

The efficacy of continuous versus intermittent celecoxib treatment in osteoarthritis patients aged <60 and ≥60 years

Aim: To characterize the effect of age on the efficacy of continuous versus intermittent celecoxib treatment. **Materials & methods:** Prespecified exploratory analysis of a double-blind, parallel-group, randomized, multicenter international study. A total of 858 patients with osteoarthritis of the knee or hip were randomized to receive celecoxib 200 mg/day either as continuous or intermittent treatment. Efficacy was measured by the Western Ontario and McMaster Universities Osteoarthritis Index total and subscale scores, and the number of flare events. **Results:** Least squares mean increases (worsening) in Western Ontario and McMaster Universities Osteoarthritis Index total scores were significantly less in the continuous than in the intermittent treatment group in patients aged <60 years (1.10 vs 5.32; $p = 0.002$). In patients aged ≥60 years, the difference between treatment groups was not significant (2.24 vs 4.60; $p = 0.111$). Fewer flares were reported in the continuous than in the intermittent treatment group in patients aged <60 years (0.50 vs 0.89; $p < 0.0001$) and ≥60 years (0.59 vs 0.97; $p = 0.0001$). There were no differences in adverse events in the two age groups. **Conclusion:** Continuous celecoxib treatment was significantly more efficacious than intermittent use, irrespective of patient's age. These data may be useful in considering the treatment of osteoarthritis patients aged ≥60 years.

KEYWORDS: age • continuous • flare • intermittent • osteoarthritis • WOMAC

Advancing age is a significant risk factor in osteoarthritis (OA) [1–3], which is the most commonly occurring disease of the elderly [4]. While every age group is affected by OA, the occurrence of OA increases from the age of 50 years in males and 40 years in females [5]. Owing to the natural progression of arthritis development, more than 25% of the population aged >60 years require treatment for arthritis [6].

Age-related changes in the musculoskeletal system (cells and extracellular matrices of joint tissues) increase the susceptibility of the elderly developing OA in the presence of other OA risk factors such as joint injury, obesity, genetics and anatomic factors that affect joint mechanics [4,7]. The number of patients with arthritis requiring treatment is expected to increase over the next few decades as the general population ages [8].

OA is a painful and progressively debilitating condition characterized by 'waxing and waning' symptoms (flares). OA flares can be unpredictable in nature, varying in strength and severity. Flares often occur following changes in activities of daily living [9] and can negatively impact patients' physical function and health-related quality of life [10]. Some patients with OA may experience asymptomatic periods alternating with OA flares, while others may have continuous symptoms. Optimal management of OA is based on both pharmacologic

and nonpharmacologic modalities [11]; however, treatment should be guided by sound clinical judgment, and on an individual patient basis.

Current treatment with nonselective or COX-2 selective NSAIDs may take the form of either intermittent or continuous administration; however, intermittent treatment is often perceived as the safer option owing to concerns regarding the gastrointestinal and cardiovascular adverse effects associated with these therapies [12]. Potentially fewer adverse outcomes are experienced with intermittent therapy since it leads to less exposure of the drug and it takes a longer time to develop consistent serum levels of the drug in the body. Furthermore, as older patients appear to be at a higher risk for NSAID-induced adverse drug reactions such as upper gastrointestinal bleeding, they may gain more benefit from intermittent treatment.

The premise that intermittent treatment is better than continuous treatment had not been extensively studied until recently. However, based on the findings of a recent double-blind, randomized, multicenter, international trial, in which the efficacy and safety of continuous celecoxib (a COX-2 selective NSAID) treatment was compared with intermittent celecoxib treatment in symptomatic patients with OA, continuous treatment with celecoxib 200 mg/day was shown to be significantly more efficacious than

Margaret Noyes Essex^{*1},
Pritha Bhadra Brown¹
& George H Sands¹

¹Pfizer Inc., 235 East 42nd Street,
New York, NY 10017, USA
*Author for correspondence:
Tel.: +1 212 733 8018
margaret.essex@pfizer.com

Future
Medicine  part of 

intermittent treatment in preventing OA flares of the hip and knee, without increasing overall serious adverse events (AEs) [12].

