

# Viscosupplementation with stabilized hyaluronic acid in the treatment of osteoarthritis of the knee joint

A non-interventional-study (NIS) has confirmed the good tolerability of viscosupplementation therapy with Synocrom forte (stabilized hyaluronate from biofermentation). Significant pain alleviation was still observed one year after treatment.

## Introduction

Because of its lubricating and shock-absorbing properties, hyaluronic acid (HA) contributes significantly to joint function. In osteoarthritic joints both the percentage of hyaluronic acid and also its molecular weight (chain length) are significantly reduced. These deficits can be offset by viscosupplementation, i.e. the intraarticular injection of high molecular weight hyaluronic acid.

Synocrom forte (Croma-Pharma) contains stabilized hyaluronic acid obtained by biofermentation and cross-linking of the molecular chains. Cross-linking produces slowing of enzymatic degradation and thereby a significant prolongation of half-life in the joint. The goal of this observational study was to collect data under practice conditions on the safety and tolerability of Synocrom forte and to follow the pain course for a period of one year after the treatment.

## Patients and method

The non-interventional study was performed in a total of 30 orthopaedic centres in



or, if necessary, after worsening of pain symptoms. In addition, they were asked to assess efficacy and to report the occurrence of undesirable effects and the use of additional pain relievers. The physician questionnaire included questions about demography, the course of illness, adjunct medications, and the occurrence of undesirable events. Some patients could not be included in the analysis because the relevant data were missing on the questionnaire.

## Results

The treatment period extended from 1 March, 2006 (first patient, first injection) to 23 July, 2006 (last patient, third injection); as planned, all patients received three injections. The last follow-up visit took place on 1 August, 2007. Demographic information on the patients may be found in Table 1. The median body mass index (BMI) was just below 27, i.e. more than half of the patients are classifiable as "overweight" according to WHO-BMI criteria (BMI >25.00).

Demographic information		Women (n)	Men (n)
Age (MV ±SD, years)	63.1 ± 11.7	(69)	59.2 ± 10.3 (46)
Height (MV ±SD, m)	1.64 ± 0.07	(69)	1.77 ± 0.05 (45)
Weight (MV ±SD, kg)	74.8 ± 12.5	(68)	84.7 ± 9.1 (45)
BMI (MV ±SD, kg/m <sup>2</sup> )	27.6 ± 4.2	(68)	27.2 ± 3.4 (45)
Grade of gonarthrosis number/grade (I/III)	10/40/19	(69)	10/23/13 (46)

Table 1: Demographic information (MV = mean value, SD = standard deviation)

test reported illness duration was 0.2 years, and the maximum reported duration was 40 years. 76 patients (66.1 %) indicated they were treatment-naïve, while 38 patients had been treated previously with hyaluronic acid.

The safety and tolerability evaluations made by the physicians are summarized in Figure 1. Efficacy was predominantly rated as "very good" or "good", while tolerability was predominantly rated as "very good". On the question about the occurrence of swelling during treatment, "yes" was marked in 8 cases (7.0 %); the severity of the swelling was indicated as "mild" in 2 cases, and as "moderate" in 5 cases.

In one case no information about the severity was given. Swelling was treated in two cases with cryotherapy, in one case with diclofenac, and in another case with puncture. No serious health deteriorations were reported. Pain and inflammation medication was used as adjuvant therapy by 29 patients (25.2 %), while further 8 patients (7.0 %) received chondroitin sulphate preparations.

Figure 2 shows the course of VAS 100 pain intensity. Mean pain intensity decreased in the first months after the treatment and reached its nadir with a mean of 26.7 only at 8 months after the end of treatment. All mean values after the start of treatment differed significantly from the baseline value (Friedmann test, p = 0.000).

## Discussion

The data support the favourable safety of hyaluronic preparations for viscosupplementation (summary: Bellamy et al. 2006). Reactions were mild or moderate in intensity and were managed easily with standard therapy. Severe inflamm-

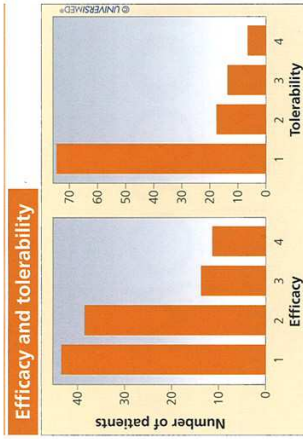


Fig. 1: Assessment of the efficacy and tolerability of Synocrom forte treatment by the participating physicians

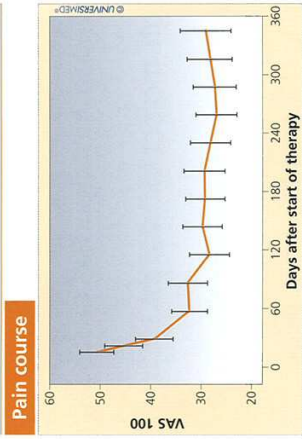


Fig. 2: Pain course according to patient declarations (mean, 95 % confidence interval)

atory swelling (pseudosepsis), as found in isolated cases with hyaluronate preparations of animal origin (Hyland G-F 20), was generally not observed with Synocrom forte.

The causality between the treatment and the outcome cannot be verified in a non-interventional study. The long-term pain course observed here, however, deserves attention since the follow-up period is usually only 4–26 weeks in controlled studies (Bellamy et al. 2006). Therefore it appears to be legitimate to discuss how far the pain improvement is attributable to the efficacy of viscosupplementation.

Evident placebo effects were frequently observed in the first weeks after injections into the knee joint (Chou 2009), but a placebo effect lasting up to one

## Literature

Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wakis G. 2006 Cochrane Database Syst Rev. 2:CD005321

Chou CW, Lue KH, Lee HS, Lin KC, Lu KH. 2009 J Formos Med Assoc. 108: 663–72

Moreland LW. 2003 Arthritis Res Ther. 5: 54–67

Authors:  
Thomas Ruester, MD, Senior Physician  
Martin Friedrich, MD, Clinical Prof.  
Speising Orthopaedic Hospital  
Speisinger Straße 109  
A 1130 Vienna  
Phone: + 43 (1) 801 82-0  
Fax: + 43 (1) 801 82-1487  
E-mail: thomas.ruester@oss.at