

MULTICENTER OPEN-LABEL TRIAL ASSESSING SAFETY AND EFFICACY OF A SINGLE INJECTION OF MANNITOL-MODIFIED CROSSLINKED HYALURONIC ACID (HAPPYMINI®) IN TRAPEZOMETACARPAL OSTEOARTHRITIS

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HAnox-M-XL in TMC OA

- ✓ Osteoarthritis of the trapeziometacarpal (TMC) joint of the thumb is a frequent and painful condition that has a significant impact on quality of life.
- ✓ The conservative treatment usually consists in a nocturnal splint, analgesics, NSAIDs and intraarticular injections of corticosteroids or hyaluronic acid (HA) preparations.
- ✓ In case of non-response to medical therapy, surgical procedure should be contemplated and consists in trapezectionomy or prosthesis.





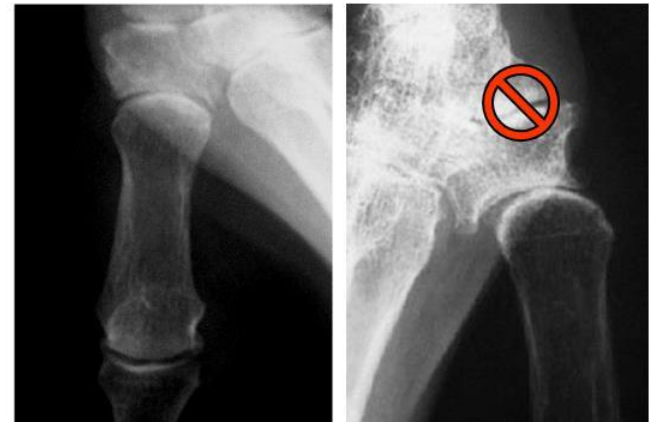
- ✓ To assess the **safety and the efficacy** on pain relief of a **single intra-articular injection of a new mannitol-modified cross-linked hyaluronic acid (HANOX-M-XL)** viscosupplement, in patients suffering from trapeziometacarpial (TMC) osteoarthritis (OA).
- ✓ To study the **predictive factors of response** to viscosupplementation, with a particular focus on the radiological stage.

HAnox-M-XL in TMC OA

- ✓ Patients with **symptomatic TMC OA** were included in a 3 month prospective multicentre open-label trial.
- ✓ Investigators were **rheumatologists or orthopedic surgeons**, specialized in hand OA
- ✓ The study received the French health authorities approval and was conducted in accordance with the Ethical standards of the Declaration of Helsinki. EUDRACT N°2015-AO1874-45
- ✓

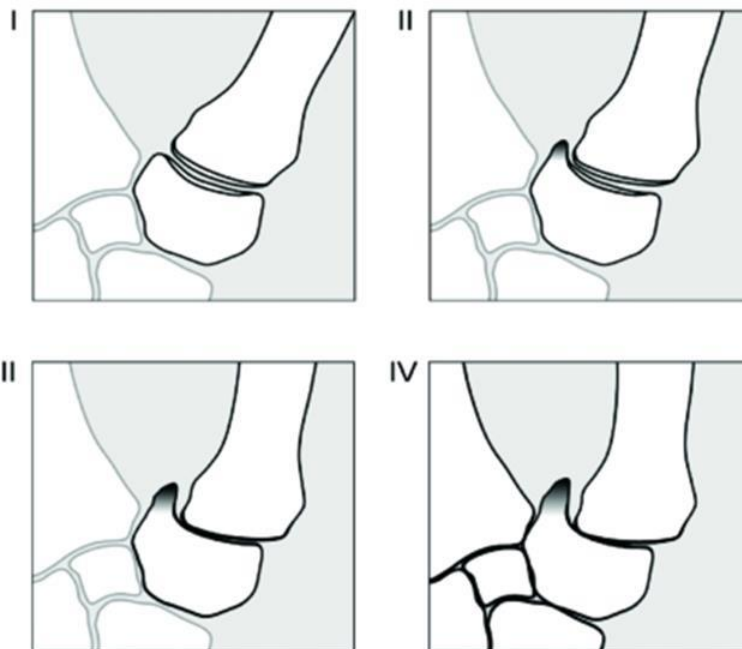
HAnox-M-XL in TMC OA

- ✓ To be included in the study patients must have **symptomatic TMC OA, not adequately relieved** by analgesics/ NSAIDs therapy and/or by the use of a thumb orthotics.
- ✓ Patients with inflammatory arthritis, trapezio-scaphoidal OA and those who previously received intra-articular injections with corticosteroids into the target thumb were excluded.
- ✓ Before treatment all patients must have had **plain radiographs with the Kapandji incidences, for the Dell grade (0-4) assessment.**



