Powerful & Long-lasting
Pain Relief.

DUROLANE has more Level-1 clinical studies
than any other single-injection HA

DUROLANE
The original single injection
since 2001*

*First introduced to the European Union in 2001

Key Clinical & Preclinical Resource Guide

Clinical | Preclinical | Reviews | Indications

bioventus®

Index of Clinical Studies

Level - 1

Study 1.
Altman RD, Åkermark C, Beaulieu AD, et al.
Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee

Study 2.
Arden NK, Åkermark C, Andersson M, et al.
A randomized saline-controlled trial of NASHA hyaluronic acid for knee osteoarthritis

Study 3.
Leighton R, Åkermark C, Therrien R, et al.
NASHA hyaluronic acid vs methylprednisolone for knee osteoarthritis: a prospective, multi-centre, randomized, non-inferiority trial

Study 4.
Zhang H, Zhang K, Zhang X, et al.
Comparison of two hyaluronic acid formulations for safety and efficacy (CHASE) study in knee osteoarthritis: a multicenter, randomized, double-blind, 26-week non-inferiority trial comparing Durolane to Artz

Level - 2

Study 5.
Estades-Rubio FJ, Reyes-Martín A, Morales-Marcos V, et al.
Knee viscosupplementation: cost-effectiveness analysis between stabilized hyaluronic acid in a single injection versus five injections of standard hyaluronic acid

Study 6.
McGrath AF, McGrath AM, Jessop ZM, et al.
A comparison of intra-articular hyaluronic acid competitors in the treatment of mild to moderate knee osteoarthritis

Study 7.
Romero Jurado M, Enrique Fidalgo A, Rodríguez Villar V, et al.
Factors related with the time to surgery in waiting-list patients for knee prostheses

Level - 3

Study 8.
Åkermark C, Berg P, Björkman A, et al.
Non-animal stabilised hyaluronic acid in the treatment of osteoarthritis of the knee. A tolerable study

Study 9.
Berg P, Olsson U.
Intra-articular injection of non-animal stabilised hyaluronic acid (NASHA) for osteoarthritis of the hip: A pilot study

Study 10.
Conrozier T, Couris CM, Mathieu P, et al.
Safety, efficacy and predictive factors of efficacy of a single intra-articular injection of non-animal-stabilized-hyaluronic-acid in the hip joint: results of a standardized follow-up of patients treated for hip osteoarthritis in daily practice

DUROLANE®
hyaluronic acid, stabilized single injection

Index of Clinical Studies

Level - 3

Study 11.

Krocker D, Matziolis G, Tuischer J, et al.
Reduction of arthrosis associated knee pain through a single intra-articular injection of synthetic hyaluronic acid

Study 12.

Lindqvist U, Tolmachev V, Kairemo K, et al.
Elimination of stabilised hyaluronan from the knee joint in healthy men osteoarthritis of the knee. A tolerability study

Study 13.

Velasco E, Ribera MV, Pi J.
Single-arm open-label study of Durolane (NASHA non-animal hyaluronic acid) for the treatment of osteoarthritis of the thumb

DUROLANE®
hyaluronic acid, stabilized single injection

Study 1

Study Title

Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee

Full List of Authors

Altman RD, Åkermark C, Beaulieu AD, Schnitzer T., DUROLANE International Study Group.

Full AMA Reference

Altman RD, Åkermark C, Beaulieu AD, Schnitzer T., Durolane International Study Group. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage.* 2004;12(8):642-9.

Study Design

Level-1 clinical study: multicentre, randomized, double-blind, saline controlled.

Indication

Knee

Objective

This study was performed to investigate the safety and efficacy of single-injection NASHA compared with placebo in patients with OA of the knee.

Results

346 patients with knee OA were randomised to a treatment group (172, DUROLANE; 174, saline). WOMAC and SF-36 scores were recorded at baseline and follow-up visits at weeks 2, 6, 13 and 26 post injection. For the overall population, there were no statistically significant between-group differences in response rates for any efficacy parameters. In patients with OA confined to the knee (n = 216), a greater responser rate* to DUROLANE than placebo was observed at week 6 (p=0.025).

*Pain responder rate: the percentage of patients with ≥40% improvement from baseline in WOMAC pain score and an absolute improvement of ≥5 points.

Open Access

Yes Click here to download the full version

DUROLANE®
hyaluronic acid, stabilized single injection

Study 2

Study Title

A randomized saline-controlled trial of NASHA hyaluronic acid for knee osteoarthritis

Full List of Authors

Arden NK, Åkermark C, Andersson M, Todman MG, Altman RD.

