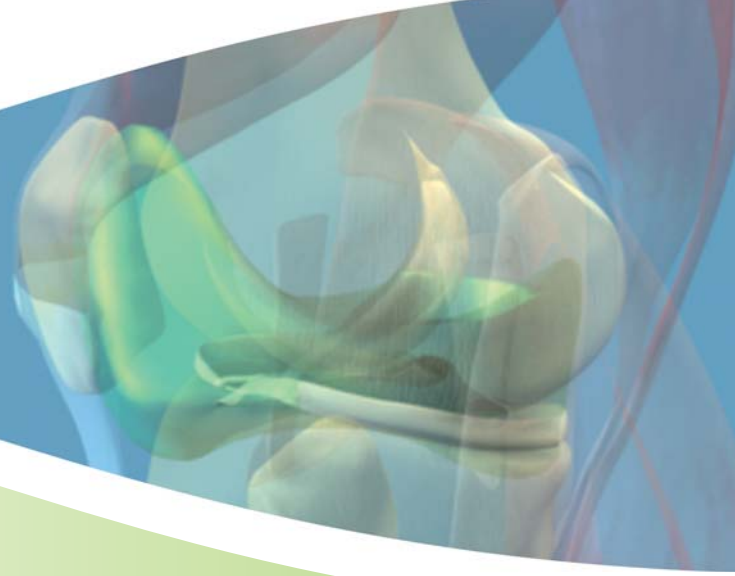




SUPLASYN[®]

Sterile sodium
hyaluronate solution
Synovial Fluid Replacement

Non Avian Derived (NAD)
Non Heat Degraded (NHD)
Sodium hyaluronate



BIONICHE
PHARMA GROUP LIMITED
www.suplasyn.com

Evidence-based medicine

Suplasyn is your physio-logical choice for intraarticular Na-HA treatment. 4 recent publications involving over 1'000 patients with knee OA show that :

1

Suplasyn is similar to NSAID for pain relief and improvement of physical function¹

Randomized, double-blind, placebo-controlled study. 120 patients randomized to 4 treatments groups. Suplasyn: 3 x 2 ml at weekly intervals. Assessments at baseline, 4 & 12 weeks.

Conclusions

- ▶ **Suplasyn was similar to NSAID therapy in improving pain at rest.**
- ▶ **For pain with physical activity and functional performance, Suplasyn may be superior to placebo alone or NSAID alone.**

SIGNIFICANT IMPROVEMENT AT WEEK 4 VS BASELINE.				
Criteria	Suplasyn (25)	Suplasyn + NSAID (29)	NSAID (26)	Placebo (28)
WOMAC				
Pain	•	•	•	•
Disability	•	•	•	•
Stiffness	•	•	•	•
VAS rest pain	•	•	•	•
Self Paced Stepping pain	•	•	•	•
Self Paced Stepping time	•	•	•	•
Self Paced Walking Pain	•	•	•	•
Self Paced Walking time	•	•	•	•

Adapted from (1) – tables 2, 3, 4

2

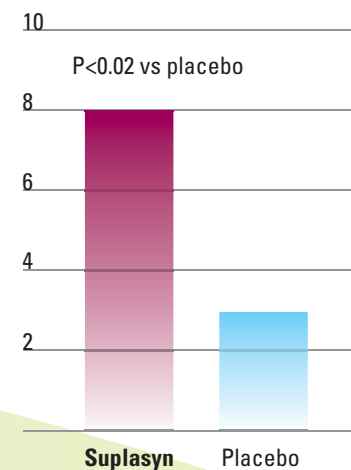
Suplasyn is superior to placebo in improving knee pain and function²

Randomized, double-blind, placebo-controlled, 2-arm parallel design. 106 patients. Follow up 12 weeks. Primary endpoint = WOMAC score at week 3.

Conclusions

- ▶ **After 3 weeks of study treatment, patients who received Suplasyn had significantly greater improvement in knee pain and function than placebo patients.**
- ▶ **No difference in primary efficacy criteria was observed whether 3 or 6 injections were delivered.**
- ▶ **Benefits were unchanged at 12 weeks.**

MEAN CHANGE IN WOMAC PAIN SCORE (Week 3)



Suplasyn is efficient and safe after repeated treatment series³

537 patients referred to a large primary care centre for OA of the knee. Suplasyn 3 x 2 ml at weekly intervals.

