



STOPP Press release

New Study Shows that Chondroitins 4 and 6 Sulfate Retard Progression of Disease and Alleviates Pain in Patients with Knee Osteoarthritis

PARIS, February 20, 2009 — Top-level experts of musculoskeletal rheumatic diseases commented on results of the Study on Osteoarthritis Progression Prevention (STOPP)¹ showing marked benefits of treatment with chondroitins 4 and 6 sulfate (CS) in patients suffering from knee osteoarthritis (OA). The study provided compelling evidence that CS significantly retard joint structure degradation while providing symptomatic relief to treated patients.

This international, randomized, double-blind, placebo-controlled study was conducted in 622 patients aged 45 to 80 years with knee OA. Patients received either an 800-mg sachet of highly purified CS (Genévrier Laboratories, Sophia Antipolis, France, and IBSA, Pambio Noranco, Switzerland) (n = 309 patients) or placebo (n = 313 patients) once daily for 2 years. The study was conducted in France, Belgium, Switzerland, Austria, and the USA.

The primary outcome criterion was modification in the minimum joint space width (JSW) of the medial compartment of the target tibiofemoral joint.

High-quality radiological method ensuring high level of evidence

Posteroanterior radiographs (Lyon schuss view) of the target knee were obtained, the patient being in a position that ensures a constant flexion of the knee leading to high reproducibility of joint positioning.

Automated digitized image analysis was used in the STOPP study.

The minimum JSW of the medial compartment of the tibiofemoral joint was assessed by digital image analysis using validated digitized image analysis software.

Intent-to-treat (ITT) analyses were performed for all randomized patients. Per-protocol completer analyses were performed on patients who completed the 2-year observation period.

Both ITT and per protocol analyses show that CS significantly retard joint structure degradation

¹ Kahan A, Daniel Uebelhart D, Florent De Vathaire F, Pierre D. Delmas PD, Reginster JY. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis. The study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis & Rheumatism* 2009;60:524–33.

The intent-to-treat analysis demonstrated:

- A significant reduction ($P < 0.0001$) in minimum JSW loss in the CS group (0.07 ± 0.03 mm versus 0.31 ± 0.04 mm) (**Figure 1**). Of note, the effect of treatment significantly increased with time.
- A significant reduction ($P < 0.0005$) of the percentage of patients with radiographic progression >0.25 mm in the CS group (28% versus 41%; relative risk reduction 33% [95% confidence interval 16–46%]). The number of patients needed to treat was 8. A significant reduction of JSW loss was observed with any threshold between 0.05 mm and 0.7 mm. For example, fewer patients experienced JSW loss of at least 0.5 mm with CS as compared to placebo (13% versus 27%, respectively; $P < 0.0001$) (**Table 1**).

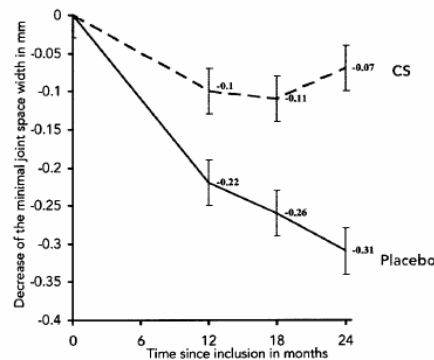


Figure 1. Change of minimum space width over time in patients treated with chondroitins 4 and 6 sulfate (CS) or placebo. Intent-to-treat analysis (Kahan A et al., Arthritis Rheum 2009;60:524-33).