Full AMA Reference

Arden NK, Åkermark C, Andersson M, Todman MG, Altman RD. A randomized saline-controlled trial of NASHA hyaluronic acid for knee osteoarthritis. *Curr Med Res Opin.* 2014;30(2):279-86.

Study Design

Level-1 clinical study: multi-centre, randomized, double-blind, saline-controlled.

Indication

Knee

Objective

A 6 week saline-controlled study to investigate the safety and efficacy of DUROLANE in patients with mild–moderate structural OA confined to the study knee.

Results

218 patients with KL grades II-III OA in a single knee were randomised into two treatment groups (DUROLANE, 108; saline, 110). No statistically significant difference in responder rate* was found between the two groups at 6 weeks (DUROLANE: 30.6%; saline: 26.4%). A post-hoc subgroup analysis of patients without clinical effusion in the study knee at baseline showed a significantly higher (p=0.0084) 6 week WOMAC pain responder rate with DUROLANE (DUROLANE: 40.6%; saline: 19.7%).

*Pain responder rate: the percentage of patients with ≥40% improvement from baseline in WOMAC pain score and an absolute improvement of ≥5 points.

Open Access

Yes Click here to download the full version

DUROLANE® hyaluronic acid, stabilized single injection

Study 3

Study Title	**NASHA hyaluronic acid vs methylprednisolone for knee osteoarthritis: a prospective, multi-centre, randomized, non-inferiority trial**
Full List of Authors	Leighton R, Åkermark C, Therrien R, Richardson JB, Andersson M, Todman MG, Arden NK.
Full AMA Reference	Leighton R, Åkermark C, Therrien R, et al. NASHA hyaluronic acid vs methylprednisolone for knee osteoarthritis: a prospective, multi-centre, randomized, non-inferiority trial. *Osteoarthritis Cartilage*.2014;22(1):17-25.
Study Design	Level-1 clinical study: prospective, multicentre, randomised (1:1), corticosteroid-controlled, double-blind.
Indication	Knee
Objective	To compare, in a non-inferiority trial, the effectiveness and safety of a single intra-articular injection of NASHA® (DUROLANE®) with a commonly used steroid; methylprednisolone acetate (MPA).
Results	442 patients with knee OA were randomly assigned to a treatment group (221, DUROLANE; 221, MPA). Results were similar between MPA and DUROLANE at 6-18 weeks (WOMAC pain responser rate). However, there was a significant reduction in the pain responders* from weeks 18-26 in the MPA group that was not observed in the DUROLANE group. The criteria for non-inferiority was met at Week 12. In response to a second DUROLANE treatment at 26 weeks (during the open-label phase of the study), sustained improvements were seen in WOMAC outcomes irrespective of initial treatment. No serious device-related AEs were reported.
Open Access	Yes Click here to download the full version

*Pain responder rate: the percentage of patients with ≥40% improvement from baseline in WOMAC pain score and an absolute improvement of ≥5 points.

DUROLANE®
hyaluronic acid, stabilized single injection

Study 4

Study Title

Comparison of two hyaluronic acid formulations for safety and efficacy (CHASE) study in knee osteoarthritis: a multicenter, randomized, double-blind, 26-week non-inferiority trial comparing Durolane to Artz

Full List of Authors

Zhang H, Zhang K, Zhang X, Zhu Z, Yan S, Sun T, Guo A, Jones J, Steen RG, Shan B, Zhang J, Lin J

Full AMA Reference

Zhang H, Zhang K, Zhang X, et al. Comparison of two hyaluronic acid formulations for safety and efficacy (CHASE) study in knee osteoarthritis: a multicenter, randomized, double-blind, 26-week non-inferiority trial comparing Durolane to Artz. *Arthritis Res Ther.* 2015;17:51. doi: 10.1186/s13075-015-0557-x.

Study Design

Level-1 clinical study: Multicentre, randomised, double-blind, active-controlled, 26-week, head-to-head, non-inferiority comparison of efficacy and safety.

Indication

Knee

Objective

Compare safety and efficacy of intra-articular hyaluronic acid (HA) in two formulations: one 3.0-mL injection of DUROLANE versus five 2.5-mL injections of Artz for the treatment of knee (OA) pain.