HAnox-M-XL in TMC OA

The Dell's radiological criteria for classification of trapeziometacarpal osteoarthritis



Stage I – Joint space narrowing and subchondral sclerosis but no evidence of subluxation or osteophyte formation.

Stage II- Increased subchondral sclerosis and joint space narrowing. Formation of osteophyte at the ulnar border of the trapezium. Metacarpal is subluxated less than 1/3rd of the diameter of the base of trapezium.

Stage III- Further loss of joint space. More prominent osteophyte at the ulnar border of the trapezium. The metacarpal is subluxated more than 1/3rd of base of the trapezium.

Stage IV- Total loss of joint space, greater amount of subluxation/dislocation and the presence of pan-trapezial arthritis

HAnox-M-XL in TMC OA

- ✓ **Primary endpoints** were the variation between injection (D0) and D90 of the thumb pain on 11 point-Likert scale (0-10) and the patient's self-assessment of efficacy (0-3).
- ✓ **Predictive factors of response** including clinical, demographic and radiographic data were studied
- ✓ **Statistical tests were carried out on ITT population** . The statistical analysis was performed using Statview© software version 5.0 (SAS institute Inc).
- ✓ The study received the **French health authorities approval** and was conducted in accordance with the Ethical standards of the Declaration of Helsinki. EUDRACT N°2015-AO1874-45

HAnox-M-XL in TMC OA

Treatment consisted in a single injection of 0.6 to 1 ml of HANOX-M-XL in the TMC joint under fluoroscopic or ultra-sound guidance.

✓ **HANOX-M-XL** (Happymini®, Laboratoire LABRHA, Lyon, France) is a novel viscosupplement, that combines:

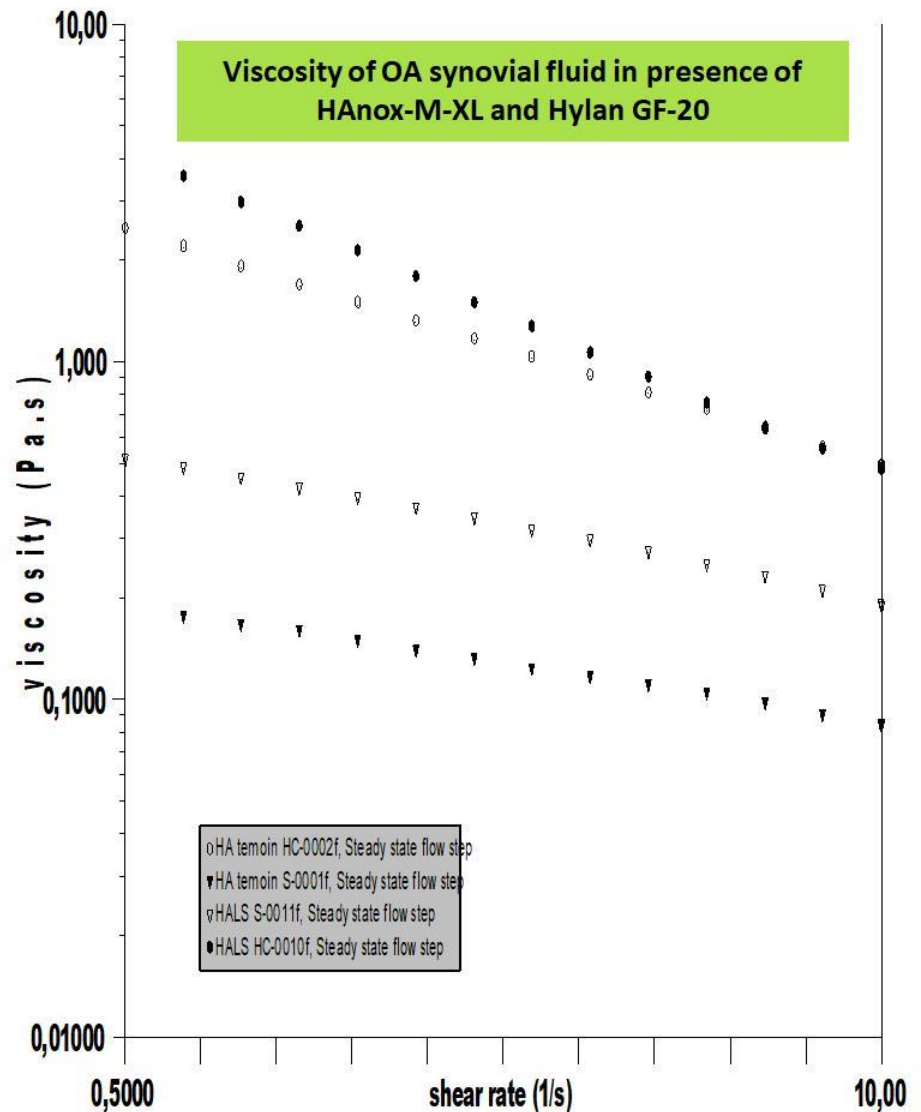
- ✓ Cross-linked **HA** of non-animal origin (16 mg/mL)
- ✓ high concentration (35 g/L) of **MANNITOL**, a polyol known for its antioxidant properties by scavenging radical oxygen species (ROS)