The effect of age on continuous versus intermittent celecoxib treatment has not previously been studied. Moreover, it is not known whether younger patients, who may have less severe or longstanding OA, demonstrate a superior response to continuous and/or intermittent response when compared with older patients. Therefore, the objective of this exploratory analysis of a double-blind, randomized, multicenter international study [12] was to characterize the effect of age on the efficacy of continuous daily celecoxib treatment compared with intermittent celecoxib treatment.

Materials & methods

A prespecified exploratory analysis of a 24-week, double-blind, parallel-group, randomized, multicenter, international study was conducted to determine Western Ontario and McMaster Universities OA Index (WOMAC) total and subscale (pain, stiffness and physical function) scores and the number of OA flares, during the blinded postrandomization period, in patients grouped according to age (<60 and ≥60 years). The sub-analysis was designed to compare two age groups of patients from the trial, those who are considered 'older' from a medical perspective (over the age of 60 years) and those who are younger. Since this was not an exclusionary analysis, it would not be suitable to exclude young subjects. The distribution of subject age (mean, median, minimum and maximum) is shown in the table of demographics (TABLE 1). A detailed description of the study design has been previously published [12] and is briefly described below.

■ Study design

A total of 858 patients aged 18–80 years with knee or hip OA, determined by ACR criteria, were randomized (1:1 ratio stratified by site) to receive celecoxib 200 mg/day either as continuous (daily) or intermittent (celecoxib 200 mg/day when needed to treat OA flares meeting predefined criteria) treatment. All patients received two bottles containing capsules identical in appearance: bottle A (to be taken each morning) and bottle B (to be taken each morning only during an OA flare day[s]). Those randomized to continuous treatment received bottle A containing celecoxib capsules and bottle B containing placebo; those randomized to intermittent use received bottle A containing placebo and bottle B containing celecoxib.

The trial consisted of three periods. Period I lasted up to 14 days (±2 days) and included the screening visit (visit one) and washout period. During period I, OA patients who had an OA flare within 14 days following discontinuation of NSAID treatment were identified, and entered period II. Period II lasted up to 14 days (±2 days) and included the flare visit (visit two) and the open-label run-in treatment period with celecoxib 200 mg/day. During period II, only patients who had successful treatment of an OA flare following celecoxib treatment without additional flares entered period III. Period III lasted 22 weeks and included randomization (visit three) followed by the double-blinded treatment period, during which the efficacy of continuous versus intermittent use of celecoxib was investigated. A detailed figure showing the study design is described in Strand *et al.* [12].

The occurrence and resolution of an OA flare were defined objectively based on the scores on the Patient's Assessment of Arthritis Pain Numeric Rating Scale and the Patient's Global Assessment of Arthritis and were confirmed based on the outcome of the Physician's Global Assessment of Arthritis administered by the investigator.

■ Efficacy analysis

Efficacy assessments were performed during the double-blind treatment period (period III). Efficacy assessments included WOMAC Index scores (total, pain, stiffness and physical function subscores from randomization to final visit [visit nine]), and the mean number of flare events experienced by patients per time of exposure (mean number of flares per month). Patients were asked to complete the WOMAC questionnaire prior to each scheduled office visit, and at onset and resolution of OA flares. Safety was monitored from period II to the end of period III. Only AEs reported during period III – the blinded treatment period – are reported.

■ Statistical analysis

Analyses were performed on the intent-to-treat (ITT) population (patients who received at least one dose of study medication postrandomization) and flare-modified ITT (FmITT) population (all patients meeting criteria for the ITT population who also had flare durations ≤14 ± 2 days), using a two-sided type 1 error of 0.05. WOMAC scores were analyzed as change in WOMAC total, and pain, stiffness and physical function subscores from randomization to

final visit. Least squares means (LSMs) were used to present changes in WOMAC scores.

Results

■ Patient characteristics

In the continuous celecoxib treatment group, the mean age was 51.3 years in the patients aged <60 years and 67.2 years in the patients aged ≥60 years. In the intermittent celecoxib treatment group, the mean age was 51.2 years in patients aged <60 years and 66.7 years in patients aged ≥60 years (TABLE 1). The mean duration of OA was 5.0 years and 8.0 years in patients aged <60 and ≥60 years, respectively, in the continuous celecoxib treatment group. In the intermittent celecoxib treatment group, the duration of OA was 5.6 and 8.1 years in patients aged <60 and ≥60 years, respectively. In the continuous celecoxib treatment group, the mean BMI was 31.1 and 29.8 kg/m² in the patients aged <60 and ≥60 years, respectively. In the intermittent group, the mean BMI was 31.1 kg/m² in patients aged <60 years and 29.9 kg/m² in patients aged ≥60 years.