Table 1. Progressor analysis (JSW 0–0.7 mm), by ITT analysis			
JSW threshold	Day 1 to month 24		
	Chondroitins 4 and 6 sulfate	Placebo	P
0.05 mm	45%	58%	0.002
0.10 mm	40%	52%	0.003
0.15 mm	37%	48%	0.004
0.20 mm	30%	43%	0.007
0.25 mm*	28%	41%	0.0005
0.30 mm	25%	40%	<0.0001
0.35 mm	20%	36%	<0.0001
0.40 mm	17%	33%	<0.0001
0.45 mm	14%	31%	<0.0001
0.50 mm**	13%	27%	<0.0001
0.55 mm	11%	23%	<0.0001
0.60 mm	10%	23%	<0.0001
0.65 mm	9%	21%	<0.0001
0.70 mm	8%	18%	0.0003

*Minimal value defining patients with radiographic progression

**Minimal value defining patients with clinical progression

Rapid and long-lasting improvement of pain

Patient's estimates of pain, using a 100-mm visual analogical scale (VAS) and the Western Ontario and McMaster Universities OA Index (WOMAC) were pre-specified secondary outcomes.

The ITT analysis (VAS and WOMAC) demonstrated significantly faster improvement in pain in the CS group than in the placebo group ($P < 0.01$ for the interaction between time and treatment effect). For the decrease in pain scores (VAS), the differences between the 2 groups in favor of CS were already significant after one month of treatment and still significant at 3, 6, 9 months (**Figure 2**).

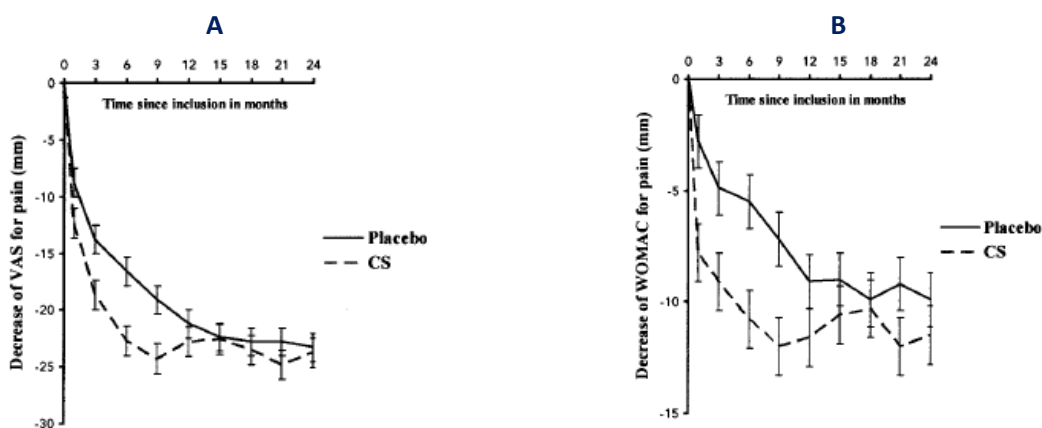


Figure 2. Change in pain over time in patients treated with chondroitins 4 and 6 sulfate (CS) or placebo. (Kahan A et al., *Arthritis Rheum* 2009;60:524-33). A, pain as measured on a Visual Analog Scale (VAS); B, pain as measured by the Western Ontario and McMaster Universities Osteoarthritis Index.

No significant differences were observed between the two groups in terms of consumption of acetaminophen, while a trend toward a decrease in the consumption of NSAIDs was observed in the CS group during the study.

The CS preparation was as well tolerated as placebo; the most frequently adverse events reported being transient and mild gastrointestinal symptoms (6% in the CS group and 5.9% in the placebo group).

A significant advance in the management of knee osteoarthritis

Prof. André KAHAN (University of Paris Descartes and Cochin Hospital, Paris, France), lead investigator of the study, underlined the high quality of radiologic assessment. "The study provides clear evidence that the highly purified CS preparation used is not only a symptomatic slow-acting drug for osteoarthritis (SYSADOA), but also, and most importantly, a disease-modifying osteoarthritis drug (DMOAD).



This CS preparation has been approved as a prescription treatment for OA in many European countries; for this reason, the results cannot be generalized to all CS products or compounds, as those available as dietary supplement in the US” he said.

“In practical terms, pain is reduced, which has an obvious impact on patient’s quality of life; the structural effect of this well-tolerated treatment represents a significant advance in the management of knee osteoarthritis and a possibility to limit the increased economic burden of the disease” he concluded.

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