Mannitol-modified cross-linked HA (HAnox-M-XL) versus Hylan GF-20

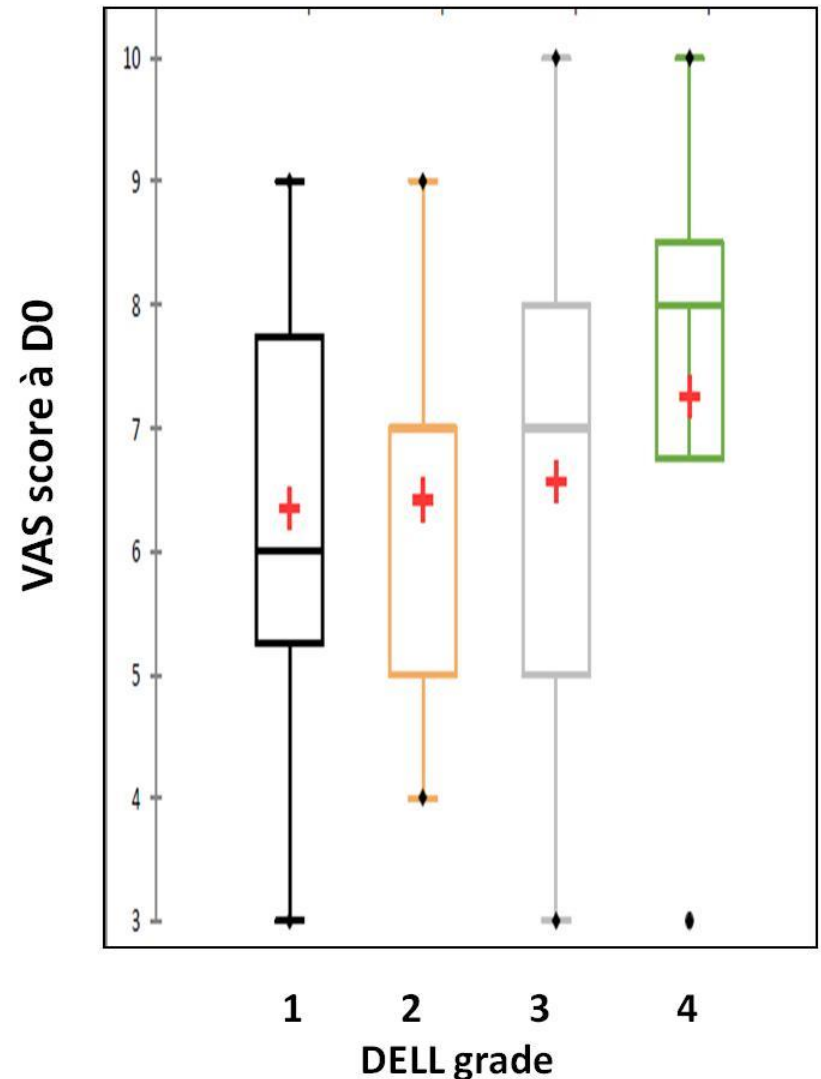
HAnox-M-XL increases, much more than Hylan GF-20, the viscosity of osteoarthritic synovial fluid:

