IAL-SYSTEM project

Bio-Revitalization
Reveal Your Beauty

“Gold standard” in the Cutaneous Bio-Revitalization

The skin tissue naturally contains the Hyaluronic Acid, which is biologically important, as it determines skin quality and freshness. With time the concentration of the Hyaluronic Acid decreases and the signs of time become visible. The Bio-Revitalization is a very important step in combating skin ageing, because it helps to regenerate components of the dermal structure and improves the hydration and elasticity properties of the skin.
Cutaneous Bio-Revitalization

Ial-System is the very first treatment that launched Bio-Revitalization, becoming also its “Gold standard”; this product – renowned all over the world – is based on bio-interactive and not chemically modified Hyaluronic Acid.

Ial-System is an important goal in aesthetic medicine, reached thanks to the cooperation between Phitogen Holding and Fidia Farmaceutici. Since then the scientific research never stopped, leading instead to the creation of Ial-System ACP which implements a new molecule, called ACP (auto-cross-linked polymer) composed of natural Hyaluronic Acid “auto-cross-linked” through an exclusive internal esterification process, without the use of external chemical components. The advantage of this molecule is due to its longer permanence inside the tissues.

Ial-System Project is constantly developing, in fact the Ial-System DUO, has been added to this range. This is a bio-revolumetry product, obtained through a chemical process, that binds BDDE cross-linked HA and auto-cross-linked HA (ACP).

The IAL-System injection products fully comply with the Green Injections’ standard, which means absolute safety and environment friendliness of the manufacturing process. The use of Green techniques and technologies assures natural results and maintenance of beauty throughout the years.

Moisturizing and Restructuring Action

The Hyaluronic Acid is responsible for the compactness of tissues. Its function in the three-dimensional organization of the extra-cellular root is highly important.

- It binds together enormous amounts of water
- Keeps the skin adequately and naturally hydrated
- Provides for firmness and freshness

Action on Fibroblasts

In-vitro and in-vivo studies have shown that the presence of Hyaluronic Acid, in specific concentrations, recreates a perfect physiological environment for the proliferation and migration of fibroblasts and for the neo-synthesis of collagen, elastin and endogenous Hyaluronic Acid.

Scavenger Action on Free Radicals

The Hyaluronic Acid protects the fibroblasts from the cytotoxic action of free radicals.
IAL-SYSTEM

The Supremacy of Cutaneous Bio-Revitalization

IAL-System is a medical device based on Hyaluronic Acid sodium salt, manufactured by Fidia Farmaceutici and is indicated for hydration and regeneration of the skin. Stimulates the proliferation and migration of fibroblasts, supporting the neogenesis of collagen, hyaluronic acid and elastin. Moreover, the product performs a strong anti-radical action, improves the level of hydration and elasticity of the skin while donating a much younger appearance.

Cutaneous Bio-Revitalization

- PREVENTS AND COMBATS SKIN AGEING
- REGENERATES COMPONENTS OF THE DERMAL SUPPORT STRUCTURE
- IMPROVES VARIOUS DERMAL AND EPIDERMAL PARAMETERS

Properties

- HYALURONIC ACID OF BIO-SYNTHETIC ORIGIN
- HA CONCENTRATION 1.8%
- 1.1 ML AND 0.6 ML MONO-USE SYRINGES
- FULLY BIO-COMPATIBLE

The efficiency is guaranteed by a patented synthesis, purification and sterilization process – exclusive property of Fidia Farmaceutici, that ensures standardized manufacturing of a Hyaluronic Acid, identical to the natural form of the polymer and free of chemical modifications, that could alter its bio-interactivity.

Intra-dermal injections of the product help to re-create an ideal physiological environment, stimulating cellular functionality through the action performed by the fragments of Hyaluronic acid on cellular receptors (FIG 1).

Hyaluronic acid lysis: fast process

![FIG 1]
**Slow-release Bio-Revitalizer**

*Ial-System ACP* (auto-cross-linked polymer) is an exclusive patent of Fidia Farmaceutici.

It is an innovative polymer, that besides having the same properties as the natural form of Hyaluronic acid, is more persistent due to the bio-synthetic auto-cross-linked Hyaluronic acid, which it is based on. *Ial-System ACP* is a result of an exclusive internal esterification process without the use of any external chemical components alien to the molecule of the Hyaluronic Acid itself.

