Safety and efficacy of intra articular injections of a combination of hyaluronic acid and mannitol (HAnox-M) in patients with symptomatic knee osteoarthritis. Results of a double-blind, controlled, multicenter, randomized trial.

Background

Hyaluronic acid (HA) would be a therapeutic option when the sensible decline (up to 5 weeks) of in the quality of life (QoL) compared to 1 year of intense mobility (0.85), is one of the main concern about viscosupplementation. HAnox-M (2000 kDa), that contains sodium hyaluronate with a high concentration (50%) of mannitol, a polyol known for its inflammatory properties, has been widely used. This combination suggests that addition of mannitol to HA might increase the intra-articular residence time of the latter and consequently might show a more rapid onset of action than HA alone.

Objective

To compare the safety and efficacy of a novel intra-articular viscosupplementation made of intermediate molecular weight (IMW) HA combined with high concentration of mannitol, HAnox-M, with a marketed high IMW HA, Bio-HA in patients with knee osteoarthritis (OA).

Methods

226 patients

Aged 45-85 with symptomatic knee OA, radiological OA (OARSI grade 1-2), were enrolled in a controlled, double-blind, parallel group, non-inferiority trial. Patients were randomized to receive 3 weekly IA injections of either HAnox-M or Bio-HA.

Primary criteria: WOMAC A (0-20) changes between baseline and week 24

Non inferiority Margin = 1.35

Follow-up: 6 months

Data at baseline:
- Demographics
- History of knee OA
- WOMAC index (0-20), B (0-10), C (0-40), Total (0-86)
- Analgesic or NSAIDs consumption
- Pain on a 10 point Likert scale (0-5)

Data at week 1, 2 and 3 (status of injection):
- WOMAC Pain subscore A
- Analgesic or NSAIDs consumption
- Pain on a 10 point Likert scale (0-5)
- Patient’s self-evaluation of efficacy using a 4 point LS
- Tolerability (4 pt LS)
- Safety (EAEs report)

Data at week 12 and 26 (Follow-up):
- WOMAC index A, B, C, Total
- Analgesic or NSAIDs consumption
- Pain on a 10 point Likert scale (0-5)

Conclusion 1

HAnox-M is an effective and well tolerated treatment for knee OA, which allows long lasting pain relief, decrease of analgesic consumption and functional improvement comparable to those obtained with Bio-HA

Results 1

HAnox-M and Bio-HA groups did not differ statistically at baseline.

The primary analysis was conducted in PP population, then confirmed in IT population.

The average WOMAC pain score at baseline was 8.5 in both groups. Mean (SD) variations in WOMAC pain score were -4.4 (2.8) and -4.5 (4.3) mm, for HAnox and Bio-HA respectively, satisfying the claim for non-inferiority.

Similar results were obtained for all other secondary endpoints.

Conclusion 2

- Both vissupplements showed similar safety profiles, indicating that addition of mannotol to HA does not modify the tolerability of HA.
- A trend to an earlier reduction of pain with HAnox-M, suggests that mannotol may have an own analgesic effect due to anti-inflammatory properties and/or through its ability in reducing the in situ HA degradation.