

## Rofecoxib

### A Viewpoint by Kenneth Saag

Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Alabama, USA.

Rofecoxib is one of only 2 truly cyclo-oxygenase-2 (COX-2) selective nonsteroidal anti-inflammatory drugs (NSAIDs) currently being developed in many countries. It has equal efficacy to ibuprofen and diclofenac and was significantly superior to placebo in clinical trials of osteoarthritis-related pain. Of even greater interest, rofecoxib is statistically indistinguishable from placebo and considerably less likely than nonselective NSAIDs to induce endoscopically documented gastric and duodenal lesions in trials of short duration. Although this finding is encouraging, larger long term studies evaluating gastrointestinal (GI) bleeding as the ultimate outcome of GI safety are eagerly awaited. The fact rofecoxib does not prolong bleeding time, an effect significantly different from that seen with ibuprofen, provides further evidence of a clinically meaningful benefit compared with traditional NSAIDs.

Rofecoxib and other COX-2-specific agents, however, do not offer a superior renal tolerability pro-

file because of the presence of COX-2 receptors in the kidney. As such, caution is required when administering this and other NSAIDs to patients with difficult-to-control hypertension and intravascular volume depletion. Rofecoxib is extensively metabolised by predominately non-cytochrome P450 cytosolic enzymes in the liver and, thus, it appears to interact with very few drugs metabolised by this pathway. The relatively long elimination half-life of rofecoxib (approximately 17 hours) may allow for true once daily dosing.

At this time, unresolved issues with regard to rofecoxib are its use in the relatively understudied high risk elderly patient population who may be preferentially administered this agent, and tolerability and efficacy comparisons with 'safer' traditional NSAIDs (such as nonacetylated salicylates) as well as with other COX-2-selective NSAIDs (e.g. celecoxib). Although current data indicate that rofecoxib has considerable tolerability advantages and equal efficacy when compared with traditional NSAIDs, confirmation of its long term tolerability will ultimately influence who receives this and other COX-2-specific agents from a societal cost-effectiveness perspective. ▲