OARSI late breaking abstract, Denver, March 2023

(Abstract character limit 5000, including spaces. Title and affiliations not included. Tables and figures are 100 characters each)

3 YEAR RESULTS FROM A PROSPECTIVE STUDY OF POLYACRYLAMIDE HYDROGEL FOR KNEE OSTEOARTHRITIS

Marius Henriksen[1], Jannie Beier[2], Andreas Hartkopp[3], Philip G Conaghan[4], Henning Bliddal[1]

1 The Parker Institute, Bispebjerg Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark

2 Gigtdoktor, Odense, Denmark

3 A2 Rheumatology and Sports Medicine, Hillerød, Denmark

4 Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds & NIHR Leeds Biomedical Research Centre, United Kingdom

Purpose

In previous clinical studies intra-articular injection of polyacrylamide hydrogel (Arthrosamid®) has been investigated using 2 injections of 3 ml separated by a month. The primary objective of this study was to evaluate the efficacy and safety of a single injection of 6 ml intra-articular Arthrosamid® on knee symptoms in participants with moderate to severe knee OA. The study has been extended to evaluate the long-term efficacy and safety of Arthrosamid® for up to 5 years after treatment.

Materials & Methods

This was a prospective, multicentre study (3 sites in Denmark) where 49 participants received a single intra-articular injection of 6 mL Arthrosamid®. The investigational plan and amendments were approved by the Danish Health authorities and the local Health Research Ethics committee (ref.no: H-19031685) and the study was registered at www.clinicaltrials.gov (NCT04179552) before any study related activities. All participants provided informed consent prior to study activities, and the study was conducted according to the principles of good clinical practice. The study was initially planned to end after 1 year but was extended to follow the participants for up to 5 years. Participants signed a new consent form to participate in the extension phase.

Injections were given by an investigator experienced in administering intra-articular injections. Participants could continue analgesics (except 48 hours prior to visits) and non-pharmacological therapy, but topical (on target knee) and systemic corticosteroids or additional injections were not allowed. Follow-up visits were conducted at 4, 13 and 26 weeks and 1, 2 and 3 years after

treatment, with further follow-ups planned yearly for up to 5 years after treatment. This abstract presents data from the 3-year follow-up visit.

Outcomes included the transformed WOMAC pain, stiffness and function subscales (0-100 score where 100 was worst) and Patient Global Assessment of disease impact (PGA). Changes from baseline to 52 weeks in these outcomes were analysed using a mixed model for repeated measurement (MMRM) with a restricted maximum likelihood-based approach. The model included fixed, categorical effects of week, baseline and baseline by week interaction. The estimated changes based on the least square means were presented including 95% confidence limits and corresponding p-values. Additional sensitivity analyses were performed on the 3-year data. The MMRM analysis was repeated, but only data from the 35 participants that continued into the extension phase were included. In another analysis an ANCOVA model was used where missing values at 3 years were replaced by the participants baseline value.

Results

49 participants (31 females) with an average age at treatment of approximately 70 years (range 44 – 86 years) were treated with Arthrosamid. Demographic and baseline characteristics are shown for these 49 participants in Table 1. 46 participants completed the 52 weeks assessment and 35 participants (22 females) continued into the extension phase, with a site closure and the increased length of the study being the most common reasons for not continuing. 29 participants completed the 3-year follow-up.

The originally planned MMRM analysis including all available data from the 49 treated participants showed clinically relevant and highly statistically significant decreases from baseline to 3 years for each of the 3 WOMAC subscale scores and the PGA (Table 2).

The analysis using the data available from the 35 participants in the extension phase showed a similar change from baseline in the WOMAC pain subscale (17.7 units) compared to the result of the planned MMRM analysis (18.0 units). The baseline carried forward analysis also showed a clinically relevant and highly statistically significant decrease in the WOMAC pain subscale from baseline to 3 years (12.1 units). Figure 1 shows the trajectory of the WOMAC pain subscale from treatment to 3 years.

19 new adverse events were reported during the 2-year and 3-year visits, none of which were assessed as related to treatment. 3 of the events were SAEs (Covid-19 infection, pre-syncope, uterine prolapse). Covid-19 infection was the most frequently reported AE in this period.

Conclusion

Single injections of 6 ml intra-articular Arthrosamid® are well tolerated and continue demonstrate clinically relevant and statistically significant effectiveness 3 years after treatment.

Table 1: Demographic and baseline characteristics

	Arthrosamid N=49
Age (years)	
Mean (SD)	70.0 (8.6)
Median	72.0
Range	44 - 86
Sex (N,%)	
Female	31 (63.3)
Male	18 (36.7)
BMI (kg/m²)	
Mean (SD)	27.5 (3.3)
Median	27.2
Range	21.0 - 34.6
Baseline WOMAC pain score (0-100)	
Mean (SD)	50.3 (11.8)
Median	50.0
Range	20 - 75
Baseline WOMAC stiffness score (0-100)	
Mean (SD)	55.6 (17.5)
Median	62.5
Range	0 - 88
Baseline WOMAC phys. function score (0-100)	
Mean (SD)	46.6 (16.1)
Median	45.6
Range	9 - 87

N: Number of subjects, SD: Standard deviation

Table 2: Analyses of change from baseline to 3 years in transformed (0-100) WOMAC subscales

	Number of participants		LSMean (95% CI)	p-value
	At baseline	At 3 years		
WOMAC pain subscale				
Planned analysis	49	29	-18.0 (-24.9; -11.1)	<0.0001
Extension participants	35	29	-17.7 (-24.7; -10.8)	<0.0001
Baseline carried forward	49	49	-12.1 (-17.0, -7.3)	<0.0001
WOMAC stiffness subscale	49	29	-16.4 (-22.5; -10.3)	<0.0001
WOMAC Phys. Function subscale	49	29	-14.9 (-21.4; -8.4)	<0.0001
Patient Global Assessment	49	29	-15.0 (-27.6; -2.4)	0.0223

CI: confidence interval; N: Number of subjects, LSMean: Least squares mean; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

The planned analyses was performed on change from baseline using a mixed model for repeated measures including fixed, categorical effects of treatment, week, treatment-by-week interaction and site, as well as the baseline value and baseline-by-week interaction as covariates. All available data from the 49 treated participants is included.

The analysis of the extension participants used a similar model to the planned analyses but only included available data from the 35 participants that consented to the extension study.

The baseline carried forward analysis was performed on change from baseline using an ANCOVA model where missing values at 3 years were replaced by the participants baseline value.

Figure 1: Change from baseline in WOMAC pain subscale from treatment to 3 years after treatment