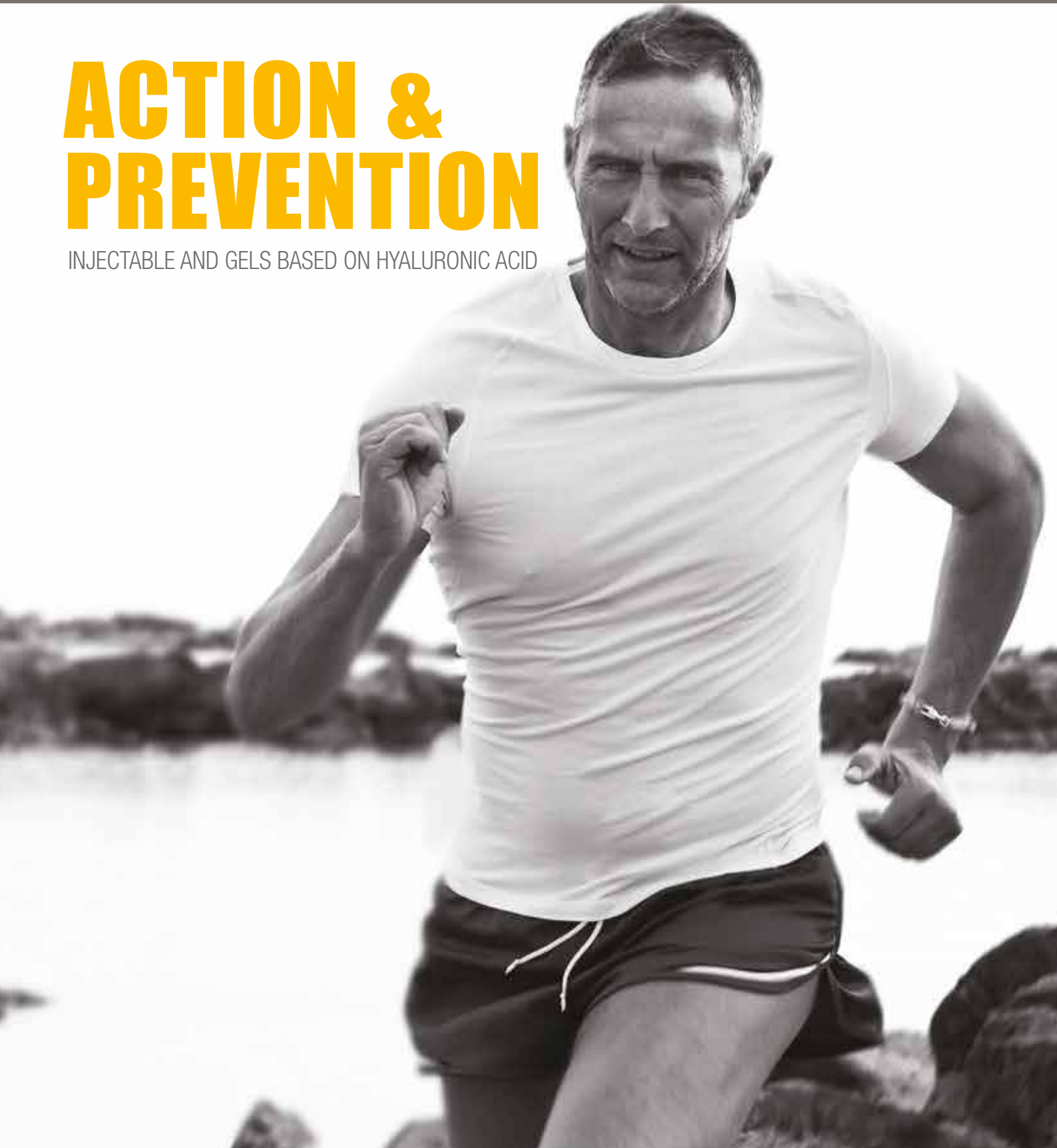


REGENflex
PROJECT

ACTION & PREVENTION

INJECTABLE AND GELS BASED ON HYALURONIC ACID



HYALURONIC ACID FOR JOINTS TENDONS AND MUSCLES

REGENYAL
LABORATORIES

ACTION & PREVENTION

HYALURONIC ACID FOR JOINTS, TENDONS AND MUSCLES



What is Hyaluronic Acid (HA)

- It is a natural component of the connective tissue
- Given its ability to form connections with collagen, proteoglycans, fibronectin and water, it is the basis of large molecular units that support the extracellular matrix
- It is an important component of the synovial fluid
- Helps to lubricate the joint and to damp down mechanical stress (lubricating and damping function)
- Protects the cartilage against the penetration of inflammatory cells and from the lytic enzymes
- It binds to LUBRICIN, glycoprotein that protects articular surfaces by lubricating them and that plays a fundamental role in osteoarthritis and tendinopathies.

