Celecoxib Gets Another Look

In the recently published Celecoxib Versus Omeprazole and Diclofenac in Patients With Osteoarthritis and Rheumatoid Arthritis (CONDOR) trial, investigators compared the risk of gastrointestinal (GI) events associated with cyclo-oxygenase (COX)-2-selective non-steroidal anti-inflammatory drugs (NSAIDs) vs nonselective NSAIDs plus a proton-pump inhibitor. They found the rate of clinically significant GI events was 4 times higher in study participants taking diclofenac plus omeprazole than in those taking celecoxib.

The CONDOR researchers conducted a 6-month, double-blind, randomized trial involving patients from 196 active centers worldwide with osteoarthritis or rheumatoid arthritis who were at increased GI risk. Patients aged 18 to 59 years were included only if they had a documented history of gastroduodenal ulceration or GI hemorrhage more than 90 days prior to screening, while patients aged 60 years and older were included with or without a history of gastroduodenal ulceration or GI hemorrhage. Inclusion criteria also included testing negative for *Helicobacter pylori*.

The patients were assigned randomly in a 1:1 ratio to receive either celecoxib 200 mg twice per day or diclofenac slow release 75 mg twice per day plus omeprazole 20 mg once per day for 6 months. After randomization, patients returned to the clinic at months 1, 2, 3, and 6 for assessment. The primary endpoint was a composite of clinically significant events occurring throughout the GI tract, and intention to treat analysis was performed on the data.

A total of 2,238 patients received celecoxib and 2,246 patients received diclofenac plus omeprazole. Of the 281 patients who withdrew early because of GI adverse events, 114 (6%) were in the celecoxib group and 167 (8%) were in the diclofenac plus omeprazole group. Twenty patients in the celecoxib group (0.9%) and 81 patients in the diclofenac plus omeprazole group (3.8%) met criteria for the primary endpoint. (The researchers say the driving force behind the primary endpoint was a hemoglobin level decrease of 20 g/L or more.) Fifteen patients in the celecoxib group and 77 patients in the diclofenac plus omeprazole group had a significant decrease in hemoglobin level.

As in the researchers' earlier trial, rates of upper GI bleeding did not differ between treatment groups. However, the researchers noted large differences for the likelihood of clinically significant blood loss from the GI tract. For patients with substantial decreases in hemoglobin and defined lesions, the data "support the contribution of the upper gastrointestinal tract as a potential site of blood loss," the researchers say. Notably, the frequency of upper GI ulcers or erosions associated with hemoglobin reductions was significantly higher in the diclofenac plus omeprazole group than in the celecoxib group.

Reductions in hemoglobin level in the absence of a defined lesion were more than 5 times more likely for patients receiving diclofenac plus omeprazole than for those receiving celecoxib. Celecoxib also was associated with a lower rate of moderate-to-severe abdominal symptoms and withdrawal because of GI adverse events. The small but significant differences contradict the results of a recent meta-analysis in which authors suggested co-therapy with nonselective NSAIDs plus a PPI was better tolerated than therapy with a COX-2 selective NSAID alone, the researchers say, although they note the meta-analysis was hampered by a scarcity of head-to-head data.

They say that their study has provided new relevant data that may help reduce the risk associated with NSAID treatment. As guidelines recommend that selection of NSAID therapy should be based on consideration of both cardiovascular and GI effects of treatment, other trials are required to further understand the cardiovascular outcomes of these 2 strategies of GI risk reduction.

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