# NEOIAL HC

The innovation of the **HYALURONIC ACID**
with **SILKWORM COLLAGEN**

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# NEOIAL HC

STERILE HYDROGEL, TRANSPARENT, VISCOELASTIC, ADSORBABLE

Based on HIGHLY PURIFIED **HYALURONIC ACID**
with **TWO MOLECULAR WEIGHTS** and
**SILKWORM RECOMBINANT COLLAGEN**


40 mg/2 ml


60 mg/4 ml


80 mg/4 ml

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# NEOIAL HC

**Class III MEDICAL DEVICE** for **INTRA-ARTICULAR USE**

*certified by the Notified Body in Italy with the* CE 0477

**INDICATED:**

**- PAIN TREATMENT** in **OSTEOARTHRITIS**

- **REDUCED MOBILITY** in the degenerative or traumatic alterations of

***KNEE***, ***HIP*** and ***SHOULDER***

**- INCREASE THE VISCOELASTICITY** of the SYNOVIAL FLUID

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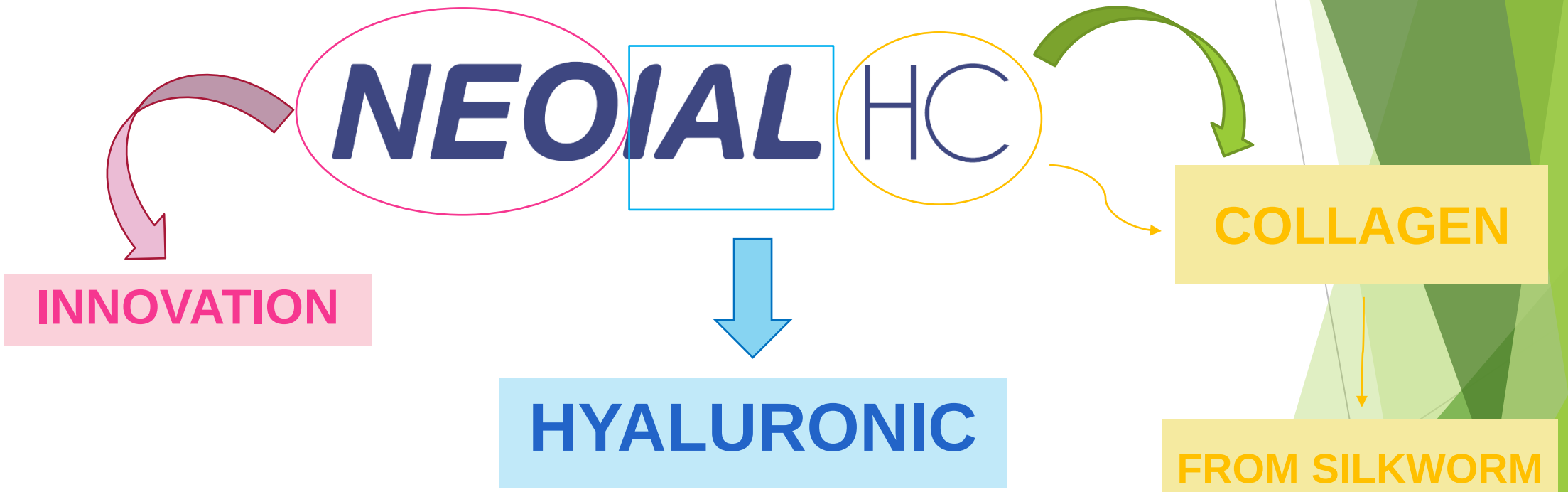
# WHY THE NAME?




IT'S the **ONLY PRODUCT** containing silkworm collagen !

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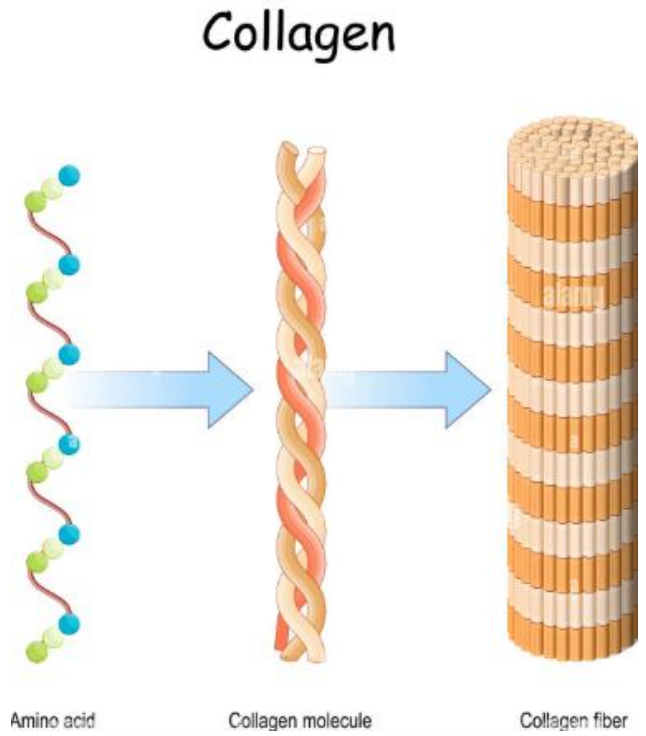
# COLLAGEN

The collagen basic structure is a **TRIPLE HELIX** made by different combinations of **type a1 and type a2 polypeptide chains.**

The main characteristic of the typical collagen molecule is its long helical, rigid, triple filament structure, in which three collagen polypeptide chains (the a chains) are winded each other in a SUPER HELIX similar to a rope.