HA and Joints



In trauma-caused and degenerative diseases of the joints there is an in situ decrease of hyaluronic acid, due to which the synovial fluid is less viscous. Such deficiency determines a compression of the articular function and causes pain.

The intra-articular administration of exogenous hyaluronic acid helps to:

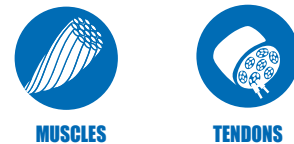
**PREVENT THE NATURAL
DEGRADATION OF THE JOINTS**

**REDUCE THE PAIN
AND INFLAMMATION**

**RESTORE
THE VISCO-ELASTIC PROPERTIES
OF THE SYNOVIAL FLUID**

IMPROVE ARTICULAR MOBILITY

HA Tendons & Muscles



In traumatic and degenerative pathologies of the tendon body of the muscle-tendon and bone-tendon transition area, (also determining a better muscular contractility) the administration of hyaluronic acid, in combination of 5 fractions with progressive molecular weight, carries out a bioinduction, able to activate:

REPAIR

REGAIN ELASTICITY

REVASCULARISATION – NEOANGIOGENESIS

ACTIVATION OF BIOLOGICAL FACTORS



REGENFLEX PROJECT is a line of **INTRA-ARTICULAR INJECTABLE** products, **TENDON INJECTABLES** and **TOPICAL USE GELS** based on Hyaluronic Acid. Injectables are recommended in **PREVENTION** and **TREATMENT** of degenerative and traumatic pathologies of joints, tendons and muscles. Gels are recommended in **PAIN THERAPY** for joints and muscles.

REGENflex
PROJECT

STARTER
REGENflex



1 INTRA-ARTICULAR INJECTIVE 32mg / 2ml

REGENflex



1 INTRA-ARTICULAR INJECTIVE 16mg / 2ml

BIO RIV@LUMETRIA

BIO-PLUS
REGENflex



1 INTRA-ARTICULAR INJECTIVE 75mg/3ml

T&M
REGENflex



1 TENDONS AND MUSCLES INJECTIVE 32mg / 2ml

Kit
REGENflex



1 STARTER 32mg / 2ml - 1 BIO-PLUS 75mg/3ml

Gel
REGENflex



2 HOT / COLD GELS 100 ml

STARTER
REGENflex

Concentration
HA 1.6%
HA LINEAR



- ◀ HIGH HA DENSITY 1.6%
- ◀ INHIBITION OF THE INTERLEUKIN
- ◀ IMMEDIATE REDUCTION OF PAIN AND INFLAMMATION
- ◀ FAST RESTORATION OF THE FUNCTIONS
- ◀ VISCO-SUPPLEMENT, ANALGESIC EFFECT
- ◀ TROPISM FOR ARTICULAR CAPSULAR PAIN RECEPTORS
- ◀ INHIBITION OF ACID PHOSPHATASE

REGENflex

Concentration
HA 0.8%
HA LINEAR



- ◀ LOW HA DENSITY 0.8%
- ◀ RECOVERY OF RHEOLOGY AND MAINTAINS OF RHEOLOGY AND METABOLIC HOMEOSTASIS OF THE ARTICULAR CHAMBER
- ◀ ANTIPHLOGISTIC EFFECT, INCLUDING RHEUMATIC PATIENTS WITH
- ◀ ASSOCIATED CORTISONIC TREATMENT NORMALISED CONCENTRATION OF THE MATRIX METALLOPROTEASE
- ◀ MAINTAINMENT OF THE OBTAINED RESULTS