- Higher HA concentration
- Denser crosslinking
- Stabilization by mannitol



HAnox-M-XL in TMC OA

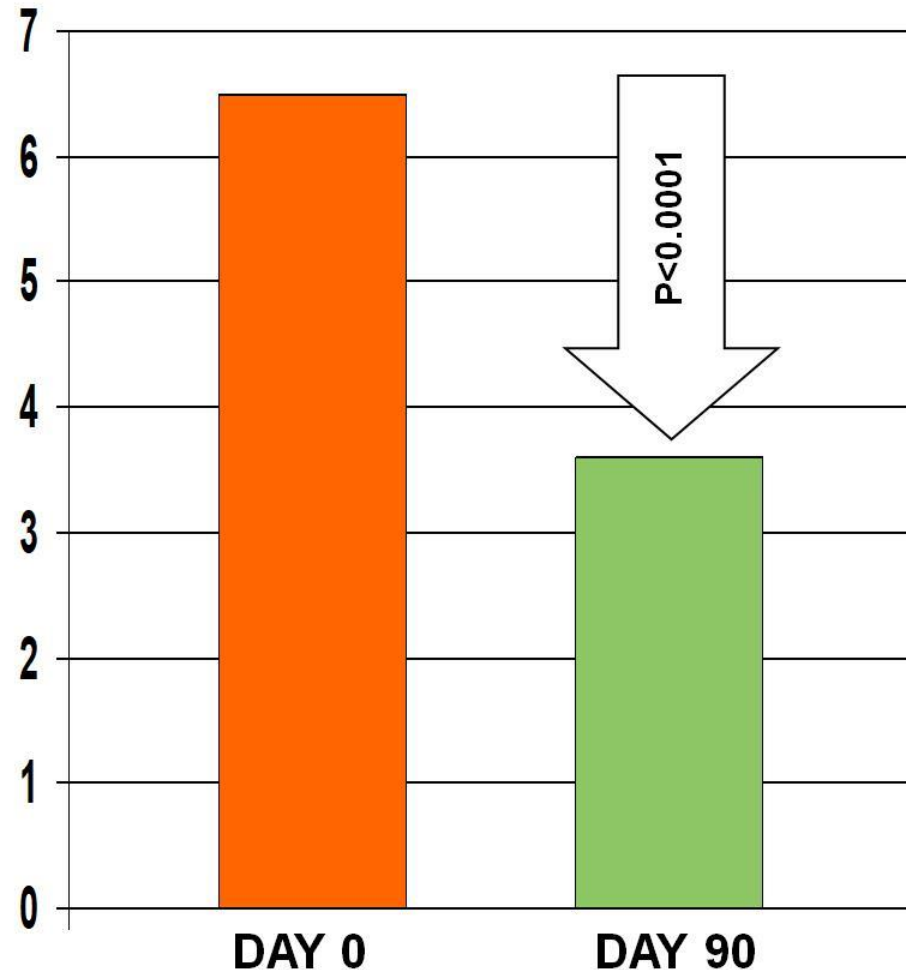
- ✓ **106 patients**, 79 F, age (SD) 60.0 (10.1), disease duration 36 (33.2) months, BMI 25.9 (4.9) were recruited.
- ✓ TMC OA was bilateral in 64%. Orthotics, NSAIDs and analgesics were used in 60.4%, 24.5% and 51%.
- ✓ **Dell grade** was 1 in 22 cases, 2 in 37 patients, 3 in 41 and 4 in 4 subjects (2 missing data).
- ✓ **At baseline** the mean (SD) **pain score was 6.5 (1.6)**. It was not significantly different according the Dell stage.