# STANDARD COLLAGEN

Type I standard triple helix collagens, like the BOVINE, OVINE, PORCINE must be inserted in high quantities in their different compositions because the digestive process drastically reduces their bioavailability.

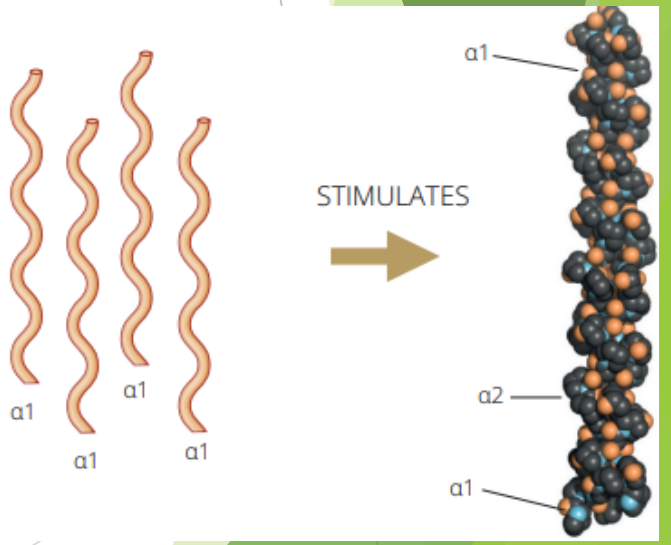
**VS**

# SILKWORM COLLAGEN

This **COLLAGEN is NOT the standard** triple helix **collagen,** but is directly the

## α1 hydroxylated type I COLLAGEN

Fundamental element of the endogen collagen production process.
**DIRECTLY STIMULATES THE COLLAGEN FIBRIL CREATION PROCESS**, without any degradation, but maintaining a **high BIOAVAILABILITY,** easing and accelerating the regenerative process.

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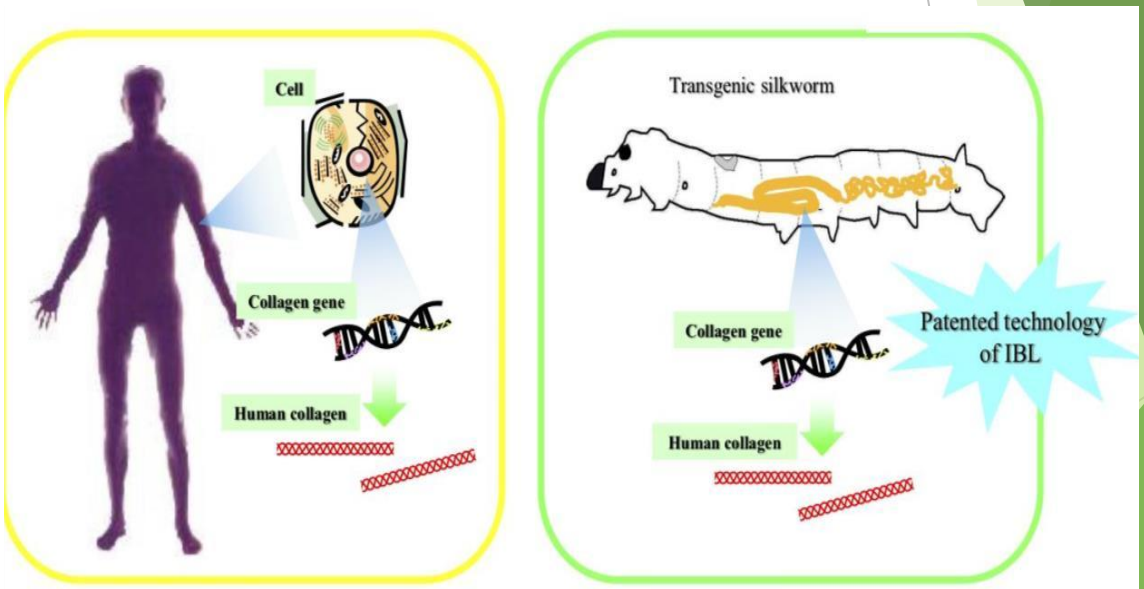
The RECOMBINING COLLAGEN, or R α1 polypeptide chain of the collagen has been obtained by a group of Hiroshima University biologists, which inserted a gene which produces collagen in the silkworm genetic heritage, exactly replacing the one which produces *fibrosin,* one of the proteins which compose silk fibres, produced in the silkworm silk glands.

