Effect of Rofecoxib Therapy on Measures of Health-Related Quality of Life in Patients With Osteoarthritis

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Background: Bodily pain and physical disability can negatively impact health-related quality of life (HRQL) in patients with osteoarthritis (OA).

Objective: To assess the effects of treatment with a new agent, rofecoxib, on HRQL in patients with OA.

Study Design: Randomized, double-blind, 6-week clinical trial comparing treatment with rofecoxib, 5 to 50 mg, with placebo in 672 patients with OA of the hip or knee.

Main Outcome Measure: Patient HRQL was assessed at baseline and at the end of treatment using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36).

Results: At 6 weeks, mean change from baseline in all SF-36 mental and physical health domain scores demonstrated significant improvement with rofecoxib use ($P < .05$ for all doses for all SF-36 domains), with evidence of a dose-response relation. Improvements in mental and physical HRQL domains with rofecoxib treatment were significantly greater than those with placebo treatment ($P < .05$ for each dose of rofecoxib vs placebo for all domains except general health) and highly correlated with improvements observed using disease-specific OA outcome measures such as the Western Ontario and McMaster Universities Osteoarthritis Index-visual Analog 3.0 OA index pain and physical function subscales. The effect of rofecoxib vs placebo treatment on mental health largely disappeared after adjustment for improvement in OA disease-specific measures.

Conclusions: Rofecoxib treatment increased physical and mental HRQL domain scores on the SF-36. Improvements in mental health with rofecoxib use primarily resulted from effective treatment of OA (ie, reduction in pain and improvement in physical function).

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Osteoarthritis (OA), the most common joint disorder worldwide, is age related and is characterized by joint pain, swelling, and stiffness.[1] Bodily pain and limitations in physical functioning are common features of OA that negatively impact patients' overall quality of life. Health-related quality of life (HRQL) describes patients' perceptions of their health and its effects on their overall well-being and physical, psychological, and social functioning.[2,3] Measures of HRQL are used increasingly in clinical trials to assess new therapies for a variety of disorders.[4,5] Given the relation between OA and decline in HRQL, assessment of HRQL is an important component of an overall evaluation of OA therapies.

Rofecoxib (VIOXX®, Merck & Co Inc, Whitehouse Station, NJ), 4-[4-(methylsulfonyl)phenyl]-3-phenyl-2(5H)-furanone, is an inhibitor of the inducible isoform to cyclooxygenase (COX-2).[6] Rofecoxib shows no significant inhibition of the constitutive cyclooxygenase isoform (COX-1) in humans within several multiples above the clinical dose range.[6,7] Nonselective nonsteroidal anti-inflammatory drugs

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(NSAIDs) inhibit both COX isoforms. Because COX-2 is the primary isoform in the setting of inflammation and COX-1 is the primary isoform in the gastrointestinal (GI) tract, it has been hypothesized that an agent that specifically inhibits COX-2 will have efficacy similar to that of NSAIDs but with superior GI tract safety. Consistent with this hypothesis, clinical trails with rofecoxib at doses of 12.5 to 25 mg daily have demonstrated efficacy in OA comparable to full doses of standard NSAIDs[8] but with a significantly lower risk of GI tract ulcers and bleeding.[9]

We report the results of an analysis of the effects of rofecoxib treatment on measures of HRQL in a 6-week, placebo-controlled, randomized clinical trial of patients with OA of the hip or knee. The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), a commonly used HRQL instrument, was used in the study. The SF-36 consists of 36 items that compose 8 domains relevant to HRQL: 4 physical health domains (general health perceptions, physical functioning, role-physical, and bodily pain) and 4 mental health domains (vitality, social functioning, role-emotional, and mental health). Individual patient responses to items are combined to produce domain-specific (or scale) scores.[3,10] The 8 scale scores are summarized into 2 scores: physical (PCS) and mental (MCS) component summary scores.[11]

This analysis was designed to investigate the association between rofecoxib treatment and HRQL in patients with OA. Comparisons to SF-36 US normative population data were made to gauge the clinical meaningfulness of the results with rofecoxib treatment. Further analyses were performed to explore the relation between improvements in HRQL and improvements in disease-specific OA measures.

