

## STOPP (STUDY ON OSTEOARTHRITIS PROGRESSION PREVENTION): CHONDROITIN SULFATE REDUCES THE PROGRESSION OF JOINT SPACE NARROWING IN KNEE OA

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### Objective:

STOPP is a multicentre, randomised, double blind, clinical study designed to evaluate the structure and modifying properties of orally 800 mg chondroitin 4&6 sulfate (CS) vs. placebo over 2 years in patients with knee osteoarthritis.

### Material and methods:

600 patients of either sex, aged between 45 and 80 years, affected by tibio-femoral knee osteoarthritis defined by clinical and radiological criteria were recruited in 4 European countries (F, B, CH, A) and North America. The symptomatic knee (VAS  $\geq$  30 mm) of each patient was selected as the target knee at the time of enrolment. If both knees were symptomatic, the knee with the narrower joint space width was selected. If both knees had the same joint space width, the most symptomatic knee was chosen. Patients received 800 mg CS or placebo once a day for 2 years. The primary efficacy criterion was the minimal joint space narrowing (JSN) analysed by means of digitised radiographs. Secondary efficacy criteria were pain, measured using the Huskisson's VAS, WOMAC algo-functional index, total consumption of paracetamol, and authorised NSAIDs. Global efficacy and tolerability were independently assessed by investigators and patients by means of a VAS and a semi-quantitative verbal scale, respectively. Patients underwent control visits on Day -30, Day 1, Month 1, 3, 6, 9, 12, 15, 18, 21, and 24. Evaluations of every single patient were always carried out by the same investigator. Knee X-rays (Lyon-Schuss view) were taken at the inclusion visit and after 12, 18, and 24 months. The digitised X-rays were analysed blindly with respect to treatment and time at the end of the study by an automated image analysis. Statistical analyses (ITT and PP) were carried out by an external, independent centre.

### Results:

A total of 622 patients meeting the inclusion criteria, 309 in the CS group and 313 in the placebo group, were enrolled between the years 2000 and 2002. The study groups were balanced at baseline with respect to demographic and clinical variables, including severity of OA of the target knee. Ninety-three patients (30.1%) of the CS group and 80 patients (25.6%) of the placebo group did not complete the 2-year treatment course. There were no significant differences between groups regarding the reasons for withdrawal. Likewise, the number of patients showing good compliance according to the protocol was not significantly different between the groups. The patients receiving placebo had a progressive JSN with a mean loss  $\pm$  SE of  $0.24 \pm 0.03$  mm after 2 years (ITT). The mean progressive narrowing was of lower extent in the patients receiving CS ( $0.10 \pm 0.03$  mm). The minimal joint space narrowing over the two years was significantly less in the CS group than in the placebo according to ITT analysis of variance ( $p < 0.01$ ). The PP analysis confirmed the results obtained by the ITT analysis. The data regarding the secondary efficacy parameters confirmed the trend in favour of CS with statistical significance at several end-points. The tolerability was very good in both treatment groups.

### Conclusions:

In this randomised, double blind, placebo-controlled study CS reduces the joint space narrowing in knee OA in comparison to placebo as assessed by radiographic follow-up over 2 years.

Long-term treatment with CS appears to delay radiographic progression in patients with OA of the knee. These results are consistent with those already published by others (B.A. Michel et al., Arthritis and Rheumatism 2005; 3(52): 779-786).