Silkworm cocoons whence collagen is extracted




PATENTED TECHNOLOGY

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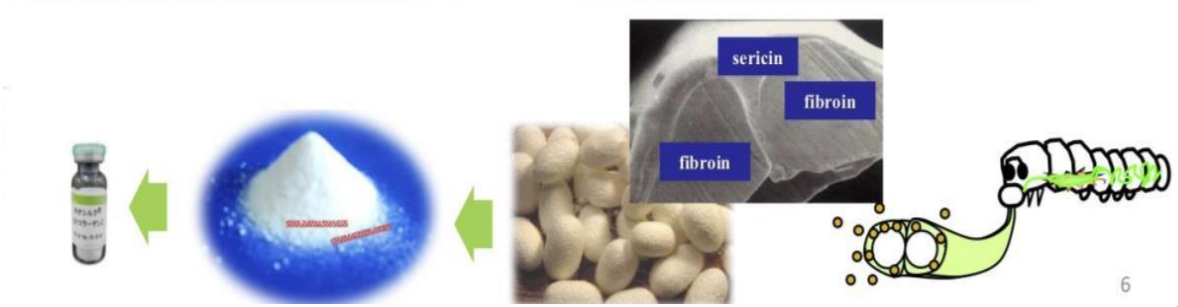
Will be sufficient to heat the cocoon, killing the larva inside, to extract the silk and separate the strands. Through chemical processes is than extracted the **COLLAGEN.**



# NEOIAL HC

## α1 R polypeptide chain of type I COLLAGEN

- 99,9% SIMILARITY TO THE HUMAN TYPE COLLAGEN
- GREATER USAGE SAFETY, since ANALLERGIC and NOT IMMUNOGENIC
- HIGHLY AND QUICKLY BIOAVAILABLE since α1 chain
- STIMULATES CARTILAGINOUS CELLS PROLIFERATION

**Can be defined PROCOLLAGEN**

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# NEOIAL HC

Silkworm collagen injected intra-articularly with hyaluronic acid **provides mechanical support** with a clear **positive effect** on the **stabilization of joint mobility, pain reduction, and the patient's quality of life.**

Furthermore, it also serves a structural function: it **restructures, protects, and reinforces cartilage, because stimulate chondrocytes to produce cartilage and hinder the normal inflammatory response.**

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# NEOIAL HC

## COMPOSITION

- Hyaluronic acid LW
- Hyaluronic acid MW
- Recombinant silkworm collagen
- Sodium carboxymethylcellulose

**RECOMBINANT COLLAGEN is EFFECTIVE**

**as demonstrated by “IN VITRO” studies on human knee cartilage chondrocytes** → **THE CELLULAR PROLIFERATION INCREASE** →

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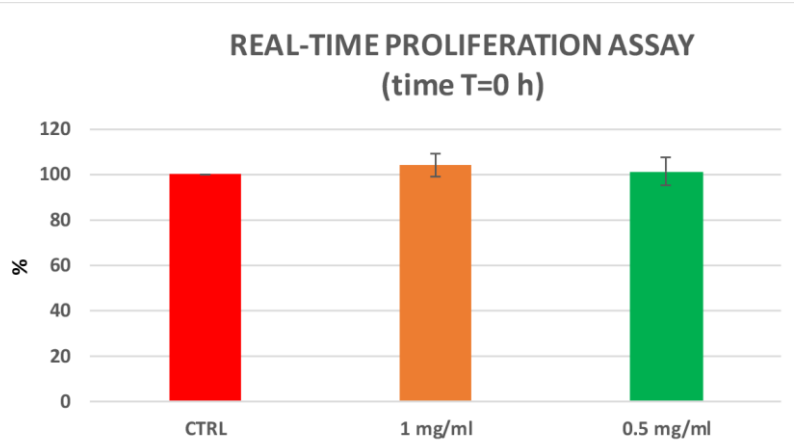
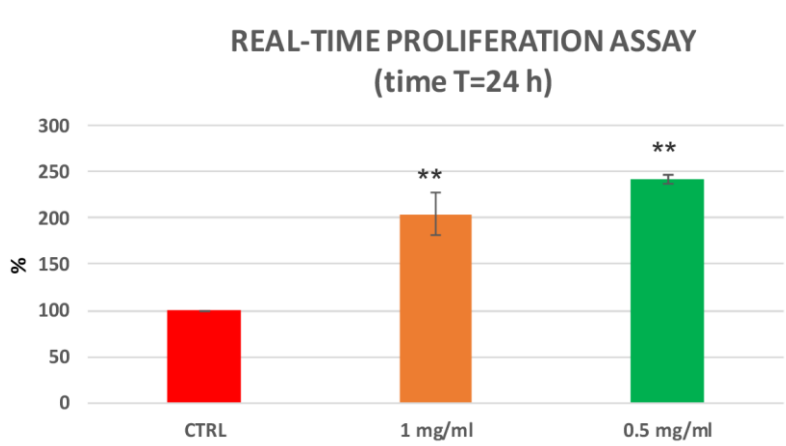
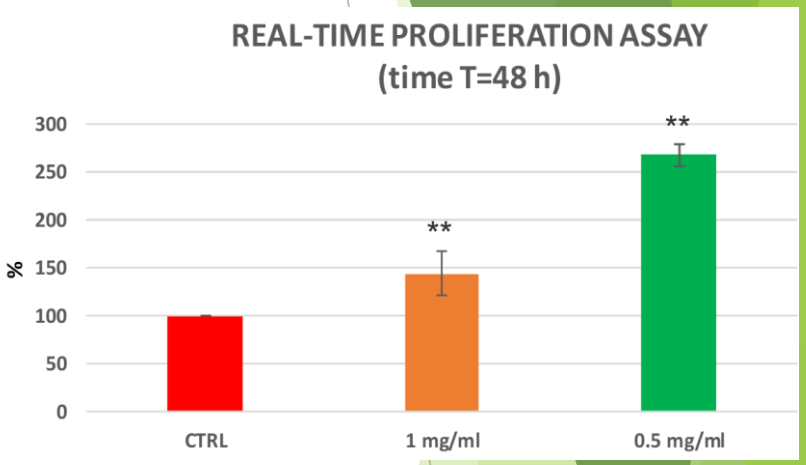
# NEOIAL HC