Results

DUROLANE and Artz were both equally effective in relieving knee OA pain. DUROLANE was found to be non-inferior in terms of knee pain, physical function, stiffness, and global self-assessment. WOMAC pain scores equally improved from baseline in both treatment groups, at 18 and 26 weeks (p<0.001 for each value, for both groups, at both weeks), suggesting a single injection of DUROLANE can be as beneficial in improving OA-related pain as a five-injection course of HA. Differences between the two HA treatments in the primary and secondary assessments were statistically insignificant through week 26, showing non-inferiority of DUROLANE. However, at weeks 18 and 26, there were twice as many nonresponders to the WOMAC pain walking on a flat surface item in the DUROLANE group (7.5% and 8.1%, respectively) vs. the Artz group (3.8% and 3.2%, respectively; p=0.0176 and 0.0082, respectively). There was an overall 14% incidence of rescue medication use in both groups between weeks 4 to 6, which was considered low compared to a similar study of knee OA treatment. Moreover, fewer patients used a rescue medication between weeks 10 to 26 in the DUROLANE group compared to those in the Artz group. Interestingly, a spike in the use of rescue medication was seen in both groups between weeks 18 to 26, but in both cases, this was most likely due to the effect of the drugs wearing off. In terms of safety, the incidence of treatment-related adverse events (TRAEs) was similar and considered low for both groups. TRAEs: 13.1% in the DUROLANE group vs. 9.8% in Artz group. The most common TRAE was arthralgia: 8.6% DUROLANE group vs. 7.5% in Artz group. Serious AEs: 3 in the DUROLANE group vs. 6 in Artz group; none were considered TRAEs. Due to its unique analysis, the results from this study were very robust, and demonstrate that a single injection of DUROLANE for the treatment of mild-to-moderate OA knee pain is just as safe, efficacious, and tolerable as five injections of Artz.

Open Access

Yes Click here to download the full version

DUROLANE®
hyaluronic acid, stabilized single injection

Study 5

Study Title

Knee viscosupplementation: cost-effectiveness analysis between stabilized hyaluronic acid in a single injection versus five injections of standard hyaluronic acid

Full List of Authors

Estades-Rubio FJ, Reyes-Martín A, Morales-Marcos V, García-Piriz M, García-Vera JJ, Perán M, Marchal JA, Montañez-Heredia E

Full AMA Reference

Estades-Rubio FJ, Reyes-Martín A, Morales-Marcos V, et al. Knee viscosupplementation: cost-effectiveness analysis between stabilized hyaluronic acid in a single injection versus five injections of standard hyaluronic acid. *Int J Mol Sci.* 2017;18(3). doi: 10.3390/ijms18030658.

Study Design

Level-2 clinical study: prospective, randomised, non-blinded study

Indication

Knee

Objective

Compare the effectiveness and treatment cost of NASHA in a single injection with standard preparations of HA in five injections in OA of the knee

Results

Fifty-four patients with knee OA (KL grades II-III) and WOMAC pain score greater than 7 were included. Patients were randomized into two groups: Group I was treated with NASHA (DUROLANE) and Group II with HA (GO-ON®). At week 26, statistically significant improvements were observed for patients treated with DUROLANE vs GO-ON in WOMAC summary scores, as well as subscale scores for pain, stiffness, and function. In addition, the need for analgesia was significantly reduced at week 26 in the DUROLANE-treated group. Finally, the economic analysis showed an increased cost of overall treatment with HA injections with GO-ON vs DUROLANE.

Open Access

Yes Click here to download the full version

DUROLANE®
hyaluronic acid, stabilized single injection

Study 6

Study Title	**A comparison of intra-articular hyaluronic acid competitors in the treatment of mild to moderate knee osteoarthritis**
Full List of Authors	McGrath AF, McGrath AM, Jessop ZM, Gandham S, Datta G, Dawson-Bowling S, Cannon SR.
Full AMA Reference	McGrath A, McGrath AM, Jessop ZM, et al. A comparison of intra-articular hyaluronic acid competitors in the treatment of mild to moderate knee osteoarthritis. *J Arthritis*. 2013;2:108. doi:10.4172/2167-7921.1000108.
Study Design	Level-2
Indication	Knee
Objective	To compare the efficacy and complications of two single-injection HA treatments for knee OA (Synvisc-One® and DUROLANE).
Results	182 knees were treated with KL grades II-III OA. Patients were followed up at 3, 6, 9 and 12 months. Significant improvements were seen in the VAS, SF-36 v2 and Oxford Knee Scores (p=0.01). At 6 months, the difference from baseline values was significantly different in the DUROLANE group (p=0.0001), but not for the Synvisc® group (p=0.783). Adverse reactions occurred significantly less with the more effective product. Nine (9) patients experienced an adverse event. Results suggest that HA treatment for mild to moderate OA can provide pain relief for up to six months, along with reducing the need for analgesic and anti-inflammatory medication.
Open Access	Yes Click here to download the full version