**Properties**

- **BIO-SYNTHETIC HYALURONIC ACID**
  - AUTO-CROSS-LINKED THROUGH INTRA-AND INTERMOLECULAR ESTER LINKS

- **LONG-LASTING BIO-REVITALIZATION**
- **1 ML MONO-USE SYRINGE**
- **FULLY BIO-COMPATIBLE**

No external chemical substances are used and, due to the water present, lysis of the ester link takes place enabling the release of bio-interactive Hyaluronic Acid.

Thanks to the special structure of the ACP molecule it is possible to position the Hyaluronic Acid in a “complex” stereo-chemical form, that is able to significantly oppose the catabolic action, thus performing positively for a longer period of time without the use of external components, avoiding to compromise the purity and bio-compatibility of the product.

The bio-revitalizing action of the Hyaluronic Acid is prolonged with visible benefits for the patient.

1. *Ial-System ACP* absorbs the water activating a hydrolysis process (de-esterification), which breaks the cross-link and frees Hyaluronic Acid chains.
2. The Hyaluronic Acid chains are degraded by the Hyaluronidase enzyme, whereby fragments of Hyaluronic Acid at different molecular weights are released; these fragments present all properties of cellular bio-interactivity *(FIG. 2)*

The HA is thus released slowly, which constantly increases the hydration of skin and for a long time stimulates the fibroblast receptors, CD44, and the receptors of blood vessels, the ICAM.

The advantage of this exclusive molecule is given by its prolonged permanence in situ, impossible to obtain with natural Hyaluronic Acid.

**Hyaluronic acid ACP lysis: slow process** *(FIG. 2)*
Ial-System DUO is a sterile, clear, transparent monophasic gel based on multi-crosslinked hyaluronic acid (Mu.C.H. Technology™), with strong viscoelastic characteristics that ensure resistance to degradation and residence times of the order of 6 months after intra-dermal administration.

Properties

- Ensures a volumizing effect in the long-term and performs a bio-stimulating effect
- Improves the three-dimensional space capability
- No inflammatory effect in the short and long term
- Fully biocompatible
- Residence time of 6-8 months
- Easy to administer
- Clinical investigation ongoing

MU.CH.™ Technology: Multi Cross-linked Hyaluronan Technology

The MU.CH. technology provides for a “perfect” physical association of 2 kinds of cross-linked Hyaluronic Acid that together generate a mono-phase and homogeneous gel. The two cross-linking types, according to the chemical variation, generate two different degradation profiles that guarantee for:

1. A longer lasting volumizing effect thanks to the increased resistance of the BDDE Cross-Linked Hyaluronic Acid (HBC) to degrading
2. A major persistence of the bio-stimulating effect through the release of the original Hyaluronic Acid by the ACP

<table>
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<tr>
<th>INGREDIENTS</th>
<th>TECHNOLOGY</th>
<th>CONCENTRATION</th>
<th>DYNAMIC VISCOSITY</th>
<th>OSMOLARITY</th>
<th>RESIDUAL BDDE</th>
<th>ENDOTOXINS</th>
<th>STORAGE</th>
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<tbody>
<tr>
<td>75% cross-linked Hyaluronic Acid (with BDDE)</td>
<td>Mu.C.H.™ (Multi-cross-linked Hyaluronan)</td>
<td>25 mg/ml</td>
<td>on average 100 Pas</td>
<td>330 mOsm/lt</td>
<td>&lt; 2 ppm</td>
<td>&lt; 2.4 EU/ml</td>
<td>2-8°C</td>
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<tr>
<td>25% ACP (Auto-cross-linked Hyaluronic Acid)</td>
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IAL-SYSTEM project

Protocols / Implant Techniques / Studies
Protocols of Bio-Revitalization

The application protocols are based on a synergistic use of the injection products. Our team has created two protocols of bio-stimulation:

1. **PROTOCOL FOR REGENERATION OF TISSUES** - Combined use of IAL-SYSTEM, IAL-SYSTEM ACP and IAL-SYSTEM DUO
2. **PROTOCOL FOR INTERACTIVE BIO-REVITALIZATION** - Combined use of SCULPTURA PEEL, IAL-SYSTEM ACP and IAL-SYSTEM DUO

The first step of the **Protocol for Regeneration of Tissues** is performed (one or two times) with IAL-SYSTEM (bio-synthetic Hyaluronic Acid) in order to rapidly hydrate the skin tissues.

