

ONE-YEAR PERFORMANCE OF POLYACRYLAMIDE HYDROGEL VS. HYALURONIC ACID: A RANDOMISED CONTROLLED STUDY

Henning Bliddal¹, Jannie Beier², Andreas Hartkopp³, Philip G Conaghan⁴, Marius Henriksen¹

PURPOSE

To compare the effectiveness of a single intra-articular injection of polyacrylamide hydrogel (Arthrosamid®) with that of a single injection of hyaluronic acid (Synvisc-One®) in participants with moderate to severe knee OA in a randomised controlled study.

MATERIALS & METHODS

- This was a prospective, double-blind multicentre study conducted at 3 sites in Denmark.
- 239 participants were randomised 1:1 to receive a single intra-articular injection of either 6 mL Arthrosamid (n=119) or 6 mL Synvisc-One (n=120). Injections were given by an investigator experienced in administering intra-articular injections, who was not involved further with the participants.
- 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.
- The statistical analyses were based on the intention-to-treat principle using least squares means for the treatment-by-week interaction effect using a mixed model for repeated measurement with a restricted maximum likelihood-based approach. The estimated mean treatment difference based on this model was reported with 95 % CI and the corresponding p-value. For the primary outcome, non-inferiority between the groups was demonstrated if the lower bound of the 95 % CI was > -9.

RESULTS

- Demographic and baseline characteristics were similar between groups (Table 1).
- Change from baseline in the transformed WOMAC pain subscale is shown in Figure 1.
- The primary outcome was change from baseline to week 26 in the WOMAC pain subscale. Analysis of the change from baseline to week 26 demonstrated non-inferiority between the groups, with a treatment difference of 3.6 (95% CI: -0.9; 8.1) in favour of Arthrosamid compared to hyaluronic acid (Table 2).
- Analysis of the change from baseline to week 52 showed treatment differences in favour of Arthrosamid compared to hyaluronic acid for the WOMAC pain, stiffness and physical function subscales and PGA. However, none of these numerical differences reached statistical significance (Table 2).
- The proportion of OMERACT-OARSI responders was similar in the Arthrosamid (56%) and hyaluronic acid (57%) groups.

Table 1: Demographic and baseline characteristics

| | Arthrosamid N=119 | Synvisc-One N=120 |
|--|----------------------|----------------------|
| Age (years) | | |
| Mean (SD) | 67.2 (9.5) | 66.6 (9.2) |
| Median | 67.0 | 68.5 |
| Range | 42 - 90 | 31 - 85 |
| Sex (N,%) | | |
| Female | 58 (48.7) | 68 (56.7) |
| Male | 61 (51.3) | 52 (43.3) |
| BMI (kg/m²) | | |
| Mean (SD) | 27.6 (3.6) | 27.3 (3.9) |
| Median | 27.2 | 26.8 |
| Range | 20.4 - 35.0 | 20.0 - 34.9 |
| Time since diagnosis (years) | | |
| N | 118 | 118 |
| Mean (SD) | 9.0 (7.9) | 8.5 (7.5) |
| Median | 7.5 | 6.0 |
| Range | 0.0 - 42.0 | 0.0 - 41.0 |
| Baseline WOMAC pain score (0-100) | | |
| Mean (SD) | 45.1 (13.4) | 46.5 (13.3) |
| Median | 45.0 | 50.0 |
| Range | 10 - 75 | 15 - 75 |
| Baseline WOMAC stiffness score (0-100) | | |
| Mean (SD) | 52.7 (20.8) | 51.1 (20.9) |
| Median | 50.0 | 50.0 |
| Range | 0 - 88 | 0 - 88 |
| Baseline WOMAC phys. function score (0-100) | | |
| Mean (SD) | 44.4 (15.1) | 43.5 (16.2) |
| Median | 47.0 | 45.6 |
| Range | 3 - 76 | 4 - 82 |

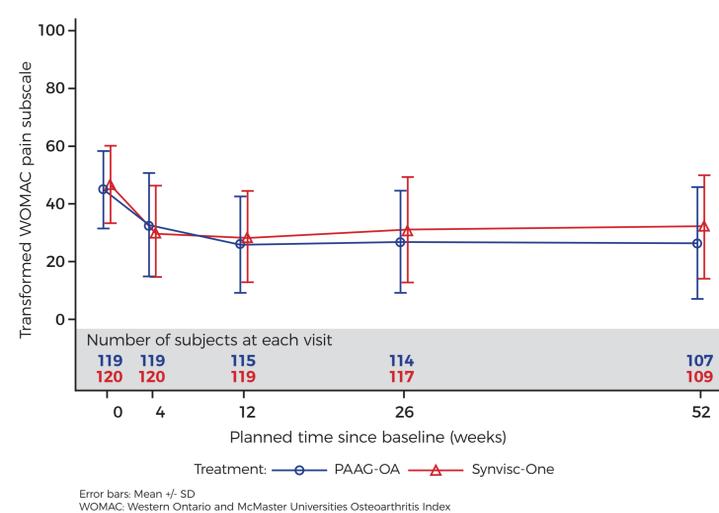
N: Number of subjects, SD: Standard deviation

Table 2: Analyses of change from baseline in transformed (0-100) WOMAC subscales in the ITT population.

| | LSMean (95% CI) | Treatment difference (95% CI) | p-value |
|--|----------------------|-------------------------------|-------------|
| WOMAC pain subscale (Week 26) | | | |
| Synvisc-One | -14.8 (-17.9; -11.7) | | |
| Arthrosamid | -18.4 (-21.5; -15.3) | 3.6 (-0.9; 8.1) | noninferior |
| WOMAC pain subscale (Week 52) | | | |
| Synvisc-One | -13.3 (-16.7; -10.0) | | |
| Arthrosamid | -17.9 (-21.3; -14.6) | 4.6 (-0.1; 9.4) | 0.0572 |
| WOMAC Stiffness subscale (Week 52) | | | |
| Synvisc-One | -12.9 (-17.2; -8.6) | | |
| Arthrosamid | -17.9 (-22.2; -13.5) | 5.0 (-1.1; 11.1) | 0.1080 |
| WOMAC Phys. Function subscale (Week 52) | | | |
| Synvisc-One | -15.2 (-18.6; -11.8) | | |
| Arthrosamid | -17.7 (-21.2; -14.3) | 2.5 (-2.3; 7.4) | 0.3006 |
| Patient Global Assessment (Week 52) | | | |
| Synvisc-One | -13.5 (-18.1; -8.9) | | |
| Arthrosamid | -17.5 (-22.2; -12.9) | 4.0 (-2.5; 10.6) | 0.2275 |

CI: confidence interval; LS: Least squares; Mean: Least squares mean; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. The analysis 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.

Figure 1: Mean plot of transformed WOMAC pain subscale (0-100) - blinded phase - ITT analysis set



CONCLUSION

At 26 weeks after treatment, the effectiveness of Arthrosamid was non-inferior to hyaluronic acid, as measured by the WOMAC pain subscale. At 52 weeks after treatment, the effectiveness of Arthrosamid was numerically superior to hyaluronic acid but not statistically significantly different.

Affiliation:

- 1: The Parker Institute, Bispebjerg Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark
- 2: Gigt doktor, 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