

# Rofecoxib, 25 mg/d, was more effective than rofecoxib, 12.5 mg/d, celecoxib, or acetaminophen in osteoarthritis of the knee

Geba GP, Weaver AL, Polis AB, Dixon ME, Schnitzer TJ, for the VACT Group. Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee. A randomized trial. JAMA. 2002 Jan 2;287:64-71.

## QUESTION

In patients with symptomatic osteoarthritis (OA) of the knee, are rofecoxib, celecoxib, and acetaminophen effective and safe?

## DESIGN

Randomized {allocation concealed\*}†, blinded {clinicians, patients, data collectors and analysts, and outcome assessors}†, \* controlled trial with 6-week follow-up.

## SETTING

29 clinical centers in the United States.

## PATIENTS

382 patients  $\geq 40$  years of age (mean age 63 y, 68% women) who had symptomatic OA of the knee for  $\geq 6$  months (American College of Rheumatology criteria and functional class rating of I, II, or III), used non-steroidal anti-inflammatory drugs (NSAIDs) or high-dose acetaminophen for  $\geq 30$  days before study entry, and met relevant entry criteria based on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (a visual analog scale [VAS] ranging from 0 [best] to 100 mm [worst]) and a global assessment measure. Exclusion criteria included pregnancy, concurrent disease, and abnormal laboratory results of clinical significance. 79% of patients completed the study, and 98% were included in a modified intention-to-treat analysis.

## INTERVENTION

Patients discontinued any NSAID or acetaminophen use and were allocated to rofe-

coxib, 25 mg ( $n = 95$ ) or 12.5 mg ( $n = 96$ ) once daily; celecoxib, 200 mg once daily ( $n = 97$ ); or acetaminophen, 4000 mg/d given as 1000 mg 4 times daily ( $n = 94$ ) for 6 weeks. Matching placebo tablets were used to retain blinding and complete the 4 tablets/d dosing schedule.

## MAIN OUTCOME MEASURES

Walking pain, night pain, rest pain, and morning stiffness assessed by individual WOMAC scores; composite pain, composite stiffness, and composite function assessed by WOMAC subscales; global response assessed by the patient global assessment of response to therapy (PGART) scale (a 5-point scale ranging from 0 [none] to 4 [excellent]); and adverse events.

## MAIN RESULTS

Analysis was by a modified intention-to-treat method with the last outcome carried for-

ward for the PGART data. Better global responses were seen with rofecoxib, 25 mg/d, than with acetaminophen or celecoxib and with rofecoxib, 12.5 mg/d, than with acetaminophen (all  $P$  values  $\leq 0.05$ ). Rofecoxib, 25 mg/d, led to greater symptom relief than did celecoxib or acetaminophen (Table). Groups did not differ for adverse events.

## CONCLUSION

In patients with symptomatic osteoarthritis of the knee, rofecoxib, 25 mg/d, was more effective than rofecoxib, 12.5 mg/d, celecoxib, or acetaminophen at 6 weeks.

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\*See Glossary.

†Information provided by author.

## Rofecoxib, 25 mg/d, vs celecoxib or acetaminophen for mean decreases in composite WOMAC VAS scores of symptoms of osteoarthritis of the knee at 6 weeks‡

Comparison	Outcomes	Mean decreases in WOMAC VAS scores (mm)	P values
Rofecoxib vs celecoxib	Pain	35 vs 29	$\leq 0.05$
	Stiffness	35 vs 28	$\leq 0.05$
Rofecoxib vs acetaminophen	Pain	35 vs 25	$< 0.01$
	Stiffness	35 vs 22	$< 0.001$
	Function	30 vs 20	$< 0.01$

‡WOMAC VAS scores = Western Ontario and McMaster Universities Osteoarthritis Index visual analog scale scores.

## COMMENTARY

OA is a chronic condition requiring long-term treatment; even assessments done at 6 weeks may not predict long-term results. The study by Geba and colleagues showed that at 6 weeks only the 25-mg daily dose of rofecoxib, which is double the recommended starting dose for OA, was more effective than acetaminophen or celecoxib. Unfortunately, this study does not answer the question of whether the higher daily dose (400 mg) of celecoxib, which is not approved for OA, would be as effective as 25 mg of rofecoxib.

The U.S. Food and Drug Administration has recently labeled rofecoxib as safer for the gastrointestinal tract than naproxen, but some cardiovascular concerns with rofecoxib exist (1). The cyclooxygenase-2 selective NSAIDs have renal side effects similar to older NSAIDs (2).

Are drugs needed at all in the treatment of OA? Studies have shown that sustained improvement in symptoms can be achieved with exercise regimens, even as low as 10 minutes of daily exercise (3). I routinely

teach isometric leg lifts to all patients with OA and knee pain.

Although in this study patients reported a better response to NSAIDs, 39% reported a good or excellent response to acetaminophen alone. Given the potential toxicity of all NSAIDs, acetaminophen and quadriceps-muscle strengthening remain an effective and safe regimen that should be used as initial therapy for OA of the knee. Further pharmacologic therapy needs to be individualized for each patient on the basis of their gastrointestinal, cardiac, and renal risk factors.

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## References

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