··· METHODS ···

A placebo-controlled, parallel-group, double-blind study of rofecoxib treatment in patients with OA of the knee or hip was conducted. The study enrolled men and women aged 40 years and older with pain in the affected joint on most days during the previous month, characteristic radiographic changes (joint space narrowing and osteophytes), and American Rheumatism Association functional class I, II, or III.[12] To be eligible, patients had to demonstrate worsening in pain after discontinuation of previous therapy with NSAIDs.

Exclusion criteria were significant renal impairment (creatinine clearance <0.50 mL/s [<30 mL/min]), evidence of active GI tract bleeding, clinical malabsorption, class III/IV angina or congestive heart failure, uncontrolled hypertension, stroke within the previous 2 years, active hepatic disease, recent neoplastic disease, or allergy to acetaminophen or NSAIDs.

Eligible patients with knee OA were randomized to receive rofecoxib, 5, 12.5, 25, or 50 mg, once daily or matching placebo for 6 weeks. Patients with hip OA were randomized to the previous treatment groups except 50 mg. Clinical efficacy was assessed using validated OA disease-specific end points, including (1) pain walking on a flat surface (Western Ontario and McMaster Universities Osteoarthritis Index-visual Analog [WOMAC question 1] and WOMAC pain, stiffness, and disability subscales (100-mm visual analog scale version 3.0 questionnaire[13]); (2) investigator global assessment of disease status (5-point categorical scale: 0 = very well and 4 = very poor); and (3) patient global assessment of response to therapy (5-point categorical scale: 0= none and 4 = excellent). The numeric scales for response to therapy were multiplied by –1 to reverse the scale to make them consistent with other OA efficacy end points for which lower scores indicate improvement.

Health-related quality of life was assessed using the SF-36, which was self-administered by patients following washout of previous NSAID therapy (baseline) and at the end of the study (week 6 or on discontinuation). The SF-36 domains were scored and the PCS and MCS scores were computed using published methods.[10,11] All SF-36 scale and summary scores were expressed on a 0- to 100-mm visual analog scale; higher scores indicate better HRQL for the represented domain.

For the assessment of clinical efficacy end points, the average change from baseline across the entire 6 weeks of treatment was analyzed as predefined. In a previous study, full clinical efficacy response was realized at the first point of measurement and maintained at a generally constant level across the entire 6 weeks of treatment. Therefore, average response across the treatment period was predefined as the primary calculation of response for each patient to minimize variability and yield the most precise estimates of treatment effects. Between-group comparisons and analysis of trends, ie, increasing response with increasing dose, were performed using an analysis of covariance (ANCOVA) model with factors for treatment, baseline covariate, study center,

and study joint stratum (primary knee vs hip OA). Using least squares means, 95% confidence intervals were computed for within-group mean changes and between-group mean differences. A similar approach was used for SF-36 scores, using the change from baseline (randomization) to week 6 (or end of study) for each scale and summary score. The analysis was conducted using an intent-to-treat approach. Dropouts were included in the analysis by carrying forward all observed data for each patient up to and including the time of discontinuation.

The SF-36 results were compared with published normative data for the US general population by age decades.[10] Because the field of quality of life research is relatively new, there is no widely accepted "benchmark" for "meaningful changes in quality of life scores." The comparison between clinical trial results and US normative data was intended to gauge the clinical significance of these effects by demonstrating that the clinical changes were comparable in magnitude to changes between specified age groups and between persons with and without chronic medical conditions. Pearson correlation coefficients were calculated between changes in SF-36 domain and component scores and OA disease-specific efficacy end points to assess the magnitude of their relation.

Additional analyses were performed to explore the relation between the efficacy of rofecoxib therapy for OA and MCS scores. Results were reanalyzed by adjusting for regression to the mean[14] and by adjusting for physical efficacy, as measured by the primary clinical efficacy end points. A composite efficacy response variable was constructed from the 3 primary end points for the rofecoxib basic study data. The 3 primary end points are average change from baseline in walking pain (WOMAC question 1); patient global assessment of response to therapy; and investigator global assessment of disease status, each across the 6 weeks of treatment. The global assessments were measured on a 0- to 4-point categorical scale, and WOMAC walking pain was measured on a 0- to 100-mm visual analog scale. The composite was created by averaging the 3 responses after adjusting the walking pain visual analog scale response by dividing by 25 to scale it to the categorical scale.