■ WOMAC Index scores

At the randomization visit, the total WOMAC and subscale scores were greater in patients aged ≥60 years in both the continuous and intermittent celecoxib treatment groups (TABLE 1). The LSM increases (worsening) in WOMAC total scores during the 22 weeks of blinded treatment were significantly less in the continuous treatment group than in the intermittent treatment group in patients aged <60 years (1.10 vs 5.32, respectively; $p = 0.002$) (TABLE 2). In patients aged ≥60 years, the difference in the LSM WOMAC total scores between the continuous

and intermittent celecoxib treatment groups were not significant (2.24 vs 4.60, respectively; $p = 0.111$). WOMAC total LSM increases were less in the continuous group than the intermittent group, irrespective of whether the patients were aged <60 or ≥60 years, although this was only significant in those aged <60 years.

Increases in pain, stiffness and physical function WOMAC subscale scores were significantly less in the continuous celecoxib treatment group in patients aged <60 years ($p < 0.05$). Increases in WOMAC subscale scores were less in the continuous celecoxib treatment group compared with the intermittent celecoxib treatment group in patients aged ≥60 years. There was a significant difference in the WOMAC pain subscale score between the two groups in patients aged ≥60 years ($p = 0.047$), but the differences in the WOMAC stiffness and physical function subscale scores were not significant.

In the FmITT population, increases in total, pain and physical function WOMAC subscale scores from baseline to final visit were significantly less in the continuous than intermittent treatment group in patients aged <60 years ($p = 0.05$), except for the WOMAC stiffness subscale ($p = 0.191$). WOMAC total and subscale scores were not significantly different between continuous and intermittent treatment in patients aged ≥60 years.

■ Number of flares

In the ITT population, patients aged <60 and ≥60 years in the continuous celecoxib treatment group experienced fewer flares per month than those in the intermittent celecoxib treatment group (aged <60 years, 0.50 vs 0.89, respectively; $p < 0.0001$; aged ≥60 years 0.59 vs 0.97,

Table 1. Subject demographics and characteristics at the randomization visit.

Characteristics	Continuous use: celecoxib 200 mg/day		Intermittent use: celecoxib 200 mg/day	
	<60 years (n = 236)	≥60 years (n = 195)	<60 years (n = 220)	≥60 years (n = 207)
Female, n (%)	183 (77.5)	134 (68.7)	154 (70.0)	149 (72.0)
Age, years; mean (SD)	51.3 (6.5)	67.2 (5.6)	51.2 (6.4)	66.7 (4.8)
Race, Caucasian; n (%)	176 (74.6)	162 (83.1)	162 (73.6)	171 (82.6)
BMI, mean (SD)	31.1 (6.4)	29.8 (5.2)	31.1 (6.1)	29.9 (5.7)
Duration of OA, years; mean (SD)	5.0 (4.6)	8.0 (7.7)	5.6 (5.8)	8.1 (7.5)
Total WOMAC score, mean (SD)	24.7 (13.4)	26.0 (14.8)	26.0 (13.6)	26.5 (14.5)
WOMAC subscale scores, mean (SD):				
– Pain	4.9 (2.8)	5.0 (3.0)	5.0 (3.0)	5.2 (3.0)
– Stiffness	2.3 (1.4)	2.4 (1.4)	2.4 (1.3)	2.4 (1.4)
– Physical function	17.6 (9.9)	18.7 (11.0)	18.6 (10.1)	19.0 (10.7)

OA: Osteoarthritis; SD: Standard deviation; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2. Least squares mean changes from randomization visit to final visit in Western Ontario and McMaster Universities Osteoarthritis Index pain, stiffness, physical function and total scores for the double-blind treatment period (intent-to-treat population).