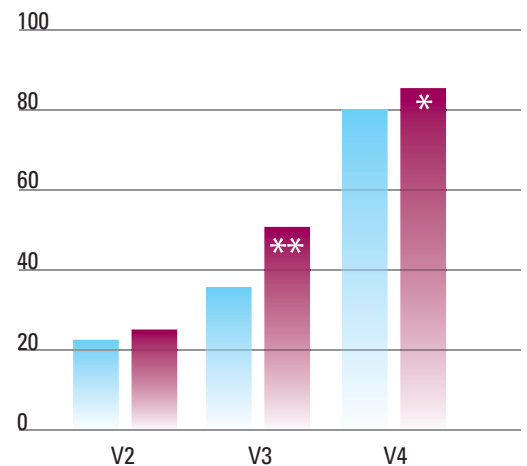
Visits: baseline V1-V2-V3 (injections), V4 (follow up).

Patients return for repeat injection series based on their perception of pain. Cohort follow up 6.7 years.

Conclusions

- ▶ **Suplasyn was highly effective in improving resting and walking pain on a 1st & 2nd treatment series.**
- ▶ **Improvement of pain on walking was significantly better after the 2nd series.**
- ▶ **Duration of symptom control was about 6 months.**
- ▶ **The therapy was highly satisfactory to patients.**

% IMPROVEMENT IN VAS SCORE VS BASELINE WALKING PAIN



■ 1st series ■ 2nd series

All differences significant vs baseline
Between series: ** $p < 0.001$; * $p < 0.03$

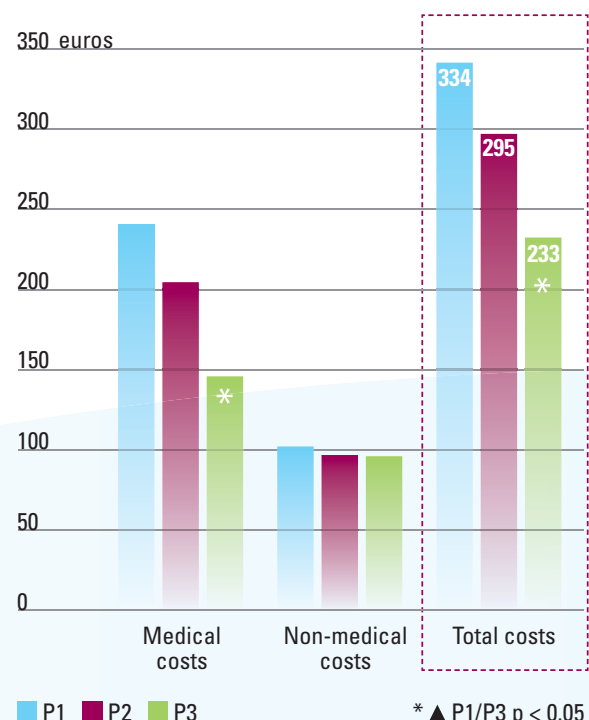
Suplasyn is cost effective⁴

Observational, multi-center, longitudinal, « before-after » design. 296 patients with knee OA. Assessments for the 3 months preceding (P1), and the 3 and 6 months following (P2, P3) treatment with Suplasyn.

Conclusions

- ▶ **All clinical efficacy criteria were significantly improved 3 months after Suplasyn therapy. Further improvements were achieved during the 4th through 6th month after therapy.**
- ▶ **The costs of knee OA decreased during the 6 months after Suplasyn therapy, indicating that the cost of medication is more than offset by the decreased need for other treatments.**

COSTS BEFORE (P1) AND AFTER (P2 & P3) SUPLASYN TREATMENT



■ P1 ■ P2 ■ P3

* ▲ P1/P3 $p < 0.05$

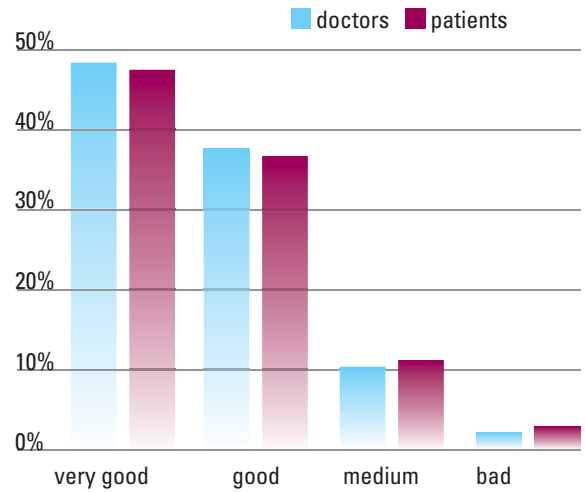
Benefits of Suplasyn are confirmed in real life practice⁵