**GROWTH OF CELLULAR PROLIFERATION already after 48 hrs.**

**In vitro studies demonstrated also the ABSENCE of CYTOTOXICITY, HYPERSENSIBILITY, SKIN REACTIVITY and implantability consequences like CYSTS, GRANULOMAS or ADHESIONS**

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# NEOIAL HC

## COMPOSITION

- **Hyaluronic acid LW**
- **Hyaluronic acid MW**
- **Recombinant collagen**
- **Sodium carboxymethylcellulose**

## HYALURONIC ACID

plays the role of viscosupplement, by increasing the viscoelasticity of synovial fluid, offering a mechanical protection on the articular cartilage, preventing bones from entering into contact during the movement.

→ *HA at MW at LW allows a Hyaluronic Acid high concentration, and increased viscosupplementing, warranting, in the meantime, an hydrogel easier extrusion from the syringe*

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# NEOIAL HC

## COMPOSIZIONE

- **Hyaluronic acid LW**
- **Hyaluronic acid MW**
- **Recombinant collagen**
- **Sodium carboxymethylcellulose**

## CARBOXYMETHYLCELLULOSE (CMC)

Is a RETICULATED polymer derived from cellulose, used as excipient and food thickener, **fully re-absorbable, biocompatible, which IMPROVES the RHEOLOGIC PROPERTIES and the product VISCOSITY**

Seems also to maintain the endogen hyaluronic acid and to promote the cartilage regeneration thanks to the hyaluronidase enzyme INHIBITION.

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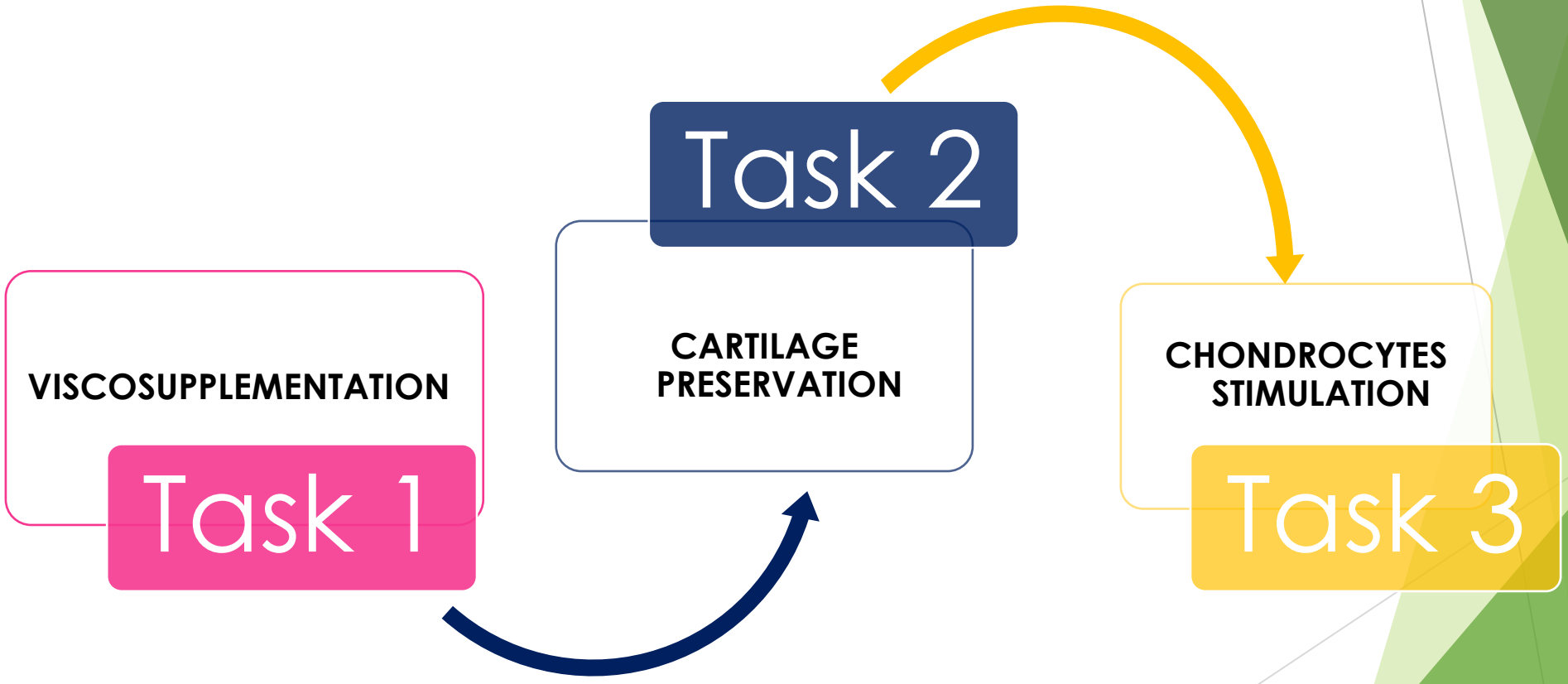
# MAIN TASKS OF NEOIAL HC