WOMAC scale	ITT population			FmITT population		
	Continuous use: celecoxib 200 mg/day (LSM; SE; 95% CI)	Intermittent use: celecoxib 200 mg/day (LSM; SE; 95% CI)	p-value	Continuous use: celecoxib 200 mg/day (LSM; SE; 95% CI)	Intermittent use: celecoxib 200 mg/day (LSM; SE; 95% CI)	p-value
<60 years						
n	236	220	–	172	139	–
Total score	1.10; 0.95; -0.76–2.96	5.32; 0.98; 3.40–7.25	0.002	-0.05; 1.08; -2.18–2.09	3.66; 1.21; 1.28–6.03	0.023
Pain subscale	0.24; 0.20; -0.16–0.64	1.20; 0.21; 0.78–1.61	0.001	-0.02; 0.23; -0.49–0.44	0.84; 0.26; 0.33–1.35	0.014
Stiffness subscale	0.12; 0.09; -0.07–0.30	0.44; 0.10; 0.25–0.63	0.015	0.07; 0.10; -0.14–0.27	0.27; 0.12; 0.04–0.50	0.191
Physical function subscale	0.76; 0.69; -0.59–2.11	3.71; 0.71; 2.31–5.10	0.003	-0.05; 0.78; -1.58–1.49	2.57; 0.87; 0.85–4.28	0.027
≥60 years						
n	195	207	–	127	133	–
Total score	2.24; 1.06; 0.15–4.33	4.60; 1.03; 2.58–6.63	0.111	-0.22; 1.26; -2.70–2.27	2.72; 1.23; 0.29–5.15	0.097
Pain subscale	0.51; 0.24; 0.05–0.98	1.17; 0.23; 0.72–1.62	0.047	0.12; 0.28; -0.43–0.67	0.81; 0.27; 0.28–1.35	0.079
Stiffness subscale	0.12; 0.10; -0.08–0.32	0.35; 0.10; 0.15–0.54	0.114	0.12; 0.10; -0.08–0.32 [†]	0.35; 0.10; 0.15–0.54 [†]	0.114
Physical function subscale	1.61; 0.77; 0.11–3.11	3.10; 0.74; 1.64–4.56	0.163	-0.29; 0.91; -2.08–1.49	1.73; 0.88; -0.01–3.47	0.112

[†]n = 195; [‡]n = 207.

FmITT: Flare-modified intent-to-treat; ITT: Intent-to-treat; LSM: Least squares mean; SE: Standard error; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

respectively; $p = 0.0001$) (TABLE 3). In the FmITT population, fewer flares per month were also reported in the continuous celecoxib treatment group both in patients aged <60 years (0.45 vs 0.87, respectively; $p < 0.0001$) and in patients aged ≥60 years (0.55 vs 1.02, respectively; $p = 0.0010$). The mean number of flares was significantly lower in the continuous group than in the intermittent group irrespective of whether the patients were aged <60 or ≥60 years.

Safety results

A total of 16 patients experienced serious AEs, six were in the continuous celecoxib treatment group (one patient aged <60 years and five patients aged ≥60 years) and ten were in the intermittent celecoxib treatment group (three patients aged <60 years and seven patients aged ≥60 years). Serious AEs in the continuous celecoxib treatment group included chest pain in patients aged <60 years and acute respiratory failure, atrial fibrillation, coronary artery disease, melena, metastases to the CNS, nephrolithiasis, pulmonary edema and rectal hemorrhage in patients aged ≥60 years. Serious AEs in the intermittent celecoxib treatment group included chest pain, gastritis, skin laceration

and squamous cell carcinoma in patients aged <60 years and abdominal pain, bipolar I disorder, hypertensive crisis, knee arthroplasty, non-cardiac chest pain, OA, pancreatitis and transient ischemic attack in patients aged ≥60 years.

In the group aged <60 years, discontinuations due to AEs occurred in 2.5% of patients receiving celecoxib continuous treatment and 5.5% of patients receiving celecoxib intermittent treatment. In the group aged ≥60 years, discontinuations due to AEs occurred in 8.2% patients receiving celecoxib continuous treatment and 5.8% of patients receiving celecoxib intermittent treatment. No deaths were reported. Numerically, fewer AEs were reported in the celecoxib continuous treatment group than in the celecoxib intermittent treatment group in patients aged <60 years (58.9 vs 61.8%), while the frequency of AEs was similar among patients aged ≥60 years receiving celecoxib continuous and intermittent treatment (54.4 vs 55.6%). Headache was the most frequently reported AE in all groups (TABLE 4).