BIO-PLUS
REGENflex

3 molecular weights

2.5%
HA 1+2 MLN DALTON
HA 500 MILA DALTON



BIO RIVOLUMETRIA

- ◀ VISCO-SUPPLEMENTATION HIGH MOLECULAR FRACTION (HA 1 M DALTON + HA 2 M DALTON)
- ◀ VISCO-INDUCTION LOW MOLECULAR FRACTION (HA 500 K DALTON)
- ◀ REGULATES THE ACTION OF MACROPHAGES AND NORMALISES THE METALLOPROTEASE
- ◀ STIMULATES THE SYNOVIOCYTES TO PRODUCE ENDOGENOUS HYALURONIC ACID
- ◀ HAS AN ANALGESIC EFFECT BY OCCUPYING THE CD42 SITES (pain receptors)
- ◀ RESTORATION OF THE CARTILAGE THE 500 THOUSAND DALTON MOLECULAR FRACTION STIMULATES
- ◀ LONG PRESENCE INSIDE THE ARTICULAR CHAMBER
- ◀ GRADUAL RELEASE OF THE HA WITH MW 500 KDALTON

T&M
REGENflex

Concentration
HA 1.6%
HA LINEAR



- ◀ 5 DIFFERENTIATED MOLECULAR WEIGHTS FROM 2000 DALTON to 1 MILL. DALTON
- BIOINDUCTION:**
- ◀ REPAIR
- ◀ REGAIN ELASTICITY
- ◀ REVASCULARISATION

REGENFLEX PRODUCTS MAIN PROPERTIES

	COMPOSITION	DOSAGE	MOLECULAR WEIGHT	CONCENTRATION HA	PROPERTIES	PACKAGE	CROSS-LINKING AGENT
REGENflex STARTER	BUFFERED PHYSIOLOGICAL SOLUTION OF THE HYALURONIC ACID SODIUM SALT	2 ML	800 KDALTON 1.200 KDALTON	1.6% 32MG / 2ML OF HYALURONIC ACID SODIUM SALT	VISCOSUPPLEMENTATION and VISCO-INDUCTION	1 PRE-FILLED SINGLE USE SYRINGE	NOT CROSS-LINKED
REGENflex	BUFFERED PHYSIOLOGICAL SOLUTION OF THE HYALURONIC ACID SODIUM SALT	2 ML	800 KDALTON 1.200 KDALTON	0.8% 16MG / 2ML OF HYALURONIC ACID SODIUM SALT	VISCOSUPPLEMENTATION and VISCO-INDUCTION	1 PRE-FILLED SINGLE USE SYRINGE	NOT CROSS-LINKED
REGENflex BIO-PLUS	CROSS-LINKED AND INTERCALATED HYALURONIC ACID	3 ML	HA 1+2 MLN DALTON CROSS-LINKED FRACTIONS + 500 THOUSAND DALTON NOT CROSS-LINKED	2.5% 75MG / 3ML	VISCOSUPPLEMENTATION and VISCO-INDUCTION	1 PRE-FILLED SINGLE USE SYRINGE	BDDE
REGENflex T&M	HYALURONIC ACID SODIUM SALT IN BUFFER PHYSIOLOGICAL SOLUTION	2 ML	2 THOUSAND DALTON 100 THOUSAND DALTON 200 THOUSAND DALTON 500 THOUSAND DALTON 1 MILLION DALTON	1.6% 32MG / 2ML OF HYALURONIC ACID SODIUM SALT	PROTECTIVE RESTRUCTURING REGENERATING	1 PRE-FILLED SINGLE USE SYRINGE	NOT CROSS-LINKED

Regenflex BIO-PLUS and Biorivolumetria

BIO-PLUS
REGENflex

BIORIVOLUMETRIA is an innovative concept in the field of **HYALURONIC ACID**-based injectable medical devices.