Two analyses were performed to adjust the SF-36 mental health component results by the composite efficacy response to estimate the rofecoxib treatment effect on HRQL not explained by effects on OA. The first added the composite efficacy end point as a covariate to the ANCOVA model used to assess treatment effect on SF-36 response (other factors in the ANCOVA model were study site, baseline covariate, study joint, and treatment group). Adjusted means from this model and associated *P* values were generated. This approach may suffer from correlation among the independent variables, treatment and composite efficacy, making it difficult to differentiate the influence of treatment on SF-36 response from that of the composite efficacy end point. Hence, a second approach, a simple linear model, was used to adjust each SF-36 response for the composite efficacy response before analysis of the treatment effect. Residuals from the model $y = a + bx$, where y = SF-36 response and x = composite efficacy response, were analyzed for treatment effect using the original ANCOVA model. Least squares means were re-expressed on the original change from baseline scale by adding the overall mean change from baseline to the least squares means predicted from the ANCOVA.

··· RESULTS ···

A total of 672 patients with OA of the hip or knee were randomized to receive placebo (n = 145) or 5 mg (n = 149), 12.5 mg (n = 144), 25 mg (n = 137), or 50 mg (n = 97) of rofecoxib. Of these, 565 patients (84%) completed the study (6 weeks of treatment); 25 patients (4%) dropped out of the study because of adverse experiences, 64 (10%) because of lack of efficacy, and 18 (3%) for other reasons. Of patients taking placebo or 5, 12.5, 25, or 50 mg of rofecoxib, 2 (1%), 6 (4%), 5 (4%), 7 (5%), and 5 (5%), respectively, dropped out because of adverse experiences and 28 (19%), 15 (10%), 12 (8%), 6 (4%), and 3 (3%), respectively, dropped out because of lack of efficacy.

Baseline characteristics, by treatment group, are shown in **Table 1**. Women composed 71% of the patient population. Mean patient age was 61.7 years (range, 38-92); 56% were older than 60 years and 21% were older than 70 years. Eighty-nine percent of patients were white and 11% were of other races. Patient weights ranged from 44.6 to 128.8 kg (mean, 86.2 kg). The average duration of OA was 10.9 years (range, 1-47 years). Sixteen percent of patients were in American Rheumatism Association functional class I, 67% were in class II, and 18% were in class III. The knee was the primary study joint in 72% of patients. No clinically meaningful differences between treatment groups were observed for sex, age, race, weight, duration of OA, or American Rheumatism Association functional class.

The mean baseline value for the primary clinical efficacy end point of pain walking on a flat surface was 74.1 mm (WOMAC questionnaire). For the primary end point of investigator global assessment of disease status, the mean baseline value was 2.9. Baseline values for these variables were comparable between the placebo and rofecoxib treatment groups. Because patient global assessment of response to therapy was intended to measure the patient's response to study medication, no pretreatment values were solicited.

The efficacy results of rofecoxib in the management of OA from this study have been reported elsewhere.[15] All rofecoxib treatment groups demonstrated statistically significant improvement over placebo, as measured by the WOMAC pain scale, patient global assessment of response to therapy, and investigator global assessment of disease status.

Mean baseline scores for all SF-36 scales were generally similar between treatment groups (**Table 2**). Adjusted within-group mean change scores showed significant improvement for all doses of