Discussion

In this exploratory analysis, lower WOMAC LSM change scores (less worsening) were observed in the continuous celecoxib treatment

group than in the intermittent celecoxib treatment group in both age groups. Patients receiving continuous celecoxib treatment aged <60 and ≥60 years also reported fewer flares than patients receiving intermittent treatment. These results are consistent with published findings where continuous celecoxib treatment was found to be significantly more efficacious than intermittent celecoxib treatment in preventing OA flares of the hip and knee [12]. However, older patients had greater worsening and more flares than their younger counterparts, regardless of whether they received continuous or intermittent treatment.

As has been previously noted [12], there is variability among patients' symptoms in OA. Some patients experience asymptomatic periods that alternate with flares, while others have more continuous symptoms. Flares can be unpredictable, varying in length and severity, sometimes occurring as a result of changes in activities of daily living such as exercise, stress, overexertion, treatment and/or surgery [12]. Continuous treatment provides a constant level of celecoxib, providing protection against the vagaries of OA flares, which could explain its improved efficacy when compared with intermittent treatment.

While intermittent treatment is thought to be a safer option compared with continuous treatment because of the potential cumulative risk of AEs, our study was not designed or powered to investigate these differences and the number of patients studied was too small to make any definitive statements about AEs in these populations. It may seem surprising

to those who believe that fewer AEs will occur with intermittent therapy, that in this study, fewer patients experienced serious AEs in the continuous treatment group compared with the intermittent treatment group. It is often stated that older patients are at higher risk for adverse drug reactions, and thus, it was no surprise that there were fewer serious AEs reported in younger patients than in the older group of patients. However, due to the short duration of follow-up (22 weeks), any findings should be interpreted with some degree of caution. A longer trial design, with a greater number of patients, is required to demonstrate the clinical robustness of these observations [13]. Age was also shown to be the most common risk factor of NSAID-induced upper gastrointestinal bleeding that resulted in hospitalization in a cross-sectional, retrospective study [14].

The current clinical guidelines for the management of OA recommend that treatment should be tailored according to age [15,16]. This analysis further supports this recommendation.

As previously described [12], patients must have successfully treated their OA flare (during the celecoxib open-label run-in period) prior to randomization into blinded study treatment. This may have resulted in an enriched study population with demonstrated efficacy and tolerability to the therapy under investigation. However, while these results are likely to be specific to this type of OA population, rather than to a more general population of patients with hip/knee OA, the study population includes

Table 3. Number of flare events per time of exposure to study medication†.

Flare events	ITT population			FmITT population		
	Continuous use: celecoxib 200 mg/day	Intermittent use: celecoxib 200 mg/day	p-value	Continuous use: celecoxib 200 mg/day	Intermittent use: celecoxib 200 mg/day	p-value
<60 years						
n	236	220	–	172	139	–
Events per month, mean (SD)	0.50 (0.60)	0.89 (0.98)	<0.0001	0.45 (0.61)	0.87 (1.15)	<0.0001
Median	0.37	0.60	–	0.19	0.52	–
Range	0.00–3.16	0.00–9.40	–	0.00–3.16	0.00–9.40	–
≥60 years						
n	195	207	–	127	133	–
Events per month, mean (SD)	0.59 (0.87)	0.97 (1.04)	0.0001	0.55 (1.02)	1.02 (1.22)	0.0010
Median	0.36	0.71	–	0.19	0.58	–
Range	0.00–7.50	0.00–7.14	–	0.00–7.50	0.00–7.14	–

†Time of exposure is the time in months from the first dose of double-blind study medication at the beginning of period III to the last dose of study medication. Patients may have more than one flare.

FmITT: Flare-modified intent-to-treat; ITT: Intent-to-treat; SD: Standard deviation.

those patients who have failed simple analgesic and/or intermittent treatment. As such, the study population is more likely to reflect those patients with more severe OA whose disease is most likely to progress.

Conclusion

In this exploratory study, irrespective of age (aged <60 or ≥60 years) daily celecoxib treatment appeared to be more efficacious than intermittent use, as assessed by WOMAC total scores and

the number of flares/month. These data may be useful when considering the treatment of older patients with OA.