Multi-center, observational survey of 3614 patients receiving Suplasyn (5 x 2 ml at weekly intervals) for knee, hip or shoulder OA.

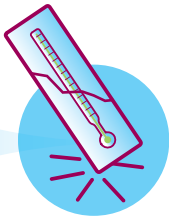
Conclusions

- ▶ **The efficacy of Suplasyn is considered good to very good for over 80% patients, by doctors and patients themselves.**
- ▶ **Suplasyn is safe and well tolerated.**

ASSESSMENT OF TREATMENT EFFICACY



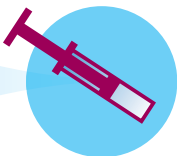
- ▶ **Suplasyn is Non-Avian Derived, produced by bio-fermentation**
 - No risk of cross-species contamination
 - No risk of allergic reaction to avian proteins



- ▶ **Suplasyn is Non Heat Degraded, sterilized by sterile filtration**
 - No risk of heat degradation of the Na-HA molecule
 - Limited risk of low molecular weight fractions



- ▶ **The average Molecular Weight of Suplasyn (500-1'000 kDa) is carefully selected and monitored to**
 - Optimize primary (mechanical) and ancillary (biological) effects of Na-HA therapy (including stimulation of endogenous production of hyaluronan^{6,7})
 - Ensure that it is comfortable to inject, easy on the joint, well tolerated and safe.



- ▶ **Suplasyn is presented in pre-filled 2 ml syringes, containing 20 mg of Na-HA (1%)**
 - Latex free rubber surfaces, pharmaceutical grade glass, finger adaptor, Luer lock & Plastic Rigid Tip Cap (P.R.T.C.).
 - Maximal safety and convenience for the injection.

1 - Effects of hyaluronate sodium on pain and physical functioning in osteoarthritis of the knee. A randomized, double-blind, placebo-controlled clinical trial R.Petrella et al. Arch.Intern.Med Vol 162 Feb 11 2002.

2 - A Prospective, Randomized, Double-Blind, Placebo controlled study to Evaluate the Efficacy of Intraarticular Hyaluronic Acid for Osteoarthritis of the Knee. RJ Petrella & M. Petrella. The Journal of Rheumatology 2006; 33:5.

3 - Hyaluronic acid for the treatment of knee osteoarthritis. Long-term outcomes from a naturalistic primary care experience. RJ Petrella. Am J Phys Med Rehabil. 2005; 84: 278-283.

4 - Medicoeconomic evaluation of hyaluronic acid for knee osteoarthritis in everyday practice: the MESSAGE study. B.Mazières et al. Joint Bone Spine 74 (2007) 453-460

5 - Practice data registry (SUP_AWB_01). Suplasyn in knee, hip and shoulder OA. Germany 01.02.2004 – 27.02.2007. Merkle-Recordati. Data on file.

6 - Potential Mechanism of Action of Intra-articular Hyaluronan Therapy in Osteoarthritis: Are the Effects Molecular Weight dependent ? P.Ghosh & D.Guidolin. Seminars in Arthritis and Rheumatism 2002; 32 (1) :10-37.

7 - Hyaluronans: Is clinical effectiveness dependant on molecular weight ? P.C Vitanzo et al. Review Paper. The American Journal of Orthopedics. September 2006.

Guidelines

- Recommendations for the Medical Management of Osteoarthritis of the hip and knee. Arthritis & Rheumatism. Vol.43, No 9 September 2000: 1905-1915.
- EULAR recommendations 2003: an evidence based approach to the management of Knee Osteoarthritis. Ann.Rheum.Dis 2003; 62:1145-1155.
- OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis & Cartilage (2008), 16, 137-162.

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