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# MAIN TARGET OF NEOIAL HC

PATIENT WITH CARTILAGE THINNING

SPORTY PATIENT

PATIENT WHOM SURGERY IS NOT RECOMMENDED

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NEOIAL HC

# CLINICAL STUDY

***"Clinical efficacy and safety of NEOIAL HC (Hyaluronic acid + Collagen) for intra-articular use in the severe knee osteoarthritis."***

*European Journal of Musculoskeletal Diseases*
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BPI

*Evaluation Study*

## CLINICAL EFFICACY AND SAFETY OF NEOIAL HC (HYALURONIC ACID + COLLAGEN) FOR INTRA-ARTICULAR USE IN THE TREATMENT OF SEVERE KNEE OSTEOARTHRITIS

R. Buda, MD[1], D. Bruni[1], A. Pantalone[1], D. Di Palma[1] and L. Perazzo[2]

[1]Orthopedic and Traumatology Clinic "Ss. Annunziata" Hospital, Chieti, Italy;
[2]Accredited Private Hospital, "Villa Laura", Bologna, Italy

*Correspondence to*:
Roberto Buda, MD PhD,
Orthopedic and Traumatology Operative Unit Complex,
"Ss. Annunziata" Hospital,
Via dei Vestini,
66100 Chieti (CH) Italy
e-mail: roberto.buda@unich.it

**ABSTRACT**

Osteoarthritis (OA) is a common cause of pain and disability in adults, with at least 40% of individuals over 65 experiencing symptomatic OA of the hip or knee, according to the Osteoarthritis Research Society International (OARSI). Knee OA is the eleventh leading cause of years lived with disability, as reported by the World Health Organization. Current guidelines recommend using intra-articular injections of hyaluronic acid (HA) to treat OA, which can provide slow and prolonged pain relief for up to six months after the first injection. However, there is limited literature regarding the intra-articular use of isolated collagen or its combination with HA for treating knee OA. The present study (pre-market clinical trial) reports a clinically safe profile. It provides evidence of the efficacy of a viscosupplementation solution containing collagen type I, and HA obtained via bacterial fermentation (NEOIAL HC) in treating symptomatic knee OA. The primary endpoint was the safety and efficacy parameters of NEOIAL HC in intra-articular infiltration to treat severe knee osteoarthritis. The evaluation was conducted through subjective and objective clinical scores and reporting of adverse events. The secondary endpoint will be knee function 6 months after treatment. The preliminary findings suggest sustained benefits in pain and physical function from the cycle of collagen Type I and HA injections.

**KEYWORDS**: *hyaluronic acid, knee osteoarthritis, viscosupplementation, collagen*

**INTRODUCTION**

Osteoarthritis (OA) is a degenerative, chronic, and progressive joint disease with a multifactorial etiology and is most common in weight-bearing joints, such as knees (1). Currently, no treatment is available to stop OA progression, and joint replacement surgery is the only solution for severe cases. Non-operative treatment options include intra-articular drug injections into affected joints, which increase local bioavailability and reduce systemic exposure, adverse events (AEs), and costs compared with traditional pharmacologic therapies (2-4). Intra-articular injections of corticosteroids

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# STUDY PROTOCOL

Evaluation of the NEOIAL HC **safety and efficacy** parameters in the infiltrative treatment for severe knee osteoarthritis (OA). The patients suffering from severe knee OA treated with **3 injections of 40mg.**