BIO

BIOCOMPATIBLE AND BIO-ABSORBABLE SUBSTANCES

RI

RE-GENERATION AND RE-STRUCTURING

VOLUMETRIA

CREATION OF NEW VOLUMES

VOLUME

NORMALISES THE HYDROSTATIC PRESSURE
INSIDE THE JOINT CHAMBER

+

REGENERATION

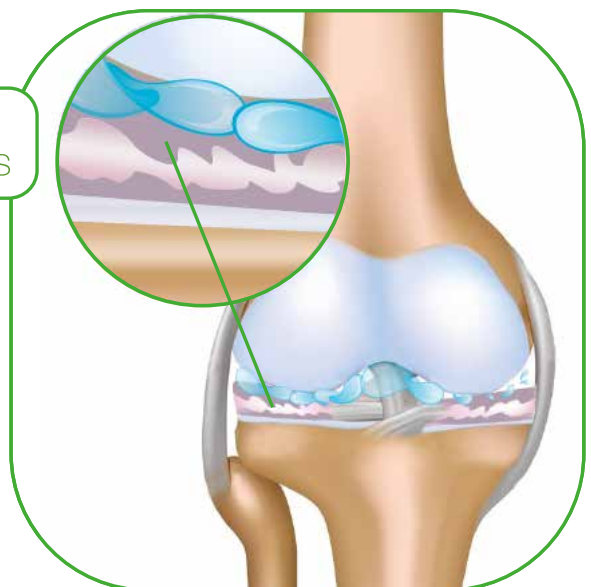
STIMULATES THE SYNOVIOCYTES TO
PRODUCE ENDOGENOUS HYALURONIC ACID



VISCO-SUPPLEMENTATION

HYDROSTATIC ACTION

green
injections



VISCO-INDUCTION

CELL STIMULATION

The same product makes it possible to simultaneously: restore the volume of the joint chamber by injecting **CROSS-LINKED HYALURONIC ACID**, and to stimulate receptors of the synoviocytes and chondrocytes thanks to the gradually released linear fraction of the **INTERCALATED HA**.

The **BIORIVOLUMETRIA** complies with the international standard of **GREEN INJECTIONS** applicable to injectable products and regarding their safety and the environmental friendliness of the manufacturing process:

GREEN PRODUCTS - Products of the highest quality created with the purest Hyaluronic Acid, with minimal levels of external chemical substances.

GREEN TECHNOLOGY - New generation products created in Italy in compliance with the strictest rules on environment protection: limited waste, energy saving, water purification, recycling, use of machinery at low energy consumption (ISO 14001 certified).

GREEN TECHNIQUES - Injective techniques with cannulae or needles, developed by highly qualified medical experts, that guarantee high performance and safe treatments, while the risk of complications in the "difficult areas" is reduced to the minimum.

BIORIVOLUMETRIA

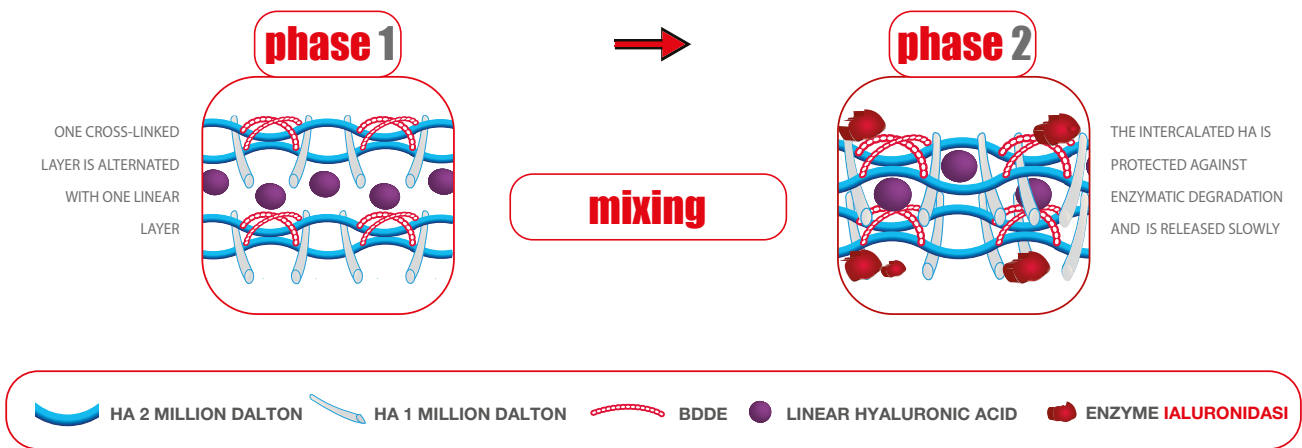
Production technology and working mechanism

The production technology used in the Regenflex BIO-PLUS is the BIOEVOLVOMETRY.