HAnox-M-XL in TMC OA

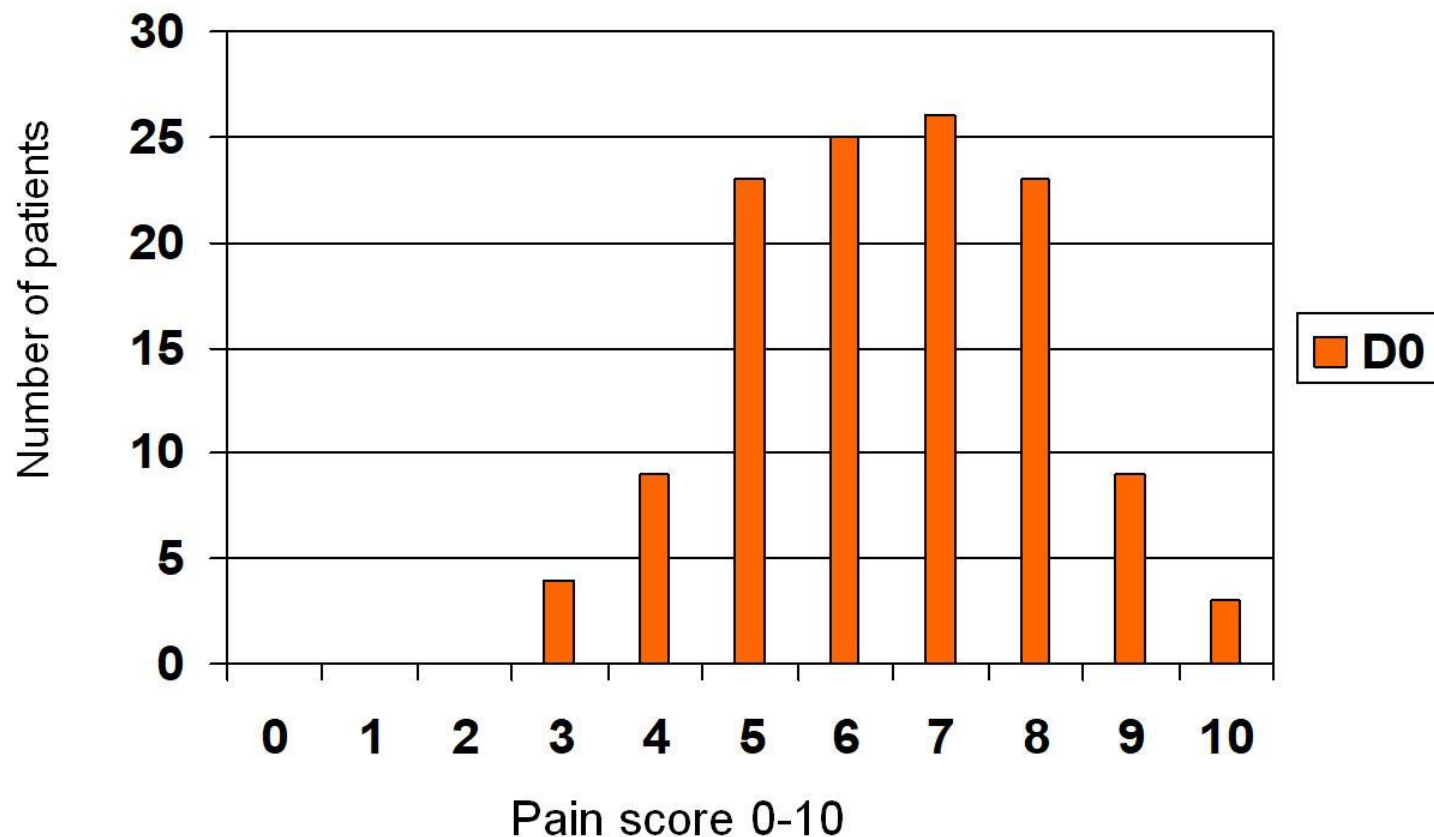
- ✓ Between D0 and D90, pain score decreased from 6.5 (1.6) to 3.6 (2.5) ($p < 0.0001$)
- ✓ 57.5% fulfilled the PASS definition at D90 (*versus 10.6% at baseline*)