In the following phase IAL-SYSTEM ACP is injected (at 15 and 45 days); the environment is rich on water and, hence, ensures a slow and long-lasting degrading where the Hyaluronic acid is released continuously and gradually. During the last session (at 75 days) IAL-SYSTEM DUO is injected.

In the **Protocol for Interactive Bio-Revitalization** the main role is played by the peeling.

The first phase consists of a treatment with SCULPTURA PEEL (superficial bi-phase peeling), followed by a treatment with Ial-System. The peeling stimulates blood vessels and attracts consistent amounts of water in the dermis, creating this way an ideal environment for the Ial-System to perform its action. The pure Hyaluronic Acid binds to itself large amounts of water and activates the bio-revitalization process.

During the following two sessions (at 15 and 45 days) the treatments with SCULPTURA PEEL and IAL-SYSTEM ACP, are carried out; the base, hydrated and revitalized with IAL-SYSTEM, is once again hydrated and stimulated (peeling).

In the end, for a longer lasting benefit, the IAL-SYSTEM ACP is injected. During the last session (at 75 days) IAL-SYSTEM DUO is injected.
Implant Techniques and Areas

The Hyaluronic Acid contained in IAL-SYSTEM and Ial-System ACP spreads homogeneously and uniformly within the derma. It is particularly versatile and easy to use.

**THE CROSS-LINKED TECHNIQUE**

This technique is used with the aim to restore tone and firmness of cheeks, and consists in infiltrating Ial-System at medium derma level by inserting the needle at its entire length as parallel as possible to the skin surface, first horizontally then vertically, so that various infiltrations intersect forming a sort of network. The distance between the parallel infiltrations should be of around one centimeter. The product is to be released in the phase of extraction. Keeping the distance lower than one centimeter, it is possible to implement the cross-linked technique in less extended areas. For example, it is possible to treat the area located under the lips, in order to contrast skin sagging.

**THE LINEAR OR MICROPAPULA TECHNIQUE**

Thanks to its ability to spread homogeneously, Ial-System is especially indicated also for treatments in the neck area. It is recommended to follow the lines one by one, staying as close as possible to the surface, so to avoid ecchymosis. With the linear or series of micropapula technique, it is possible to achieve a good correction of imperfections. In order to increase the bio-revitalization effect, it is recommended to carry out further linear infiltrations, parallel to the previous ones, or scattered micropapula.

Often, even in young patients, the lack of skin tone results in fine wrinkles, especially during mimic movements of the face. Ial-System enables to improve significantly an already fragile and not very elastic tissue. In the case of the periorbicular area it is, therefore, recommended to highlight and correct single lines, using always the superficial linear technique and releasing modest amounts of Hyaluronic Acid in the phase of extraction. Finally, to increase the aesthetic and bio-revitalizing effect, these injections will need to cross further linear infiltrations until the zygomatic area is reached.

The perioral area requires superficial injections with linear, but preferably micropapula, technique along the visible lines, and two linear injections into the medium derma, parallel to the labial rima.

**DIFFICULT WRINKLES**

In the case of wrinkles, that are difficult to correct, it can be useful to apply Ial-System with a detachment technique, 10-15 days prior to injecting a dermal filler. Thanks to its high concentration, Ial-System permits to keep a space between the de-structured collagen fibers and to activate an optimal tissue reparation process, boosting a regular dislocation of new fibers of collagen. Hence, best conditions are created for corrections to be carried out with a filling material.

**ACP: MIXED TECHNIQUE**

Ial-System ACP may be implanted with the mixed technique according to particular requirements that may vary:

- neck, décolleté and hands: series of micropapula technique along visible lines, 13mm needle
- face: either retrograde linear technique performed using a 13mm needle, or deep intradermal technique, performed with a 4mm needle at an angle of 45 degrees and inserting it at full length, maintaining 1cm distance between injections. A modest amount of product should be released.

It may be useful to make proper Ial-System ACP injections in the nasogenian area with a 13mm needle and linear technique, 15 days prior to a treatment with a dermal filler.