Biorevolumetric products are MONOPHASIC GELS obtained by "gentle crosslinking", a low-temperature and prolonged duration cross-linking process. Slow mixing allows the cross-linking agent (BDDE) to distribute itself better and more evenly. BDDE used quantity is 30% lower compared to the majority of other products, with the same viscosity, on the market and the free residual is lower than 0.1ppm. In Regenflex BIO-PLUS 3 molecular weights of Hyaluronic Acid are used, of 1 MILL., 2 MILL. and 500 THOUSAND Dalton. The latter, linear and intercalated, corresponds to 10% of the total Hyaluronic Acid. HA chains of different length allow for a better calibration of product viscosity. Linear Hyaluronic Acid is released gradually over time with a prolonged biological action (visco-induction).

Intercalation process

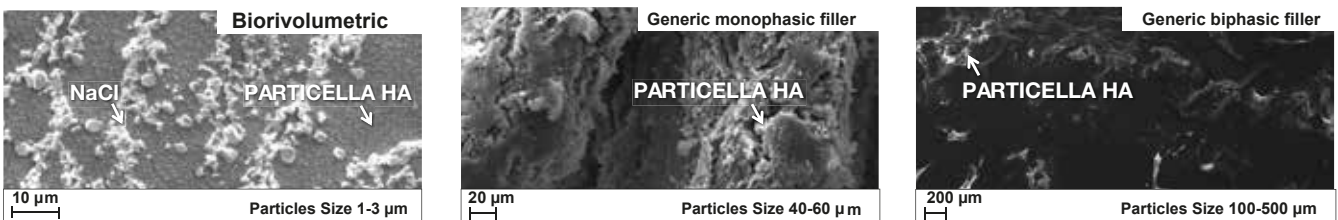
Intercalation is carried out during one of the last production phases and consists in alternating very thin layers of linear sodium Hyaluronate with thicker layers (of a few millimetres) of cross-linked hyaluronic acid inside special containers in the absence of oxygen. Everything is left resting for 12 hours at low temperature so as to form weak bonds (hydrogen and Van der Waals bonds). After 12 hours we proceed with a homogenization carried out with the use of an orbital mixer equipped with special blades designed specifically for this purpose. After some hours of mixing, micro-aggregates are obtained, formed on the outside by cross-linked hyaluronic acid and on the inside by linear sodium hyaluronate.



Hyaluronic Acid MICROPARTICLES

Images obtained with scanning electron microscopy (SEM) technique reveal that BIOEVOLVOMETRIC PRODUCTS are MORE COMPACT and HOMOGENEOUS than fillers, thanks to the smaller size of cross-linked hyaluronic acid particles.

Smaller particles allow a better distribution of the gel in the articular chamber, with a better distribution of the compression forces.