Table 1. Baseline Patient Characteristics by Treatment Group*

		Rofecoxib, mg				
	Placebo (n = 145)	**5 (n = 149)**	**12.5 (n = 144)**	**25 (n = 137)**	**50 (n = 97)**	**Total (N = 672)**
Sex						
F	99 (68.3)	107 (71.8)	103 (71.5)	104 (75.9)	64 (66.0)	477 (71.0)
M	46 (31.7)	42 (28.2)	41 (28.5)	33 (24.1)	33 (34.0)	195 (29.0)
Race						
White	126 (86.9)	135 (90.6)	127 (88.2)	122 (89.1)	87 (89.7)	597 (88.8)
Hispanic	7 (4.8)	3 (2.0)	3 (2.1)	2 (1.5)	4 (4.1)	19 (2.8)
Other	12 (8.3)	11 (7.4)	14 (9.7)	13 (9.5)	6 (6.2)	56 (8.3)
Age†						
<50 y	29 (20.0)	19 (12.8)	24 (16.7)	19 (13.8)	18 (18.5)	109 (16.2)
51-60 y	39 (26.9)	47 (31.5)	46 (31.9)	32 (23.4)	26 (26.8)	190 (28.3)
61-70 y	41 (28.3)	58 (38.9)	43 (29.9)	57 (41.6)	31 (32.0)	230 (34.2)
71-80 y	32 (22.1)	25 (16.8)	28 (19.4)	26 (19.0)	20 (20.6)	131 (19.5)
>80 y	4 (2.8)	0 (0.0)	3 (3.1)	3 (2.2)	2 (2.1)	12 (1.8)
Mean (SD)	61.4 (10.8)	61.2 (9.1)	61.4 (10.5)	63.0 (9.9)	61.3 (11.0)	61.7 (10.2)
Median	62.0	62.0	61.5	65.0	61.0	62.0
Range	39-89	39-80	38-92	39-83	40-86	38-92
Weight, kg						
Mean (SD)	87.2 (18.2)	87.1 (16.9)	85.0 (17.6)	84.8 (16.3)	87.5 (16.7)	86.2 (17.2)
Median	87.0	86.7	81.4	83.9	85.3	84.8
Range	44.6-127.0	50.4-127.0	48.5-128.8	53.1-127.0	54.4-127.5	44.6-128.8
Duration of osteoarthritis, y‡						
Mean (SD)	10.3 (8.5)	11.6 (9.5)	11.4 (9.3)	9.4 (6.5)	12.0 (8.4)	10.9 (8.6)
Median	8.0	9.0	9.0	7.0	10.0	8.0
Range	1-47	1-40	1-45	1-37	1-45	1-47
American Rheumatism Association functional class						
I	19 (13.1)	28 (18.8)	23 (16.0)	24 (17.5)	12 (12.4)	106 (15.8)
II	95 (65.5)	93 (62.4)	94 (65.3)	93 (67.9)	73 (75.3)	448 (66.7)
III	31 (21.4)	28 (18.8)	27 (18.7)	20 (14.6)	12 (12.4)	118 (17.6)
Study joint						
Knee	100 (69.0)	98 (65.8)	96 (66.7)	92 (67.2)	97 (100.0)	483 (71.9)
Hip	45 (31.0)	51(34.2)	48 (33.3)	45 (32.9)	0 (0.0)	189 (28.1)

*Data are given as number (percentage) of patients except where indicated otherwise.
†All patients were aged ≥39 years when randomized.
‡Patient reported.

Table 2. Mean SF-36 Scale Scores and Within- and Between-Group Treatment Differences