DUROLANE® hyaluronic acid, stabilized single injection

Study 7

Study Title	**Factors related with the time to surgery in waiting-list patients for knee prostheses**
Full List of Authors	Romero Jurado M, Enrique Fidalgo A, Rodríguez Villar V, Mar Medina J, Soler López B.
Full AMA Reference	Romero Jurado M, Enrique Fidalgo A, Rodríguez Villar V, Mar Medina J, Soler López B. Factors related with the time to surgery in waiting-list patients for knee prostheses. *Reumatol Clin*. 2013;9(3):148-55.
Study Design	Level-2 clinical study: single centre, retrospective cohort study.
Indication	Knee
Objective	To assess if DUROLANE treatment could delay the need for a total knee replacement.
Results	Data was collected on 224 patients requiring total knee replacement (TKR), 202 (90.2%) of these patients were treated with DUROLANE. Kellgren-Lawrence grades varied from I to IV (9% KL-I, 27.5% KL-II, 48.2% KL-III, 15.3% KL-IV). In the stratified analysis, treatment with DUROLANE extended time until surgery in the group of patients with KL-III, which was close to statistically significant (p=0.064). The median survival until TKR surgery of patients with grade III lesions and DUROLANE treatment, was 1278 days (95%, 474–2081) and for those not receiving treatment it was 596 days (95% CI, 14–1179).
Open Access	Yes Click here to download the full version

DUROLANE®
hyaluronic acid, stabilized single injection

Study 8

Study Title	**Non-animal stabilised hyaluronic acid in the treatment of osteoarthritis of the knee. A tolerability study**
Full List of Authors	Åkermark C, Berg P, Björkman A, Malm P.
Full AMA Reference	Åkermark C, Berg P, Björkman A, Malm P. (2002). Non-animal stabilised hyaluronic acid in the treatment of osteoarthritis of the knee. A tolerability study. *Clin Drug Investig.* 2002;22(3):157-66.
Study Design	Level-3 clinical study: multicentre, non-blinded, prospective, tolerability study with an extension phase.
Indication	Knee
Objective	To evaluate the safety of an intra-articular injection of DUROLANE (non-animal stabilised hyaluronic acid [NASHA]) in patients with OA of the knee, with an extension phase to assess the safety of a second repeat injection.
Results	One hundred and three patients (128 knees) with arthroscopically verified OA were treated with a single injection of DUROLANE. Patients were followed up at 2 weeks and 3 months post injection. Knee pain variables (at rest, during non-weight-bearing motion, during weight-bearing motion, and at night) were assessed on a VAS scale at each clinic visit. Overall satisfaction with treatment was assessed at the 3-month visit after the first injection. After the first injection, 7 of the reported local reactions fulfilled the criteria to be classed as a device-related adverse event (AE) (knee pain and swelling). Fifty-three patients received a second injection (6.5 to 9.5 months after the first injection). This was followed up 1 month later. After the second injection, 11 AEs were considered potentially related to the study product or the injection procedure, of which three were classed as device-related, unanticipated AEs, giving an event frequency of 4% in 72 injections. A statistically significant reduction in knee pain ($p < 0.0001$) was seen after both injections.
Open Access	No Click here to view the abstract

Study 9

Study Title	**Intra-articular injection of non-animal stabilised hyaluronic acid (NASHA) for osteoarthritis of the hip: A pilot study**
Full List of Authors	Berg P, Olsson U.
Full AMA Reference	Berg P, Olsson U. Intra-articular injection of non-animal stabilised hyaluronic acid (NASHA) for osteoarthritis of the hip: A pilot study. *Clin Exp Rheumatol*. 2004;22(3):300-6.
Study Design	Level-3 clinical study: single centre, prospective, open-label, pilot study.
Indication	Hip
Objective	To assess the safety and potential efficacy of intra-articular non-animal stabilised hyaluronic acid (NASHA) in patients with hip OA.
Results	Thirty-one patients with KL grades II-III OA in the hip were treated with DUROLANE. Follow up was made at 2 weeks and 3 months post injection. A positive response was defined as a ≥ 40% reduction from baseline in the WOMAC pain score, together with an absolute decrease of ≥ 5 points. The response rate was 50% at 2 weeks and 54% at 3 months. In the extension population, the response rates were 69% at 3 months and 44% at 6 months. There were 9 treatment-related adverse events, the majority of which were arthralgia. Adverse reactions were generally transient and all patients made a full recovery.
Open Access	No, only available in hardcopy Click here to view the abstract

Study 10

Study Title

Safety, efficacy and predictive factors of efficacy of a single intra-articular injection of non-animal-stabilized-hyaluronic acid in the hip joint: results of a standardized follow-up of patients treated for hip osteoarthritis in daily practice

Full List of Authors

Conrozier T, Couris CM, Mathieu P, Merle-Vincent F, Piperno M, Coury F, Belin V, Tebib J, Vignon E.