1506
UNIVERSITÀ
DEGLI STUDI
DI URBINO
CARLO BO

DISB
DIPARTIMENTO DI
SCIENZE BIOMOLECOLARI

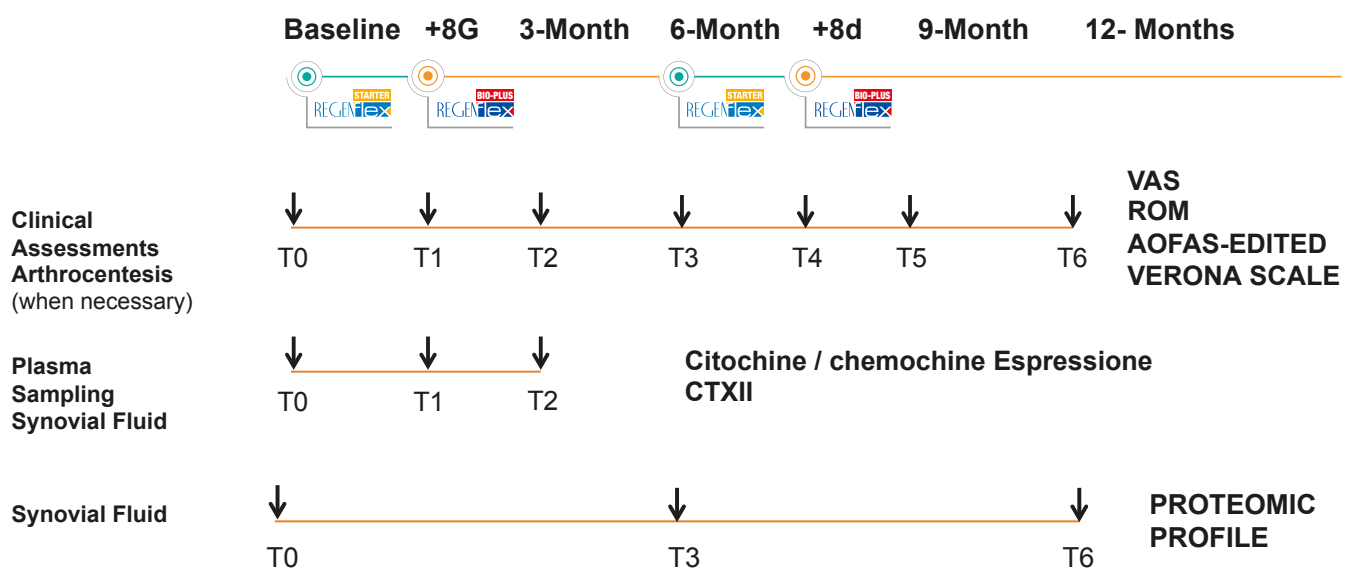
Clinical studies

The University of studies of Urbino Carlo Bo carried out a clinical study on the combined protocol of STAR-TER and BIO-PLUS. They enrolled 53 patients, 35 of them were eligible, in order to evaluate the clinical and biochemical effects on patients with osteoarthritis.

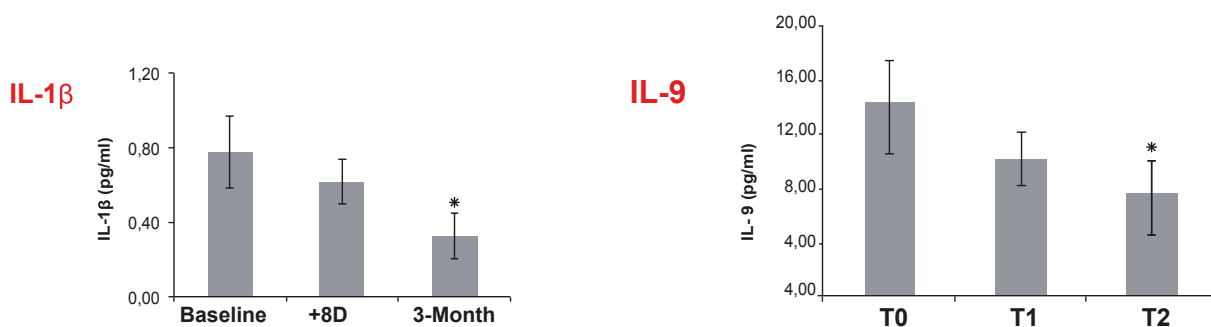
RESEARCH STUDY:

"CLINICAL ADVANTAGE AND EVALUATION OF BIOCHEMICAL PARAMETERS AFTER TREATMENT WITH INTRA-ARTICULAR INJECTION OF HYALURONIC ACID IN PATIENTS WITH KNEE OSTEOARTHROSIS WITH INTERVALS OF 6 MONTHS"

Experimental drawing

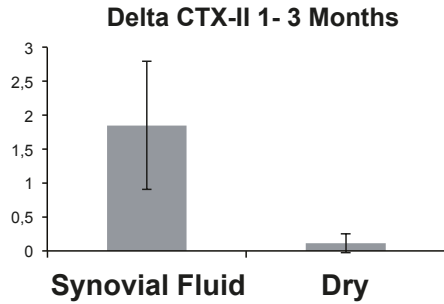


Plasma



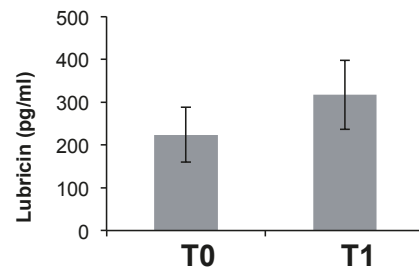
Three months after the second infiltration, there is a significant decrease in pro-inflammatory interleukins.

Local biochemical markers (synovial samples)



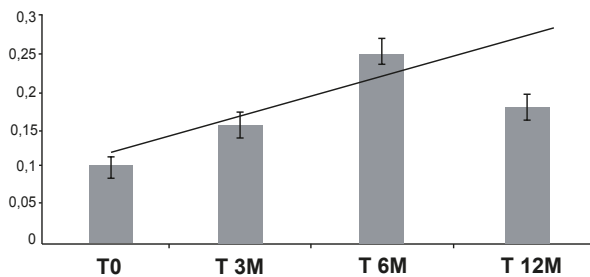
Patients with a moderate chondropathy, 3 months later, no longer have joint effusion and have a marked decrease of CTX-II.

