active medication or placebo for 7.5 days. Platelet aggregation responses to arachidonate (AA), collagen, and adenosine diphosphate (ADP); Simplate II bleeding times; and serum thromboxane (Tx) B₂ concentrations were measured at baseline; 30 min predose, 2, 4, and 8 h postdose on Day 1; and 2, 4, and 8 h after the final dose on Day 8.