Treatment	Patients, No.	Mean Score, mm		LS Mean Change (95% CI)	LS Mean Difference From Placebo (95% CI)
		Baseline	Treatment Period		
General Health Perceptions					
Placebo	129	62.96	66.17	2.32 (–0.08-4.72)	NA
Rofecoxib, mg					
5	139	64.49	68.45	3.63 (1.32-5.94)	1.31 (–2.02-4.64)
12.5	134	60.33	65.87	3.93 (1.58-6.29)	1.62 (–1.74-4.98)
25	131	64.22	67.99	3.20 (0.82-5.58)	0.88 (–2.50-4.26)
50*	91	66.06	69.71	4.30 (1.44-7.16)	1.98 (–1.75-5.71)
Physical Functioning					
Placebo	134	28.30	33.15	5.16 (1.94-8.37)	NA
Rofecoxib, mg					
5	140	27.98	39.39	11.82† (8.67-14.96)	6.66 (2.16-11.16)
12.5	135	29.81	41.27	12.56† (9.36-15.76)	7.40 (2.87-11.94)
25	131	27.81	40.04	12.59† (9.33-15.84)	7.43 (2.86-12.00)
50*	92	28.68	43.92	16.25† (12.37-20.13)	11.09 (6.05-16.13)
Role-Physical					
Placebo	134	23.78	32.74	8.97 (2.64-15.29)	NA
Rofecoxib, mg					
5	139	21.48	44.50	21.37† (15.16-27.58)	12.40 (3.54-21.27)
12.5	134	19.44	45.56	23.40† (17.07-29.72)	14.43 (5.49-23.38)
25	131	19.71	45.09	23.10† (16.70-29.50)	14.13 (5.14-23.13)
50*	92	27.58	50.40	24.27† (16.64-31.91)	15.31 (5.40-25.22)
Bodily Pain					
Placebo	134	29.31	36.09	6.16 (2.82-9.49)	NA
Rofecoxib, mg					
5	139	29.32	44.48	14.52† (11.25-17.79)	8.37 (3.70-13.03)
12.5	135	31.44	48.32	17.47† (14.15-20.79)	11.31 (6.61-16.02)
25	131	30.66	47.82	17.13† (13.76-20.50)	10.97 (6.24-15.71)
50*	92	31.10	54.10	22.90† (18.88-26.92)	16.74 (11.52-21.96)
Mental Health					
Placebo	134	70.84	70.24	–2.44 (–4.86-–0.01)	NA
Rofecoxib, mg					
5	140	72.72	76.78	2.82† (0.45-5.20)	5.26 (1.86-8.65)
12.5	135	69.77	74.43	2.47† (0.05-4.89)	4.91 (1.48-8.34)
25	131	70.53	78.03	5.28† (2.83-7.74)	7.72 (4.26-11.17)
50*	92	75.13	78.66	4.04† (1.11-6.97)	6.47 (2.67-10.28)
Role-Emotional					
Placebo	131	53.50	57.95	1.88 (–4.31-8.07)	NA
Rofecoxib, mg					
5	139	57.66	69.89	11.84† (5.83-17.85)	9.96 (1.34-18.59)
12.5	128	49.53	70.62	17.18† (10.92-23.45)	15.31 (6.50-24.11)
25	129	51.36	65.31	10.74† (4.51-16.98)	8.87 (0.08-17.66)
50*	92	56.01	73.41	17.48† (10.09-24.87)	15.60 (5.97-25.24)
Social Functioning					
Placebo	134	59.03	64.90	3.94 (0.06-7.81)	NA
Rofecoxib, mg					
5	140	60.23	70.32	8.59 (4.80-12.38)	4.65 (-0.77-10.08)
12.5	135	61.37	74.33	12.61† (8.75-16.47)	8.67 (3.20-14.15)
25	131	61.22	77.63	15.32† (11.40-19.24)	11.38 (5.87-16.90)
50*	92	64.30	79.66	16.98† (12.30-21.66)	13.04 (6.97-19.12)
Vitality					
Placebo	134	40.66	43.27	2.57 (–0.52-5.66)	NA
Rofecoxib, mg					
5	140	40.20	49.87	9.11† (6.09-12.13)	6.54 (2.22-10.86)
12.5	135	38.76	49.98	9.99† (6.91-13.06)	7.42 (3.05-11.78)
25	131	42.00	55.60	13.62† (10.50-16.75)	11.05 (6.66-15.44)
50*	92	42.47	56.12	13.80† (10.07-17.53)	11.23 (6.38-16.07)
Physical Component Summary					
Placebo	127	28.22	30.99	3.06 (1.60-4.51)	NA
Rofecoxib, mg					
5	137	27.63	33.61	5.95† (4.55-7.35)	2.90 (0.88-4.92)
12.5	127	28.37	34.47	6.23† (4.78-7.68)	3.19 (1.13-5.24)
25	129	28.07	34.17	6.21† (4.77-7.66)	3.16 (1.11-5.21)
50*	91	28.59	36.16	7.83† (6.11-9.55)	4.77 (2.52-7.02)
Mental Component Summary					
Placebo	127	49.80	50.17	–0.63 (–2.21-0.94)	NA
Rofecoxib, mg					
5	137	51.01	53.38	1.82† (0.31-3.33)	2.46 (0.27-4.64)
12.5	127	48.91	52.61	2.45† (0.88-4.02)	3.18 (0.95-5.40)
25	129	49.84	54.35	3.38† (1.82-4.94)	4.01 (1.79-6.23)
50*	91	51.79	54.98	3.49† (1.63-5.35)	4.12 (1.68-6.55)

SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey; LS = least squares; CI = confidence interval; NA = not applicable.
*Knee only.
†Statistically different from placebo ($P < .05$).

rofecoxib on all 8 physical and mental health domains (Table 2). The improvements were significantly greater than those observed with placebo for all domains except general health. There was evidence of a dose-response relation among the rofecoxib treatment groups, with the mean changes for the 5-mg group being of a smaller magnitude compared with the 12.5-, 25-, and 50-mg groups.