Full AMA Reference

Conrozier T, Couris CM, Mathieu P, et al. Safety, efficacy and predictive factors of efficacy of a single intra-articular injection of non-animal-stabilized-hyaluronic-acid in the hip joint: results of a standardized follow-up of patients treated for hip osteoarthritis in daily practice. *Arch Orthop Trauma Surg*. 2009;129(6):843-8.

Study Design

Level-3 clinical study: single centre, uncontrolled study.

Indication

Hip

Objective

To report on the efficacy and tolerability of a single intra-articular injection of DUROLANE in patients treated for symptomatic hip OA.

Results

Thirty-four patients with primary hip OA, ranging from KL grades I-IV, were treated with DUROLANE. All clinical variables (walking pain, patient global assessment, WOMAC index, and Lequesne index) decreased significantly between baseline and last evaluation at 180 days. Twenty-two of the 34 assessable patients (71%) and of the 40 total patients treated (55%) were classified as of OMERACT-OARSI responders, suggesting the majority of patients derived benefit from the treatment.

*Pham T, van der Heijde D, Altman RD, et al. OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. *Osteoarthritis Cartilage.* 2004;12(5):389-99.

Open Access

No Click here to view the abstract

DUROLANE® hyaluronic acid, stabilized single injection

Study 11

Study Title	**Reduction of arthrosis associated knee pain through a single intra-articular injection of synthetic hyaluronic acid**
Full List of Authors	Krocker D, Matziolis G, Tuischer J, Funk J, Tohtz S, Buttgereit F, Perka C.
Full AMA Reference	Krocker D, Matziolis G, Tuischer J, et al. Reduction of arthrosis associated knee pain through a single intra-articular injection of synthetic hyaluronic acid. *Z Rheumatol.* 2006;65(4):327-31.
Study Design	Level-3 clinical study: single centre, uncontrolled study.
Indication	Knee
Objective	To examine the efficacy of a single intra-articular injection of DUROLANE, based on changes in measurements of pain, functioning, and quality of life in patients with knee joint OA.
Results	Fifty patients with KL grades I-III OA of the knee were treated with a single injection of DUROLANE. Patients were followed up at 2 and 24 weeks post injection. At all three visits, range of motion (ROM), Knee Osteoarthritis Outcome Score (KOOS), European quality of life 5D (EQ5D) and visual analog score (VAS) were recorded. Two weeks post injection, there was a non-statistical improvement from baseline in quality of life, 24 weeks after the injection there was a significant improvement from baseline (p<0.01) from baseline in all parameters.
Open Access	No Click here to view the abstract

Study 12

Study Title	**Elimination of stabilised hyaluronan from the knee joint in healthy men**
Full List of Authors	Lindqvist U, Tolmachev V, Kairemo K, Aström G, Jonsson E, Lundqvist H.
Full AMA Reference	Lindqvist U, Tolmachev V, Kairemo K, Aström G, Jonsson E, Lundqvist H. Elimination of stabilised hyaluronan from the knee joint in healthy men. *Clin Pharmacokinet*. 2002;41(8):603-13.
Study Design	Level-3 clinical study: single centre, uncontrolled study.
Indication	Knee
Objective	To investigate the elimination of stabilised hyaluronan following intra-articular injection into the knee joint of healthy men.
Results	Six male subjects were injected with 3 mL of radiolabeled DUROLANE into the knee joint. Radioactivity levels were then measured to assess how long it took for the DUROLANE to be eliminated from the human knee joint. Elimination of DUROLANE from the joint was described by three distinct phases, with half-lives of 1.5 hours, 1.5 days and 4 weeks. Most likely, the last value reflects the true half-life of DUROLANE.
Open Access	No Click here to view the abstract

DUROLANE®
hyaluronic acid, stabilized single injection

Study 13

Study Title	**Single-arm open-label study of Durolane (NASHA non-animal hyaluronic acid) for the treatment of osteoarthritis of the thumb**
Full List of Authors	Velasco E, Ribera MV, Pi J
Full AMA Reference	Velasco E, Ribera MV, Pi J. Single-arm open-label study of Durolane (NASHA nonanimal hyaluronic acid) for the treatment of osteoarthritis of the thumb. *Open Access Rheumatol.* 2017;9:61-66.
Study Design	Level-3 clinical study: prospective, single-arm, multicentre, open-label study
Indication	Trapeziometacarpal (TMC) joint of the thumb (rhizarthrosis)
Objective	Confirm the safety and effectiveness of viscosupplementation with DUROLANE (NASHA) in rhizarthrosis.
Results	Thirty-five patients were treated with DUROLANE and completed the study. Treatment was well tolerated and effective in reducing symptoms. Measured on a VAS scale, pain scores improved significantly, exceeding the threshold for minimum clinically meaningful improvement (25% change in VAS score) throughout the 6-month follow-up period. A positive response to viscosupplementation was also evident in joint function (QuickDASH and Kapandji scores) and biomechanical function (radial abduction, metacarpophalangeal flexion, and strength of clamp).
Open Access	Yes Click here to download the full version