LUBRICIN



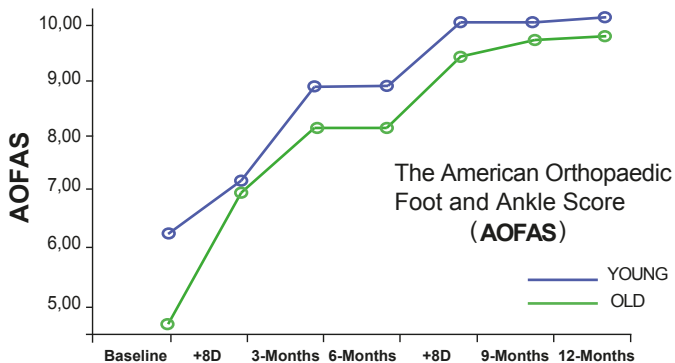
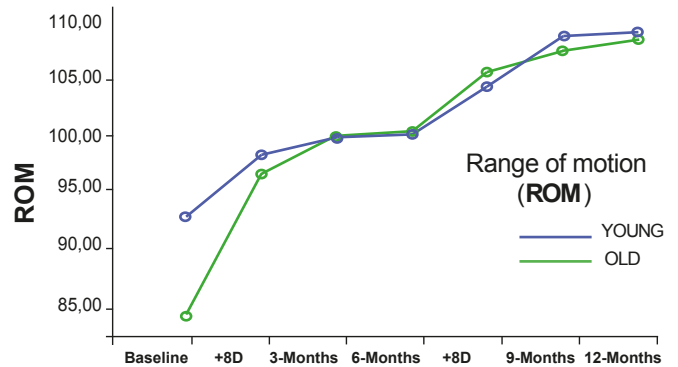
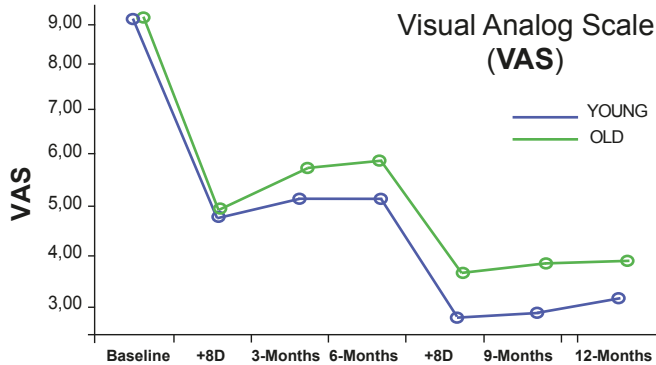
Lubricin is a glycoprotein that carries out a cartilage protective action.

TRANSTHYRETIN



Transthyretin is a constitutive inhibitor of the production of interleukin 1 (IL-1). It carries out a physiological and Anti-aging function

VAS e ROM + AOFAS DOUBLE



CONCLUSIONS

Regenflex Starter + Bio-Plus protocol has been demonstrated to be effective on both mild and high-grade chondropathies with a clinical improvement in articular function and a slowing of disease progression.

APPLICATION PROTOCOL

CARE AND PREVENTION FOR ALL JOINTS INDEPENDENTLY OF ETHIOPATHOGENESIS
WITHOUT USE OF NSAIDS OR CORTISONE PRODUCTS



KNEE



HIP



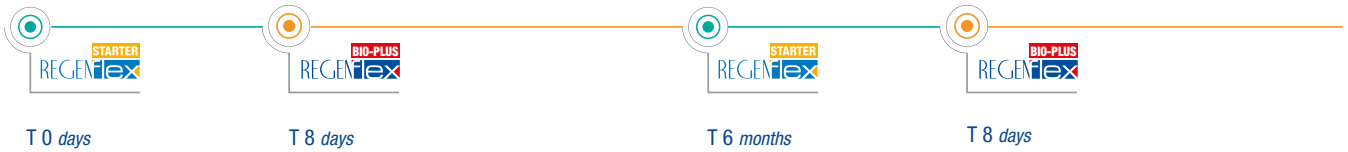
HAND



SHOULDER



ANKLE



CARE AND PREVENTION FOR TENDONS AND MUSCLES



MUSCLES



TENDONS



Who can carry out the treatment ?