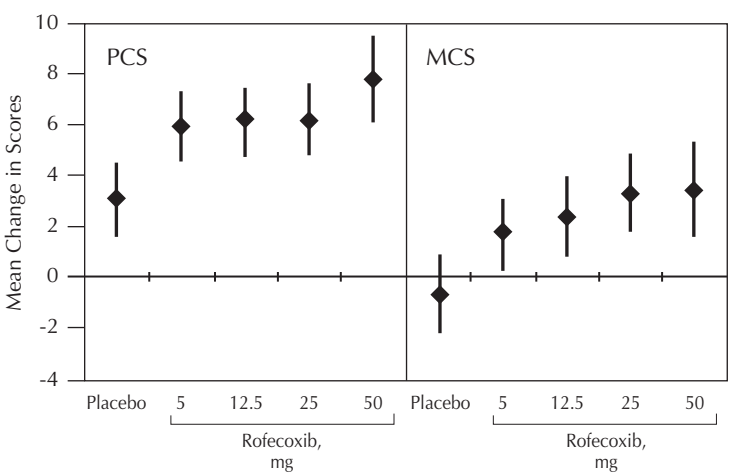
Within-group mean change scores for the PCS and MCS are shown in Table 2 and the **Figure**. As with the individual domains, all the rofecoxib treatment groups demonstrated significantly greater improvement compared with placebo on both scales.

Additional analyses were performed to assess the clinical significance of the improvements in HRQL observed with rofecoxib treatment. In **Table 3**, the effects of rofecoxib treatment (average of all rofecoxib treatment groups minus placebo) is compared with age-specific normative data from the US general population. Relative to placebo use, improvements with use of rofecoxib were generally similar to or greater than the magnitude of difference in the general population between persons aged 55 to 64 years and 45 to 54 years and between those aged 65 to 74 years and 55 to 64 years in physical domains, including physical functioning, role-physical, and bodily pain. In the general population, mental health domain scores show only limited or no decline with increasing age. As such, the improvement with rofecoxib treatment uniformly exceeded differences between persons aged 55 to 64 years and 45 to 54 years and between those aged 65 to 74 years and 55 to 64 years.

Table 4 shows the pairwise correlation coefficients between the SF-36 domain scores and the clinical efficacy measures (primary end points of the study). As expected, the physical functioning and bodily pain domains had stronger correlations with the primary end points and the WOMAC physical function subscales than did the other domains.

We also assessed the effect of adjustment for regression to the mean and for OA treatment efficacy on the mean change scores from the MCS scales. Adjustment for regression to the mean had no effect on any of the scores, regardless of treatment. Adjustment for OA efficacy attenuated the scores for all rofecoxib treatment groups and increased the scores for the placebo group on all scales and on the MCS. As a result, for most comparisons, the effect of treatment after adjustment for OA efficacy is minimally different from that of placebo. For each individual treatment tested, the overall treatment effect *P* values for individual scale scores and MCS scores using both methods of adjustment for composite efficacy were all greater than .05, and all were greater than .10 except one (data not shown).

Figure. Mean Change From Baseline (Flare) in SF-36 Component Summary Scores at 6 Weeks



SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey; PCS = physical component summary; MCS = mental component summary. Error bars represent 95% confidence intervals.

··· DISCUSSION ···

Recently, HRQL measures have been used increasingly in clinical studies, and they help provide an understanding of the broad impact of interventions on patients' everyday lives.[4,5] Measures of HRQL can be used to monitor, assess, and evaluate patient status, alternative treatments, and treatment effects. These measures also provide a means for physicians and patients to better develop a shared view of outcomes.[16] Bodily pain, physical functioning, and activity limitations are all measured in an assessment of HRQL and are especially important to patients with OA, who see the effects of their disease on HRQL in everyday activities. Compared with those without OA, patients experience losses in the ability to perform household chores, shop, complete errands, and undertake leisure activities.[17] Furthermore, OA is a chronic disease with

no associated mortality; therefore, improvements in HRQL can be of primary concern in selecting and evaluating treatments.