**Infiltrations of NEOIAL HC, at a distance of one week, followed by a fourth infiltration of the same product one month after the third one.**

**The study included 15 patients aged 50-80**.

Patients underwent a **baseline clinical evaluation, and were monitored for adverse events after each infiltration: follow up evaluations were conducted at the end of the treatment, 3 and 6 months after follow up .**

**Efficacy and safety were evaluated on the injection day and approximately 1 week, 1 month and 3 and 6 months after follow up.**

**At each follow up visit, a well-validated VAS , KOOS , WOMAC and LEQUESNE SCORE**

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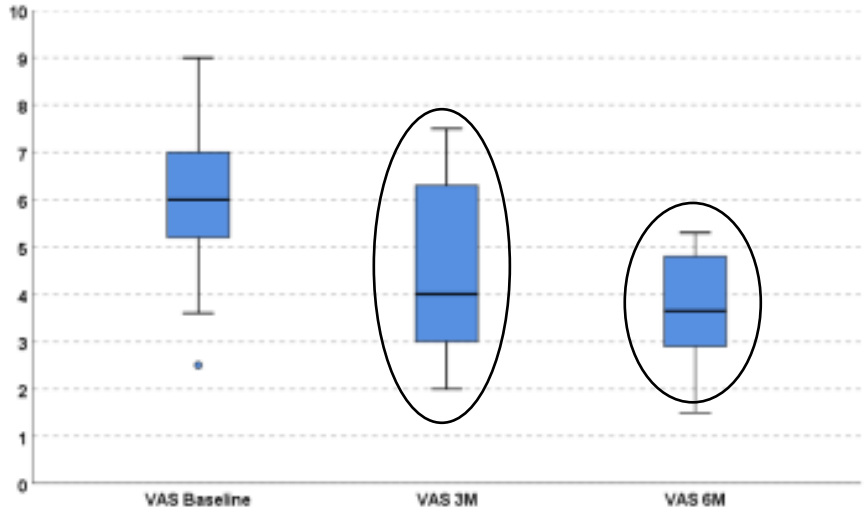
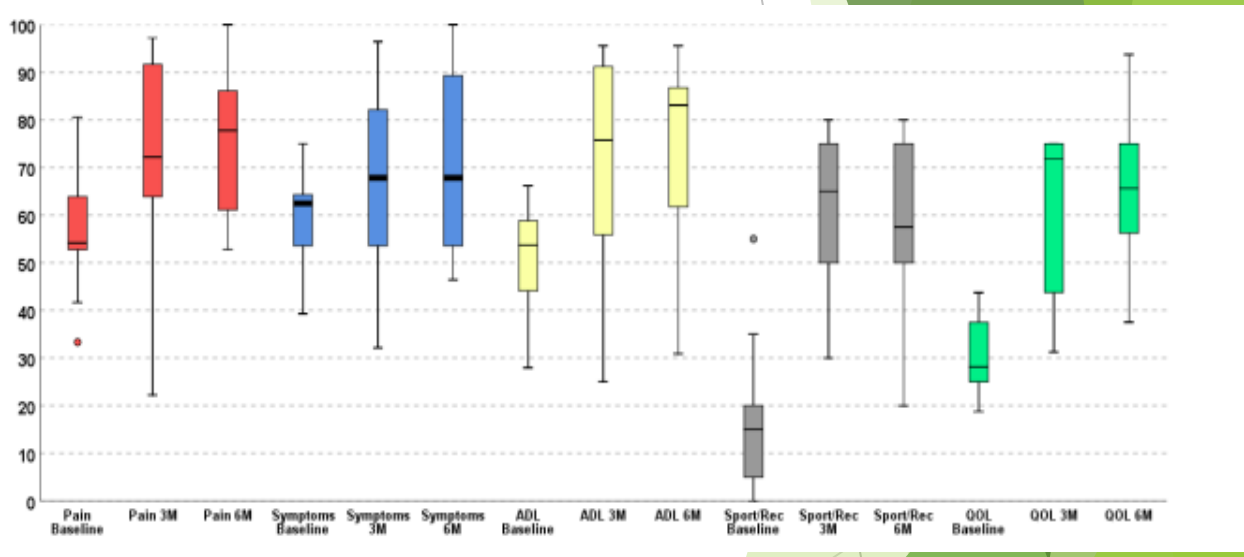
# VAS AND KOOS SCORE

Pain reduction as early as **3** months from baseline and one further as **6** months.




VAS score at baseline and after 3 and 6 months.

The results of Koos questionnaire confirmed the data observed on the Vas scale.




KOOS score items at baseline and after 3 and 6 months.