Future perspective

As prescribing physicians develop a better understanding of the differing needs of patient subgroups, it is speculated that future treatment strategies for OA will become more individualized. Data such as those presented here will complement the clinical practice guidelines, to

Table 4. Summary of treatment-emergent adverse events in the safety population.

Adverse event [†]	Age <60 years, n (%)		Age ≥60 years, n (%)	
	Continuous use: celecoxib 200 mg/day (n = 236)	Intermittent use: celecoxib 200 mg/day (n = 220)	Continuous use: celecoxib 200 mg/day (n = 195)	Intermittent use: celecoxib 200 mg/day (n = 207)
Total patients with AEs	139 (58.9)	136 (61.8)	106 (54.4)	115 (55.6)
Headache	46 (19.5)	42 (19.1)	19 (9.7)	26 (12.6)
Back pain	14 (5.9)	17 (7.7)	6 (3.1)	14 (6.8)
Arthralgia	11 (4.7)	12 (5.5)	6 (3.1)	13 (6.3)
Upper respiratory tract infection	5 (2.1)	13 (5.9)	9 (4.6)	6 (2.9)
Pain in extremity	11 (4.7)	10 (4.5)	7 (3.6)	11 (5.3)
Nasopharyngitis	12 (5.1)	11 (5.0)	7 (3.6)	9 (4.3)
Dyspepsia	12 (5.1)	3 (1.4)	5 (2.6)	3 (1.4)
Diarrhea	3 (1.3)	11 (5.0)	4 (2.1)	6 (2.9)
Sinusitis	9 (3.8)	6 (2.7)	2 (1.0)	4 (1.9)
Musculoskeletal pain	2 (0.8)	8 (3.6)	5 (2.6)	4 (1.9)
Muscle spasms	3 (1.3)	2 (0.9)	7 (3.6)	3 (1.4)
Hypertension	0 (0)	0 (0)	5 (2.6)	7 (3.4)
Edema peripheral	2 (0.8)	5 (2.3)	2 (1.0)	7 (3.4)
Insomnia	8 (3.4)	4 (1.8)	3 (1.5)	4 (1.9)
Influenza	7 (3.0)	7 (3.2)	3 (1.5)	2 (1.0)
Abdominal pain upper	3 (1.3)	6 (2.7)	4 (2.1)	4 (1.9)
Pain	1 (0.4)	4 (1.8)	5 (2.6)	5 (2.4)
Dizziness	3 (1.3)	4 (1.8)	5 (2.6)	4 (1.9)
Bursitis	1 (0.4)	1 (0.5)	5 (2.6)	1 (0.5)
Fatigue	6 (2.5)	5 (2.3)	0 (0)	4 (1.9)
Myalgia	6 (2.5)	4 (1.8)	4 (2.1)	5 (2.4)
Neck pain	6 (2.5)	2 (0.9)	1 (0.5)	5 (2.4)
Abdominal pain	6 (2.5)	1 (0.5)	4 (2.1)	3 (1.4)
Urinary tract infection	4 (1.7)	2 (0.9)	3 (1.5)	5 (2.4)
Bronchitis	3 (1.3)	4 (1.8)	0 (0)	5 (2.4)
Nausea	3 (1.3)	5 (2.3)	2 (1.0)	4 (1.9)
Pharyngolaryngeal pain	3 (1.3)	1 (0.5)	4 (2.1)	3 (1.4)
Nasal congestion	1 (0.4)	3 (1.4)	4 (2.1)	0 (0)

[†]Occurring in ≥2% of patients in either treatment group. AEs were defined by the preferred Medical Dictionary for Regulatory Activities term. AE: Adverse event.

lead to more optimized treatment for OA and more favorable patient outcomes.

Writing assistance was provided by K Bradford and C Campbell of PAREXEL, and was funded by Pfizer Inc.

Financial & competing interests disclosure

The study was sponsored by Pfizer Inc. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Executive summary

Western Ontario & McMaster Universities Osteoarthritis Index scores

- Western Ontario and McMaster Universities Osteoarthritis Index total least squares mean increases (worsening) were less in the continuous celecoxib group than the intermittent celecoxib group, irrespective of whether the patients were aged <60 or ≥60 years, although this was only significant in those aged <60 years.
- Increases in pain, stiffness and physical function Western Ontario and McMaster Universities Osteoarthritis Index subscale scores were less in the continuous celecoxib treatment group in patients aged <60 or ≥60 years.