ORTHOPAEDICS

SPORTS DOCTORS

GERIATRISTS

PHYSIATRISTS

RHEUMATOLOGISTS

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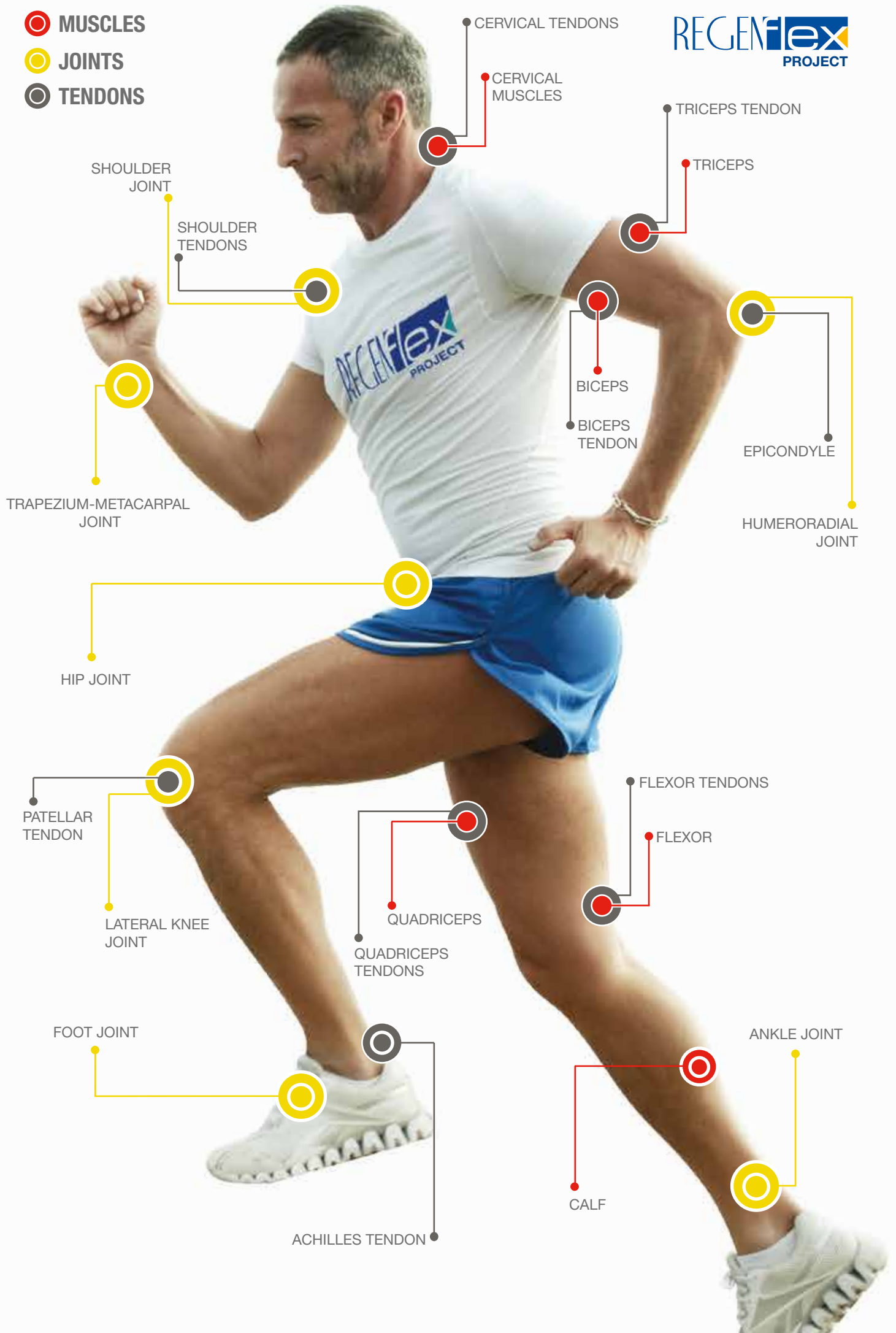


REGENflex
PROJECT

“ Let your limits be like the horizon...
The closer you get, the farther they seem ”

KEEP RUNNING

-  MUSCLES
-  JOINTS
-  TENDONS





REGENYAL LABORATORIES Srl
Via Valtellina, 21
63074 S. Benedetto del Tronto (AP) - ITALY
www.regenyal.eu

Numero Verde
800-095850



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