DUROLANE®
hyaluronic acid, stabilized single injection

Index of Preclinical Studies

DUROLANE®
hyaluronic acid, stabilized single injection

Study 1

Study Title

Non-animal stabilized hyaluronic acid: a new formulation for the treatment of osteoarthritis

Full List of Authors

Ågerup B, Berg P, Åkermark C.

Full AMA Reference

Ågerup B, Berg P, Åkermark C. Non-animal stabilized hyaluronic acid: a new formulation for the treatment of osteoarthritis. *BioDrugs.* 2005;19(1):23-30.

Study Design

Preclinical review article.

Objective

This article aims to describe the structures of HA products, how they are produced and summarises clinical findings. The two main HA treatments addressed in this review are hylan G-F 20 and DUROLANE.

Results

Ågerup et al clearly describe how hylan G-F 20 is produced by combining hylan A and hylan B strands. Hylan is extracted from rooster combs after pretreatment with formaldehyde to produce cross-links between amino acids and animal proteins. This cross-linking results in a protein content of 0.4-0.8% in hylan A. Hylan B is produced by further crosslinking hylan A with divinyl sulfone to produce a gel. The extent of cross-linking in hylan B is approximately 20%. They also discuss the half-life of hylan A being 1.5 days, and 8.5 days for hylan B and that hylan G-F 20 has been associated with AEs and complications, such as swelling and pain in the treated joint, but also serious AEs, such as aseptic acute arthritis, synovitis, pseudogout and anaphylactic shock.

In comparison, Ågerup et al describe the production of DUROLANE using NASHA technology. This involves the secretion of HA from the cellular membrane of fermented bacteria into media. The HA is then extracted from the media and cross-linked at the hydroxyl groups with 1,4-butanediol diglycidyl ether, this cross-linking is limited to 0.5-1.0%. The true half-life of DUROLANE is described considered 4 weeks. Regarding safety, the authors discuss that NASHA products have been used for cosmetic purposes without any safety concerns. Lastly, in a tolerability study as a viscosupplementation treatment, only general transient reactions were experienced which required no treatment.

Open Access

No, only available in hardcopy Click here to view the abstract

Study 2

Study Title

A study of the ability of DUROLANE™ to withstand degradation by free radicals while maintaining its viscoelastic properties

Full List of Authors

Edsman K, Melin H, Näsström J.

Full AMA Reference

Edsman K, Melin H, Näsström J. A study of the ability of DUROLANE™ to withstand degradation by free radicals while maintaining its viscoelastic properties. Poster presented at: 55th Annual Meeting of the *Orthopaedic Research Society*; February 2009; Las Vegas, NV, Poster #1149.

Study Design

Preclinical investigation.

Objective

This preclinical investigation was carried out to determine how Synvisc and DUROLANE are degraded by reactive oxygen species (ROS) compared to normal and osteoarthritic synovial fluid.

Results

Oxidative stress, with increased concentrations of ROS, results in HA degradation in inflammatory diseases of the joints. DUROLANE and Synvisc were exposed to free radicals in both their normal and diluted state. Their viscoelastic property was measured over a 90-minute period using storage (G´) and loss (G´´) moduli. These were then compared to data of normal and arthritic human synovial fluids. DUROLANE showed the ability to retain its storage modulus, which represents the elasticity of the product, over the level of normal synovial fluid during the degradation. This was found to be so for the undiluted as well as for the diluted sample. Immediately after the onset of degradation, levels of both the storage and loss moduli of undiluted Synvisc were in the same order of magnitude as normal synovial fluid, but this dropped rapidly. The diluted Synvisc showed properties closer to pathologic synovial fluid.

Open Access

Yes Click here to download the full version

DUROLANE®
hyaluronic acid, stabilized single injection

Study 3

Study Title

Intraarticular injection of hyaluronan prevents cartilage erosion, periarticular fibrosis and mechanical allodynia and normalizes stance time in murine knee osteoarthritis

Full List of Authors

Plaas A, Li J, Riesco J, Das R, Sandy JD, Harrison A.