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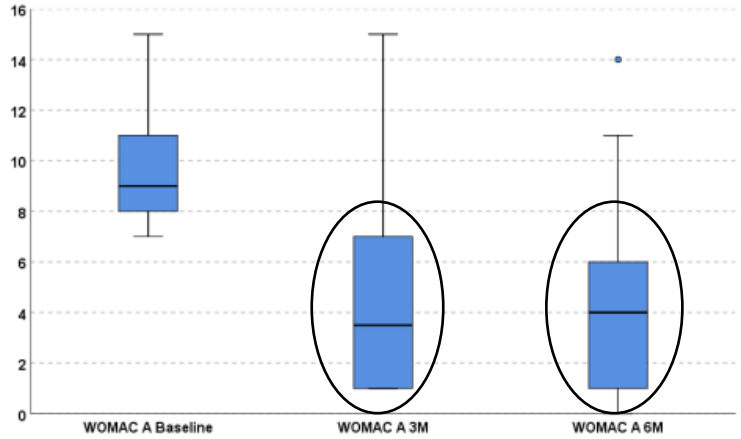
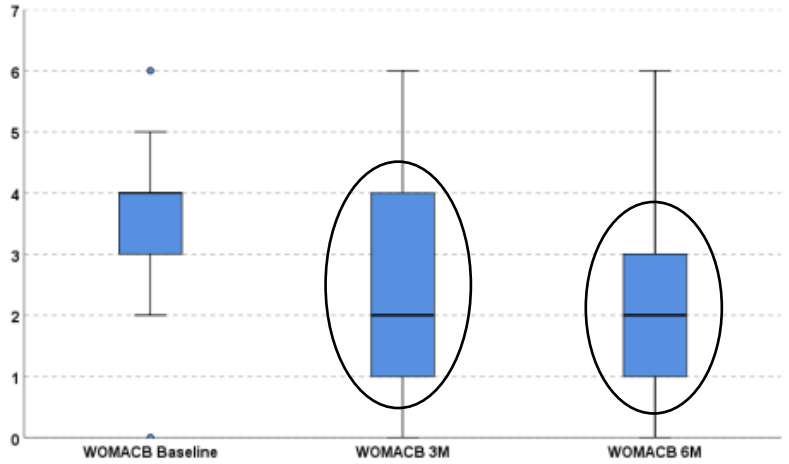
# WOMAC SCORE

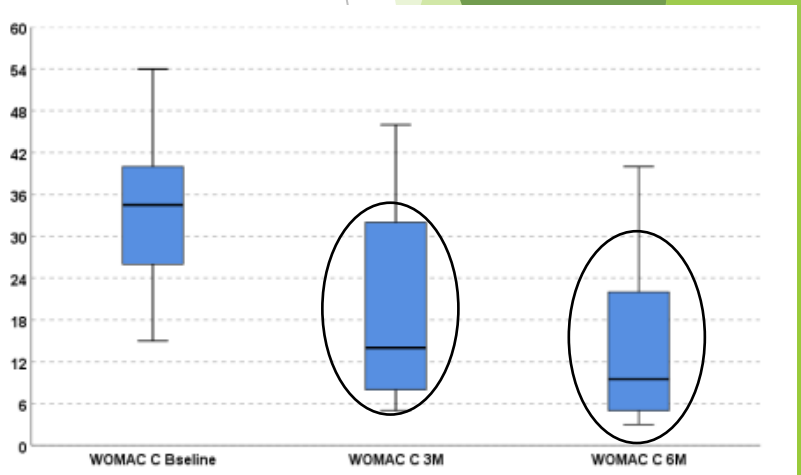
In every subscore Womac scale the reduction of **pain** and **daily living activity** it's confirmed as early as **3** months and at **6** months for **rigidity**.




WOMAC subscore A items **pain** at baseline and after 3 and 6 months.




WOMAC subscore B items **rigidity** at baseline and after 3 and 6 months.




WOMAC subscore C items **daily living activity** at baseline and after 3 and 6 months.

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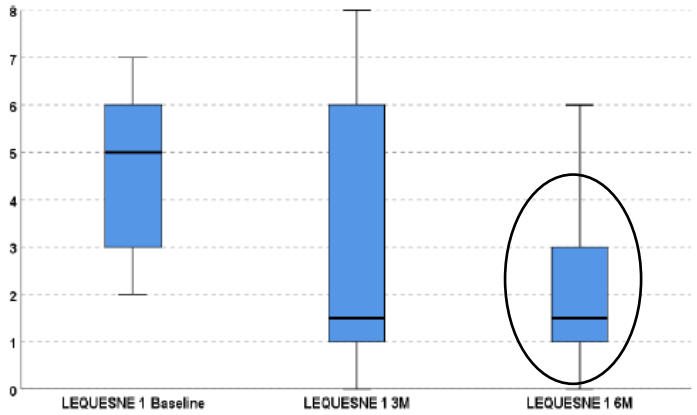
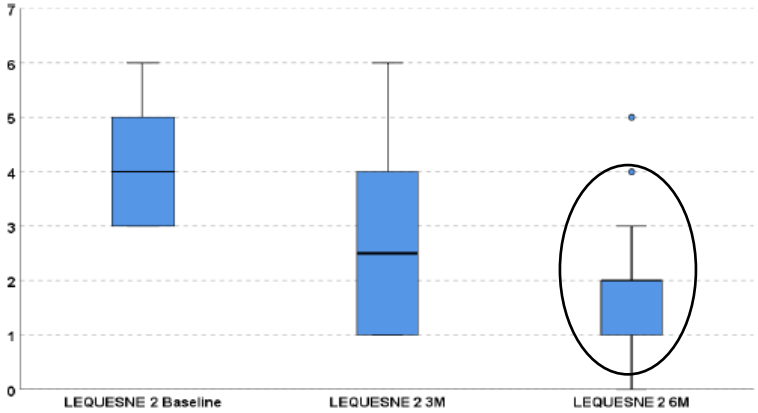
# LEQUESNE SCALE

