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Lumiracoxib
A Viewpoint by Paola Patrignani

Department of Medicine and Center of Excellence on Aging, School of Medicine, G. d'Annunzio University, Chieti, Italy

Lumiracoxib, a diclofenac analogue, is a second-generation cyclo-oxygenase (COX)-2-selective inhibitor (coxib). In randomised clinical trials, it has shown similar clinical efficacy to nonselective NSAIDs and the first generation of coxibs (i.e. celecoxib and rofecoxib) in the treatment of osteoarthritis (OA), rheumatoid arthritis and acute pain.

Lumiracoxib has peculiar pharmacodynamic and pharmacokinetic features versus other COX-2-selective inhibitors. In fact, it is characterised by the highest COX-2 selectivity (i.e. COX-1 **:** COX-2 concentrations required to inhibit 50% of enzyme activity ratio) *in vitro* and the shortest half-life (3–6 hours). It remains to be determined whether its once-daily administration (which is associated with no dose-accumulation kinetics) will translate into reduced inhibitory effects on the biosynthesis of renal prostanoids and systemic prostacyclin as a consequence of reduced drug exposure. This may have contributed to the lack of statistically significant differences in the incidences of myocardial infarction (MI), elevation of blood pressure or development of congestive heart failure between lumiracoxib and the nonselective NSAIDs naproxen and ibuprofen in TARGET (the Therapeutic Arthritis Research and Gastrointestinal Event Trial). However, the trial had inadequate statistical power to detect significant differences in rates of MI in the patients enrolled, who were generally at low risk of cardiovascular events.

The results of TARGET have shown that patients receiving lumiracoxib had a significant 79% reduction in complicated ulcers relative to patients randomised to the nonselective NSAIDs ibuprofen or naproxen. However, this benefit was almost annulled by the coadministration of low-dose aspirin (acetylsalicylic acid), an obligatory therapeutic strategy in patients at intermediate-to-high risk of cardiovascular events. Furthermore, increased hepatotoxicity was detected in patients receiving lumiracoxib.

Further studies are required to assess the occurrence of interpatient pharmacokinetic and pharmacodynamic variability with lumiracoxib, which is a more predictable determinant of therapeutic responses and adverse effects than the COX-1 **:** COX-2 ratio *in vitro*.

In conclusion, lumiracoxib has comparable clinical efficacy to that of other coxibs and nonselective NSAIDs. The drug is associated with improved gastrointestinal safety compared with nonselective NSAIDs, but this benefit is countered by the coadministration of low-dose aspirin and an increased incidence of hepatotoxicity. In patients with OA at low risk of cardiovascular events, no significant differences between lumiracoxib and nonselective NSAIDs in the incidences of MI or renal adverse events were detected. Unfortunately, the cardiovascular consequence of selective COX-2 inhibition by lumiracoxib in patients at high cardiovascular risk is still unknown. ▲