Full AMA Reference

Plaas A, Li J, Riesco J, Das R, Sandy JD, Harrison A. Intraarticular injection of hyaluronan prevents cartilage erosion, periarticular fibrosis and mechanical allodynia and normalizes stance time in murine knee osteoarthritis. *Arthritis Res Ther.* 2011;13(2):R46. doi: 10.1186/ar3286.

Study Design

Preclinical investigation using control groups and TGF-ß1 and exercise-induced OA model in mice.

Objective

The objective of this study was to examine the effect of intraarticular HA injection on well-defined stages of the initiation and progression of murine OA. Using a TGF-ß1 and exercise-induced OA model in mice, investigators performed macroscopic and microscopic evaluations of joint tissue structure, determined mechanical allodynia (pain caused by stimuli that do not normally evoke pain) and locomotive function of the hindlimbs.

Results

Osteoarthritis was induced in mice by injecting TGF-ß1 and running the mice uphill for 2 weeks. Animals were injected with either HA or saline the day before running commenced. A control group, without any intervention, also ran uphill for 2 weeks. Gait analysis showed that OA development in this model was accompanied by significant ($p < 0.01$) enhancement of the stance and propulsion times of affected legs. Hyaluronic acid injection (but not saline injection) blocked all gait changes. Analysis of the joints also showed that HA protected joints from femoral cartilage erosion as well as tibial and femoral tissue fibrosis. Both HA injection and saline injection attenuated acute allodynia, but the HA effect was more pronounced and prolonged than the saline injection.

Open Access

Yes Click here to download the full version

DUROLANE® hyaluronic acid, stabilized single injection

Study 4

Study Title	**Hyaluronic acid viscosupplements from avian and non-mammalian sources exhibit biocompatibility profiles with unique, source-specific, antigenic profiles**
Full List of Authors	Wooley PH, Song Z, Harrison A.
Full AMA Reference	Wooley PH, Song Z, Harrison A. Hyaluronic acid viscosupplements from avian and non-mammalian sources exhibit biocompatibility profiles with unique, source-specific, antigenic profiles. *J Biomed Mater Res B Appl Biomater*. 2012;100(3):808-16.
Study Design	Preclinical in-vivo study using an air pouch model in mice.
Objective	The objective of this work was to compare two HA supplements from non-mammalian sources (LMWHA and NASHA) with a viscosupplement derived from an avian source (hylan G-F 20) with respect to their biocompatibility within an inflammatory tissue model, and their immunogical profile.
Conclusion	Air pouches were created in the back of 30 mice. After 6 days, the 30 mice were divided into 5 treatment groups and injected with 500 µL saline, DUROLANE, Synvisc, low molecular weight HA, or positive control. Pouches were stimulated by the injection of 500 µL of sterile saline UHMWPE particle suspension. After 14 days, the tissue thickness of the pouch and antibody levels were measured by ELISA in order to evaluate if the injected products created an inflammatory response. Analysis of the air pouch tissue showed significant increase in thickness beyond that of the control for all HA products except DUROLANE; the largest amount of tissue inflammation was observed in the pouches injected with Synvisc. The cause of the inflammation was shown to be an infiltration of both inflammatory cells and fibroblasts, with the largest inflammatory cell infiltration being caused by Synvisc. Only DUROLANE stimulated fibroblast infiltration. Moderate increases in both TNF-alpha and IL-6 in membrane-extracted proteins supported the histological observations of modest inflammation and fibroblast proliferation. An additional 24 animals were immunized with HA products in complete Freund's adjunvant, in order to stimulate the immune system. These animals were then treated with one of the HA products. A high antibody response was seen in mice injected with HA from an avian source, while low reactivity was observed in sera from mice injected with HA from bacterial sources. There was no indication of a cross-reaction, suggesting that patients with adverse immune responses to HA from an avian source should be unresponsive to a subsequent injection with HA from a non-avian source.
Open Access	Yes Click here to download the full version

Index of Reviews

Study 1.

Altman R, Fredericson M, Bhattacharyya SK, et al.
Association between hyaluronic acid injections and time-to-total knee replacement surgery

Study 2.