Nonsteroidal anti-inflammatory drugs are commonly used to treat chronic OA symptoms. However, because OA is a chronic disease and frequently requires long-term treatment, there is a need for safer therapies that demonstrate equivalent efficacy. The COX-2 hypothesis suggests that the nonspecific mechanism of action of NSAIDs imparts

Table 3. Comparison of Treatment Effects of Rofecoxib Compared With Normative Data From the US General Population

	SF-36 Normative Data Means					Rofecoxib	
SF-36 Domain	Age 45-54 y (n = 338)	Age 45-54 y minus Age 55-64 y	Age 55-64 y (n = 269)	Age 55-64 y minus Age 65-74 y	Age 65-74 y (n = 442)	Rofecoxib minus Placebo*	Pooled Baseline Mean
Physical functioning	85	–9	76	–7	69	8†	29
Role-physical	83	–9	74	–9	65	14†	22
Bodily pain	73	–5	68	0	68	11†	30
General health	72	–7	65	–2	63	1	63
Vitality	62	–2	60	0	60	9†	41
Social functioning	84	–3	81	0	81	9†	61
Role-emotional	84	–4	80	1	81	12†	54
Mental health	75	0	75	2	77	6†	72

SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.
*Between-group mean difference in average change from baseline across the treatment period.
†$P < .01$ for difference from zero.

Table 4. Correlation Coefficients for Changes From Baseline at Week 6*

	SF-36 Domain									
Clinical Efficacy Measure	Physical Functioning	Role-Physical	Bodily Pain	General Health	PCS	Vitality	Social Functioning	Role-Emotional	Mental Health	MCS
Pain walking on a flat surface (WOMAC question 1)	–0.458	–0.445	–0.605	–0.220	–0.567	–0.392	–0.357	–0.204	–0.184	–0.185
Patient global assessment of response to therapy	–0.447	–0.425	–0.557	–0.169	–0.526	–0.396	–0.323	–0.235	–0.179	–0.199
Investigator global assessment of disease status	–0.405	–0.371	–0.537	–0.189	–0.468	–0.371	–0.324	–0.216	–0.212	–0.216
WOMAC pain subscale	–0.489	–0.450	–0.648	–0.221	–0.591	–0.414	–0.378	–0.212	–0.209	–0.201
WOMAC stiffness subscale	–0.470	–0.413	–0.608	–0.180	–0.536	–0.446	–0.377	–0.218	–0.229	–0.232
WOMAC functional subscale	–0.555	–0.494	–0.678	–0.230	–0.619	–0.464	–0.454	–0.276	–0.274	–0.277

SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey; PCS = physical component summary; MCS = mental component summary; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
*All correlation coefficients are significantly different from zero, each at $P < .01$, except for the correlation between investigator global assessment of disease status with general health ($P = .04$) and role-emotional ($P = .11$).

both clinical efficacy and undesired GI tract adverse effects and that targeting the COX-2 isozyme with coxibs such as rofecoxib has the potential to provide efficacy similar to that of NSAIDs but with fewer GI tract adverse effects.

The effects of rofecoxib therapy on the MCS score may seem surprising. However, relief from the pain and stiffness caused by OA might affect aspects of HRQL related to mental health or psychological well-being. These could be mediated through an increase in the ability to perform and enjoy everyday activities. These results are consistent with the known psychometric properties of the SF-36. It has been shown that the SF-36 physical functioning and mental health scales are most sensitive to the clinical manifestations of medical and psychiatric conditions, respectively.[18] As a result, they have high discriminant validity for these conditions and their effects on HRQL. On the other hand, the social functioning and vitality scales are poor discriminators between physical and mental health effects.

Overall, use of rofecoxib improved HRQL in patients with OA. These improvements correlated with patients' perceived relief of the signs and symptoms of OA. Furthermore, the efficacy of rofecoxib treatment in improving measures of HRQL was clinically meaningful. This clinical significance was shown to be of a similar magnitude to decrements within the general population between 10-year age groups. In this study, rofecoxib treatment had a meaningful impact on HRQL. Not only were pain and stiffness effectively decreased, but ability to perform routine tasks was improved. Furthermore, these patients also experienced improvement in their overall emotional well-being, which might be due to their increased ability to perform and enjoy routine tasks and leisure activities while experiencing relief from the signs and symptoms of OA.

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