Number of flares

- Patients aged <60 and ≥60 years in the continuous celecoxib treatment group experienced fewer flares per month than those in the intermittent celecoxib treatment group.

Safety

- Numerically, fewer adverse events were reported in the celecoxib continuous treatment group than in the celecoxib intermittent treatment group in patients aged <60 years.
- Frequency of adverse events was similar among patients aged ≥60 years receiving celecoxib continuous and intermittent treatment.

Discussion

- Older patients had greater worsening and more flares than their younger counterparts, regardless of whether they received continuous or intermittent treatment.
- Daily celecoxib treatment was more efficacious than intermittent use, irrespective of whether the patients were aged <60 or ≥60 years.

Conclusion

- These data may be useful in considering the treatment of older patients with osteoarthritis.

References

Papers of special note have been highlighted as:

■ of interest

■ ■ of considerable interest

- Abramson SB, Attur M. Developments in the scientific understanding of osteoarthritis. *Arthritis Res. Ther.* 11(3), 227 (2009).
- Bagge E, Bjelle A, Eden S, Svanborg A. Osteoarthritis in the elderly: clinical and radiological findings in 79 and 85 year olds. *Ann. Rheum. Dis.* 50(8), 535–539 (1991).
- Felson DT. The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study. *Semin. Arthritis Rheum.* 20(3 Suppl. 1), 42–50 (1990).
- Shane Anderson A, Loeser RF. Why is osteoarthritis an age-related disease? [abstract]. *Best Pract. Res. Clin. Rheumatol.* 24(1), 15–26 (2010).
- Breedveld FC. Osteoarthritis – the impact of a serious disease. *Rheumatology (Oxford)* 43(Suppl. 1), i4–i8 (2004).
- Verzijl N, Bank RA, TeKoppele JM, DeGroot J. Ageing and osteoarthritis: a different perspective. *Curr. Opin. Rheumatol.* 15(5), 616–622 (2003).
- Loeser RF, Shakoor N. Aging or osteoarthritis: which is the problem? *Rheum. Dis. Clin. North Am.* 29(4), 653–673 (2003).
- Hamerman D. Clinical implications of osteoarthritis and ageing. *Ann. Rheum. Dis.* 54(2), 82–85 (1995).
- Lawrence RC, Hochberg MC, Kelsey JL *et al.* Estimates of the prevalence of selected arthritic and musculoskeletal diseases in the United States. *J. Rheumatol.* 16(4), 427–441 (1989).
- Majani G, Giardini A, Scotti A. Subjective impact of osteoarthritis flare-ups on patients' quality of life. *Health Qual. Life Outcomes* 3, 14 (2005).
- Zhang W, Moskowitz RW, Nuki G *et al.* OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 16(2), 137–162 (2008).
- Strand V, Simon LS, Dougados M *et al.* Treatment of osteoarthritis with continuous versus intermittent celecoxib. *J. Rheumatol.* 38(12), 2625–2634 (2011).
- ■ Randomized, multicenter international trial that demonstrated that continuous treatment with celecoxib was significantly more efficacious than intermittent treatment in preventing osteoarthritis flares of the hip and knee, without increasing overall serious adverse events.
- American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. *J. Am. Geriatr. Soc.* 57(8), 1331–1346 (2009).
- Marco JL, Amariles P, Boscá B, Castelló A. Risk factors associated with NSAID-induced upper gastrointestinal bleeding resulting in hospital admissions: a cross-sectional,

- retrospective, case series analysis in Valencia, Spain [abstract]. *Curr. Ther. Res. Clin. Exp.* 68(2), 107–119 (2007).
- 15 Hochberg MC, Altman RD, April KT *et al.* American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res. (Hoboken)* 64(4), 465–474 (2012).
- ■ **Provides an update of the ACR 2000 recommendations for hip and knee osteoarthritis and presents new recommendations for hand osteoarthritis.**
- 16 Jordan KM, Arden NK, Doherty M *et al.* EULAR recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann. Rheum. Dis.* 62(12), 1145–1155 (2003).
- **Provides an update of the European League Against Rheumatism 2000 recommendations for the management of knee osteoarthritis by an evidence-based medicine and expert opinion approach.**