Johal H, Devji T, Schemitsch EH, et al.
Viscosupplementation in knee osteoarthritis: evidence revisited

DUROLANE®
hyaluronic acid, stabilized single injection

Study 1

Study Title	**Association between hyaluronic acid injections and time-to-total knee replacement surgery**
Full List of Authors	Altman R, Fredericson M, Bhattacharyya SK, Bisson B, Abbott T, Yadalam S, Kim M
Full AMA Reference	Altman R, Fredericson M, Bhattacharyya SK et al. Association between hyaluronic acid injections and time-to-total knee replacement surgery. *J Knee Surg*. 2016;29(7):564-70.
Study Design	Level-II study: retrospective review of large insurance claims databases
Indication	Knee
Objective	Assess the association between HA injections and time-to-total knee replacement surgery for patients with knee OA
Results	Results from this retrospective analysis included 22,555 patients who had TKR surgery: 14,132 in the non-HA treated cohort and 8,423 in the HA treated cohort. In patients undergoing TKR, the median time-to-TKR surgery was 326 days for the non HA cohort and 908 days for the HA cohort, a difference of 582 days. Those receiving HA injections had a median 1.6-year longer time-to-TKR surgery versus those who did not receive HA injections.
Open Access	No Click here to view the abstract

Study 2

Study Title	**Viscosupplementation in knee osteoarthritis: evidence revisited**
Full List of Authors	Johal H, Devji T, Schemitsch EH, Bhandari M
Full AMA Reference	Johal H, Devji T, Schemitsch EH, Bhandari M. Viscosupplementation in knee osteoarthritis: evidence revisited. *JBJS Rev.* 2016;4(4):e11-e111
Study Design	Review article
Indication	Knee
Objective	Review evidence and guidelines for the use of viscosupplementation in knee OA
Results	Examination of the most recently published literature shows evidence that viscosupplementation favors clinically important reductions in pain among higher-molecular-weight and cross-linked formulations and is a safe option in patients with knee OA. Large primary trials with improved methodology investigating these effects are likely needed. Rare AEs and long-term safety may be best observed through large cohort studies or registry-type databases, rather than randomized trials. Improvement in the translation of knowledge from the current literature and guidelines is required to ensure that a clear and consistent message regarding the use of viscosupplementation for knee OA is reaching clinicians faced with making evidence-based treatment decisions, in the context of their own experience and patients' values and preferences.
Open Access	No Click here to view the abstract

DUROLANE®
hyaluronic acid, stabilized single injection

Summary of Instructions for Use

Europe and Chile

DUROLANE (3 mL): Symptomatic treatment of mild to moderate knee or hip osteoarthritis. In addition, DUROLANE has been approved in the EU for the symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, shoulder, elbow, wrist, fingers, and toes.

DUROLANE SJ (1 mL): Symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, elbow, wrist, fingers, and toes. Both DUROLANE and DUROLANE SJ are also indicated for pain following joint arthroscopy in the presence of osteoarthritis within 3 months of the procedure. There are no known contraindications. You should not use DUROLANE if you have infections or skin disease at the injection site. DUROLANE has not been tested in pregnant or lactating women, or children. Risks can include transient pain, swelling and/or stiffness at the injection site.

Canada

DUROLANE (3 mL): Symptomatic treatment of mild to moderate knee or hip osteoarthritis. In addition, DUROLANE has been licenced for the symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, fingers and toes.

DUROLANE SJ (1 mL): Symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, fingers and toes.

Both DUROLANE and DUROLANE SJ are also indicated for pain following joint arthroscopy in the presence of osteoarthritis within 3 months of the procedure.

Australia, New Zealand, Mexico

DUROLANE (3 mL): Symptomatic treatment of mild to moderate knee osteoarthritis. There are no known contraindications. You should not use DUROLANE if you have infections or skin disease at the injection site. DUROLANE has not been tested in pregnant or lactating women, or children. Risks can include transient pain, swelling and/or stiffness at the injection site.

United Arab Emirates, Saudi Arabia, Jordan, Hong Kong, Indonesia, India, Colombia, Argentina, Brazil

DUROLANE (3 mL): Symptomatic treatment of mild to moderate knee or hip osteoarthritis. There are no known contraindications. You should not use DUROLANE if you have infections or skin disease at the injection site. DUROLANE has not been tested in pregnant or lactating women, or children. Risks can include transient pain, swelling and/or stiffness at the injection site. Full prescribing information can be found in product labeling, or at DUROLANE.com.

Taiwan

DUROLANE (3 mL): Treatment of pain in OA of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics, e.g., acetaminophen. Full prescribing information can be found in product labeling, or at DUROLANE.com.

DUROLANE.com
BioventusGlobal.com

DUROLANE and NASHA are registered trademarks of Galderma S.A.
The Bioventus logo is a registered trademark of Bioventus LLC.
Synvisc and Synvisc-One are registered trademarks of Genzyme Corporation.
EUFLEXXA is a registered trademark of Ferring B.V.

DUROLANE® hyaluronic acid, stabilized single injection

bioventus®

© 2018 Bioventus LLC SMK-000902c 6/18