Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis
Chan FKL. N Engl J Med 2002;347:2104-10 (December 26)

Study Type: POEM

Purpose: Does celecoxib or diclofenac + omeprazole reduce the risk of recurrent ulcer bleeding in patients at high risk?

Study Duration: 6 months; n = 290

Patients: ~67 years; ~65% female; ~68% white, 5% black; ~10 to 14% smoke; 9 to 11% drink, 6:3:1 location of bleeding ulcer (gastric or duodenal to gastric+duodenal; ~ 21% had more than one gi bleed; ~ 16% with an ulcer > 2 cm; ~ 20% with a SCr > 1.2; 85% with OA vs 4% with RA and 4% other

Trial Design: double-blinded, randomized, from China (one Center), intention-to-treat, 200 mg celecoxib bid + placebo daily verses diclofenac extended release 75 mg bid + omeprazole 20 mg daily for 6 mths

Patients could take: antacids, acetaminophen, low-dose aspirin, non-NSAID analgesics, DMARDs

Prohibited meds: other NSAIDs, misoprostol, H2-blockers, sucralfate, other PPI’s

Inclusion: patients who present with a bleeding ulcer confirmed by endoscopy; ulcer healing confirmed by follow-up endoscopy; negative h.pylori

Exclusion: anticoagulants; corticosteroids; a history of gastric surgery; presence of erosive esophagitis; gastric-outlet obstruction; renal failure (SCr > 2.2); terminal illness, cancer

Primary Outcome Events: recurrent bleeding

Secondary outcomes: efficacy of treatments, recurrent bleeding among those not taking low-dose aspirin, adverse effects

1. Are the results valid?
   * randomized? yes
   * double-blinded? yes
   * placebo-controlled? no
   * patient accountability? yes
   * were groups similar? not real sure, no p-values in table, seems to be more gastric ulcers in celecoxib group (60% vs 56%); there were twice as many patients with both gastric and duodenal ulcers in diclofenac combo group (11% vs 4%)

2. What were the results?
   * No difference between the two groups in global assessment of disease activity or arthritis pain
   * Those discontinuing the drug based on a lack of efficacy was low (2.8% in celecoxib vs 2.1% in diclofenac + omeprazole)
   * there were 16 cases of recurrent ulcer bleeds - 7 in the celecoxib grp and 9 in the diclofenac/omeprazole grp
   * all but one bleed was gastric
   * 6 required endoscopic control of bleeding; 4 needed a blood transfusion of 3 units
   * Probability of recurrent ulcer was 4.9% in the celecoxib grp and 6.4% in diclofenac/omeprazole grp, p = NS

<table>
<thead>
<tr>
<th>Adverse effects</th>
<th>Celecoxib</th>
<th>diclofenac + omeprazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>dyspepsia</td>
<td>15.3%</td>
<td>8.4%</td>
</tr>
<tr>
<td>Nausea, heartburn, diarrhea</td>
<td>0.7%</td>
<td>1.4%</td>
</tr>
<tr>
<td>hypertension</td>
<td>13.9%</td>
<td>18.9%</td>
</tr>
<tr>
<td>renal failure</td>
<td>5.6%</td>
<td>6.3%</td>
</tr>
<tr>
<td>MI</td>
<td>0.7%</td>
<td>0</td>
</tr>
</tbody>
</table>

   There were no statistical differences between groups

3. Will the results help me?
   * one patient died in the omeprazole + diclofenac group of peritonitis from multiple perforations and small bowel infarction
   * neither regimen fully protected against recurrent bleeds
   * The authors conclude that “among patients with a history of ulcer bleeds, treatment with celecoxib was as effective as treatment with diclofenac + omeprazole with respect to recurrent bleeding”.
   * If a patient is currently taking a PPI, and needs an NSAID, it seems reasonable to use a traditional generic NSAID instead of a COX-2.
   * We need data on a COX-2 + a PPI.