Drugs 2004; 64 (19): 2247-2248
0012-6667/04/0019-2247/$34.00/0

Lumiracoxib
A Viewpoint by Hyman Tannenbaum

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In 1999, the WHO designated a new subclass of NSAIDs, which were termed coxibs. Coxibs distinguish themselves from the nonselective NSAIDs by selectively inhibiting the cyclo-oxygenase (COX)-2 enzyme. Celecoxib and rofecoxib, which have sulfonamide and methylsulfone side-chains, respectively, were among the first generation of coxibs. More recently, a second generation of coxibs (valdecoxib, etoricoxib and lumiracoxib), which have greater potency in inhibiting the COX-2 enzyme than their predecessors, have been developed.

Lumiracoxib differs structurally from the other coxibs; it is a phenylacetic acid compound and is more structurally related to diclofenac and other acidic NSAIDs. It lacks the tricyclic structure of the other coxibs and contains no sulfonamide or sulfone group. It is currently the most selective of the coxibs, with a 500-fold greater selectivity for the COX-2 than COX-1 enzyme.[1]

In clinical trials, lumiracoxib appears to be an effective drug for use in patients with acute pain, dysmenorrhoea, osteoarthritis (OA) or rheumatoid arthritis (RA), and has an improved gastrointestinal (GI) tolerability and safety profile compared with nonselective NSAIDs.[2-8] Lumiracoxib, in head-to-head comparisons, is equally as effective as celecoxib and diclofenac in OA and as naproxen in RA.[2,9,10] In endoscopic studies in patients with either OA or RA, lumiracoxib was associated with fewer gastroduodenal ulcerations than ibuprofen and a similar number to celecoxib.[5,6]

TARGET (the Therapeutic Arthritis Research and GI Event Trial) was the largest safety outcome study (n = 18 325) ever undertaken to evaluate the GI and cardiovascular safety of a coxib.[7,8] In this 1-year double-blind, randomised trial, lumiracoxib 400 mg once daily (two or four times the recommended dose in OA) was compared with either ibuprofen (800mg three times daily) or naproxen (500mg twice daily) in patients aged ≥50 years with OA. About one-quarter of the patients were on concomitant low-dose aspirin (acetylsalicylic acid; 75–100 mg/day) for cardiovascular prophylaxis. The primary endpoint was the difference in time-to-event distribution of upper GI ulcer complications (perforation, obstruction and bleeding). The incidence of adverse cardiovascular events was also prospectively planned.

In patients not using aspirin, a 79% reduction in the development of ulcer complications was demonstrated in patients taking lumiracoxib (0.25%) compared with patients using the nonselective NSAIDs (1.09%). Although there was a 21% reduction in ulcer complications in those patients using concomitant aspirin, there was no significant benefit of lumiracoxib over non-selective NSAIDs. In contrast with the augmented adverse thrombotic cardiovascular events noted with rofecoxib in the VIGOR (Vioxx GI Outcomes Research) trial,[11] no significant increase in adverse cardiovascular events was observed with lumiracoxib when compared with the nonselective NSAIDs ibuprofen or naproxen. Liver transaminase levels more than three times the upper limit of normal were observed in 2.6% of the patients receiving lumiracoxib compared with 0.6% of patients on nonselective NSAIDs. However, lumiracoxib was administered at supratherapeutic dosages in this safety study and all liver abnormalities resolved fully after drug discontinuation.

Lumiracoxib appears to offer effective pain relief with GI safety and without any associated cardiovascular risk, and will be a useful alternative for patients who require either a nonselective NSAID or COX-2-selective inhibitor for management of arthritis. ▲

References

1. Marshall PJ, Berry C, Wasvary J, et al. The *in vitro* and *in vivo* selectivity of COX189, a new and highly selective inhibitor of COX-2 [abstract no. SAT0013]. Ann Rheum Dis 2002; 61 Suppl. 1: 259
2. Tannenbaum H, Berenbaum F, Reginster JY, et al. Lumiracoxib is effective in the treatment of osteoarthritis of the knee: a 13-week, randomized, double-blind study versus placebo and celecoxib. Ann Rheum Dis. Epub 2004 Feb 27
3. Bitner M, Kattenhorn J, Hatfield C, et al. Efficacy and tolerability of lumiracoxib in the treatment of primary dysmenorrhoea. Int J Clin Pract 2004 Apr; 58 (4): 340-5
4. Pavelka K, Nayiager S, Kivitz A, et al. Efficacy and tolerability of lumiracoxib in the treatment of rheumatoid arthritis: a 13-week, randomized, double-blind study [abstract no. FRI10107]. Ann Rheum Dis 2004 Jul; 63 Suppl. 1: 280
5. Kivitz AJ, Nayiager S, Schimansky T, et al. Reduced incidence of gastroduodenal ulcers associated with lumiracoxib compared with ibuprofen in patients with rheumatoid arthritis. Aliment Pharmacol Ther 2004 Jun 1; 19 (11): 1189-98

6. Hawkey CJ, Karateev D, Codreanu C, et al. Improved upper gastrointestinal (UGI) safety and tolerability of a new coxib, COX189 compared with ibuprofen in osteoarthritis patients [abstract no. THU0226]. Ann Rheum Dis 2002; 61 Suppl. 1: 126
7. Schnitzer TM, Burmester GR, Mysler E, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutics Arthritis Research and Gastrointestinal Event Trial (TARGET), reduction in ulcer complications: randomised controlled trial. Lancet 2004 Aug 21; 364 (9435): 665-74
8. Farkouh ME, Kirshner H, Harrington RA, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutics Arthritis Research and Gastrointestinal Event Trial (TARGET), cardiovascular outcomes: randomised controlled trial. Lancet 2004 Aug 21; 364 (9435): 675-84
9. Schnitzer TJ, Beier J, Geusens P, et al. Efficacy and safety of four doses of lumiracoxib versus diclofenac in patients with knee or hip primary osteoarthritis: a phase II, four-week, multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Care Res 2004; 51 (4): 549-57
10. Geusens P, Alten R, Rovensky J, et al. Efficacy, safety and tolerability of lumiracoxib in patients with rheumatoid arthritis: results of a randomized double-blind study [abstract no. 544]. Arthritis Rheum 2003; 48 (9 Suppl.): 242
11. Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis: VIGOR study group. N Engl J Med 2000 Nov 23; 343 (21): 1520-8