POSTER 483

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

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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.

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 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.
- Outcomes included the transformed WOMAC pain, stiffness and function subscales and Patient Global Assessment of disease impact (PGA).
- Changes from baseline to 52, 104 and 156 weeks in these outcomes were analysed using a mixed model for repeated measurement (MMRM) with a restricted maximum likelihood-based approach. 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 for the WOMAC pain subscale:
  - MMRM repeated, but only data from the participants that continued into the extension phase were included.
  - An ANCOVA model was used where missing values at 3 years were replaced by the participants baseline value.

RESULTS

- Demographics of the 49 treated participants are shown in Table 1.
- 46 participants completed the 52 weeks assessment.
- 35 participants (22 females) continued into the extension phase, with a site closure (personal reasons) 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 entering 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). Figure 1 shows the trajectory of the WOMAC pain subscale from treatment to 3 years.
- 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).
- 19 new adverse events were reported between 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).

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

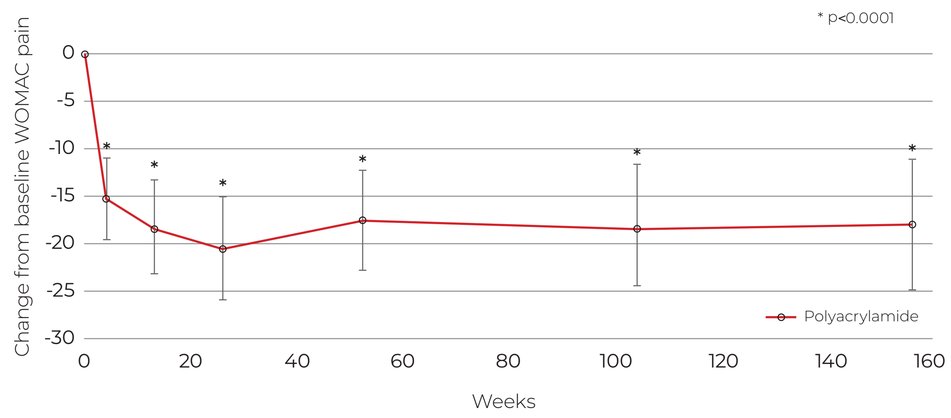
N: Number of subjects, SD: Standard deviation

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

	Number of participants			
	At baseline	**At 3 years**	**LSMean (95% CI)**	**p-value**
WOMAC pain subscale				
Planned analysis (MMRM)	49	29	-18.0 (-24.9; -11.1)	<0.0001
Extension participants (MMRM)	35	29	-17.7 (-24.7; -10.8)	<0.0001
Baseline carried forward (ANCOVA)	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



CONCLUSION

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

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