VAS score 0-10



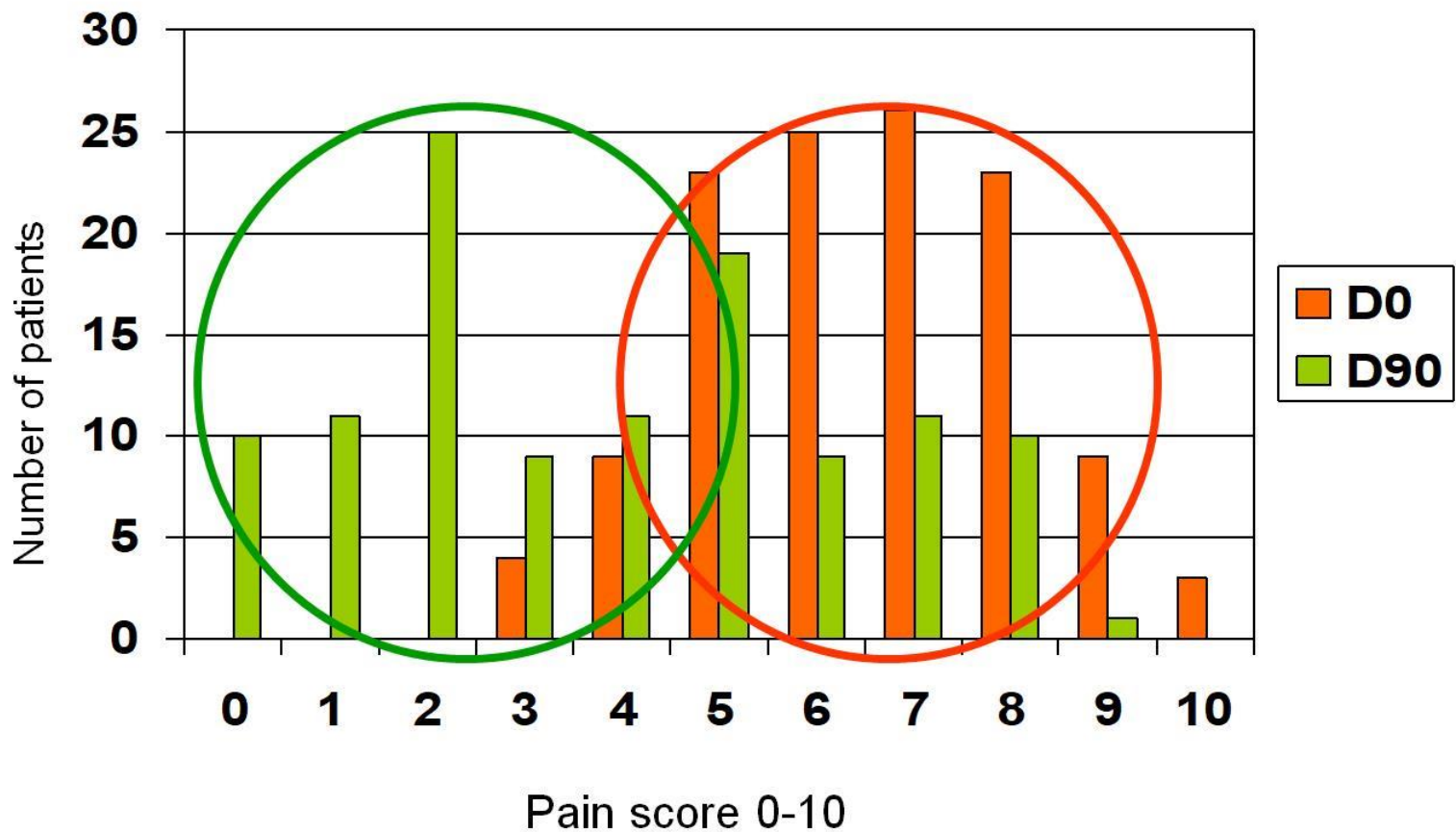
HAnox-M-XL in TMC OA

Pain score: Individual data at D0



HAnox-M-XL in TMC OA

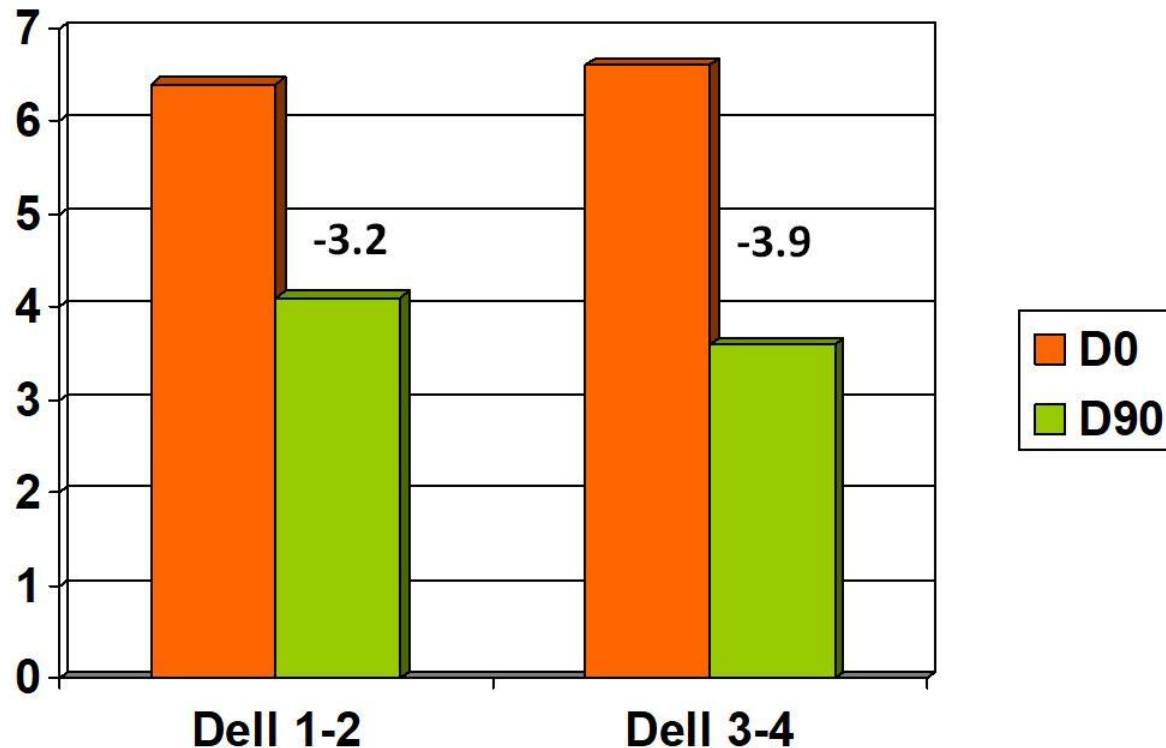
Pain score: Individual data at D0 and D90



HAnox-M-XL in TMC OA

Pain decrease was **unrelated to DELL grade**:

- ✓ Dell 1-2 : 6.4 (1.5) → 4.1 (2.4)
- ✓ Dell 3-4 : 6.6 (1.7) → 3.6 (2.6)



HAnox-M-XL in TMC OA

In univariate analysis response to viscosupplementation was:

Unrelated to:

- ✓ Age
- ✓ Gender
- ✓ BMI
- ✓ Disease duration
- ✓ Level of pain on VAS at baseline
- ✓ Dell grade
- ✓ Type of guidance (US versus X-rays)

Negatively correlated with:

- ✓ NSAIDs regular use ($p=0.012$)

In multivariate analysis no predictive factor of response to viscosupplementation was identified

HAnox-M-XL in TMC OA



There was no safety issue.

- ✓ 11 treatment/injection procedure-related adverse events (10.1%) occurred.
- ✓ All AEs were local pain during or following HA administration and resolved without sequel within 1 to 7 days.
- ✓ No severe AEs

HAnox-M-XL in TMC OA

This large scale pilot study suggests that a single injection of HANOX-M-XL is effective in relieving pain in patients with TMC OA, without safety concern.

Interestingly patients with the more advanced stages of OA seemed to benefit from the treatment as well as those with less advanced OA.



Thanks

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