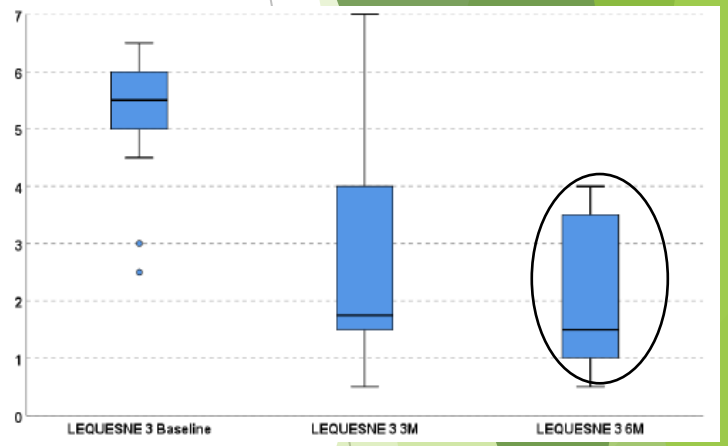
Lequesne subscore pain, maximum distance walked and activity of daily life the largest reduction was confirmed at **6** months.




Subscore **pain**




Subscore **maximum distance walked**




Subscore **daily life activity**

# CONCLUSIONS

The present study showed a clinically good safety profile and provided preliminary evidence of NEOIAL HC's efficacy in treating symptomatic knee OA.

**The data analysis obtained at 3 months showed a significant improvement in the values in all 4 evaluation scales ( VAS, KOOS, WOMAC and LEQUESNE).**

**This improvement was confirmed at 6 months.**

# NEOIAL HC

## METHODS OF USE


**40 mg**/2 ml– **3** injections at **1 week intervals**, with a possible follow-up injection after 1 month if deemed necessary by the physician.


**60 mg**/4 ml– **2** injections at **1 week intervals**, with a possible follow-up injection after 1-2 months, if deemed necessary by the physician.


**80 mg**/4 ml – **1** single injection , followed by a **possible follow-up** injection within 1–2 months at the physician's discretion.

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# NEOIAL HC

## PRECAUTIONS – WARNINGS – USEFUL INFORMATION

- The product should not be injected in the presence of **an infected or severely inflamed joint**.and in case of infections in place or **inflammatory conditions of the skin** in proximity of the infiltration site.
- Before the injection **suck any possible joint effusions** and prepare the site with an **appropriate disinfectant.** The use of quaternary ammonium compounds disinfectants is not recommended because, in presence of hyaluronic acid, can promote the **precipitates formation**.
- Inject NEOIAL HC slowly into the joint, possibly at **room temperature**.
- Do not undergo the joint to **excessive weights** the hours after the injection.
- As there is no evidence from clinical trials in **pregnancy** or breastfeeding, the use is not recommended.
- Safety and efficacy of NEOIAL HC use with other intra-articular treatments is not ascertained. Therefore, **avoid the administering** of NEOIAL HC **simultaneously to other** intra-articular products to prevent any possible alteration.
- Rarely reactions on the injection site are reported, as **pain, swelling/effusion, heat, redness, itch and synovitis. Symptoms are bearable and temporary**; spontaneously disappear in few days keeping the limb at rest with the application of ice. As for every intra-articular treatment, it may occur septic arthritis in rare cases if infection is not administered in compliance with general precautions of asepsis.

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# NEOIAL HC

1. IS THE **FIRST** TREATMENT FOR INTRA -ARTICULAR USE WHICH COMBINES DOUBLE MOLECULAR WEIGHT **HYALURONIC ACID** WITH **SILKWORM COLLAGEN.**

2. SILKWORM COLLAGEN HAS A **99,9% SIMILARITY** WITH HUMAN COLLAGEN, THEREFORE ALLERGY RISKS ARE PRACTICALLY ABSENT.

3. DOES NOT LIMIT TO BRING A **VISCOSUPPLEMENTATION ACTION**, BUT INDUCES AND STIMULATES THE **CARTILAGE FORMATION** THANKS TO THE DIRECT ACTION OF THE COLLAGEN ON THE **CHONDROCYTES**.

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