**IAL-SYSTEM DUO: MIXED TECHNIQUE**

Ial-System DUO may be implanted with a mixed technique according to particular requirements that may vary:

- nasogenian folds: retrograde linear technique using a 27G 19mm needle or a 25G 38mm cannula
- Local hypo-volumes: malar or cheekbone area, linear or radial technique using a 25G 38mm cannula.

Depth of injection: medium or deep hypoderm.
Studies

>> Restoration of Skin Elasticity and Firmness Through Intra-Dermal Injections of Hyaluronic Acid (Ial-System)


Di Pietro, A., Di Sante, G.

The study has highlighted and confirmed the restoration of cutaneous firmness and elasticity after 2 intra-dermal infiltrations of Ial-System at T0 and T15, with instrumental check up at the base and before the second, and last treatment. Further check ups were done at 30 and 90 days from the last infiltration. The evaluation over time of skin elasticity and firmness in all 20 patients has produced a significant improvement with the peak reached at 30 days after the second treatment. In the specific, the elasticity coefficient, which before the treatment was on the average equal to 5.125, after 15 days was at 5.6, after 30 days 6.265, and reached 60.75 at 90 days after the second treatment. The medium basic value of firmness was of 0.74 and grew to 0.77 after the second treatment, while at 30 days after the second treatment it reached 0.78, and remained such at 90 days after the second treatment. The results were judged excellent by the 100% of the patients treated. In this case also, the absence of adverse events has strengthened what we already know from available literature, that is to say: excellent tolerability and safety of the natural Hyaluronic Acid.

Facial rejuvenation with ACP® gel, a novel, non-animal-derived

A pilot study on twenty patients

EXPERIMENTAL

Alessandrini, Andrea M.D.; Di Bartolo, Chiara B.S.; Pavesio, Alessandra B.S.; Pressato, Daniele

[ Abstract ]

Background: Facial ageing is due to a decreased cellular deposition of dermal components responsible for skin hydration and firmness, among which the hyaluronic acid (HA).

Objective: To assess safety and efficacy of the HA based ACP hydrogel in facial rejuvenation.

Methods: Twenty patients with signs of facial ageing were treated three times with ACP in various areas of the face, at a distance of 15 days between the treatments. Efficiency was evaluated by instrumental quantification of skin hydration and by visual assessment of firmness and local edema. Safety was evaluated by assessing adverse events and by quantifying immediate pain and erythema.

Results: ACP gel injection did not cause adverse events, 15% of the patients reported mild pain and 15% reported mild rapidly regressing erythema. A 40% average improvement was achieved in skin hydration parameters after the first injection and was maintained during the study period. ACP gel injection induced local edema in all subjects (80% moderate, 20% mild), giving the skin a pleasant, firm appearance.

Conclusions: The cross-linked HA based ACP gel is efficient in facial rejuvenation and does not cause any relevant adverse events.

IAL-SYSTEM: Clinical Evaluation

in Lecture congressuale, SIME 2002, Rome

>> Pugliese, S.

A preliminary study that involved 20 patients, who were subject to a cycle of natural bio-active Hyaluronic Acid injections, has highlighted through a bio-microscopic and histological examination, that a significant change in the skin structure had taken place. The most important observation was made in terms of dermal perfusion, which perpetuated in time even after 6 months after the treatment cycle had ceased, whereas not only the thick dermal vascular network was more resistant and firm, but there were also evident bio-microscopic signs of neo-angiogenesis.

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Bio-Revitalization
FIDIA FARMACEUTICI SPA is a world-leader in the manufacturing of Hyaluronic Acid. Thanks to investments in research, the Company made their products international. Besides research and development of Hyaluronic Acid applications, the main manufacturing areas of the Company are: active principles for antibiotics and medicines for cancer treatments, drugs and medical devices for the treatment of socially and economically relevant diseases.

PHITOCEN HOLDING SPA, founded in 2003, is now a leader in the field of aesthetic medicine and professional aesthetics. Recognized nationally and internationally, the Company not only distributes products but is also active in the field of scientific communication and science awareness initiatives. It is a leader in the application of new materials and active principles, as well as in the most advanced implantation and intervention techniques. The excellent results achieved by the Company are due to clinical experiments, partnership with important Companies specializing in the field, and of course to scientific competence, quality of the products and efficient teamwork.