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low medium high

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LOW MEDIUM HIGH

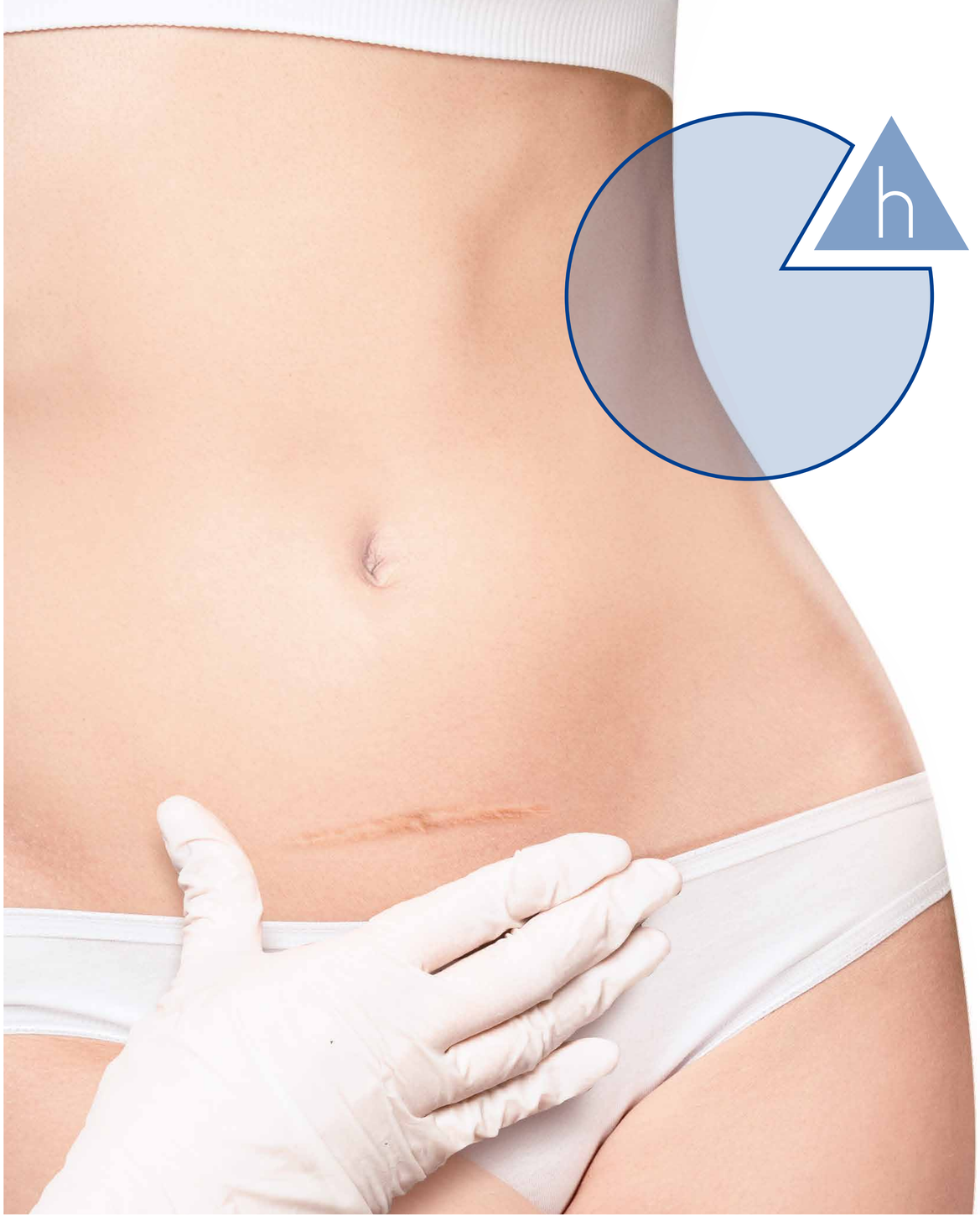
The only recombinant enzymatic system in the world

· Three products designed for specific indications

· Last-generation enzymes

· Ready-to-use, easy-to-apply and minimally invasive device

Collagenase PB220, Lipase PB500 and Lyase PB72K



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NEW HIGH

Presentation designed for scars and postsurgical fibrosis

- The only recombinant enzymatic system in the world
- Last-generation enzymes
- Ready-to-use, easy-to-apply and minimally invasive device

Collagenase PB220, Lipase PB500 and Lyase PB72K

EVALUATION OF THE EFFECTS OF HYALURONIC ACID AND ENZYMATIC SYSTEM IN SCARS

MULTICENTER CLINICAL STUDY

Multicenter Clinical Study to Evaluate the Efficacy and Safety of Hyaluronic Acid and Enzyme Cocktail in Scars

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Summary

This paper presents and evaluates the treatment results for the product High, which contains high molecular weight hyaluronic acid and a system of recombinant enzymes (collagenase PB220, lipase PB500 and lyase PB72K). The study was performed by 10 dermatologists on 42 patients who reported 44 cases of scar fibrosis; and was medically assessed following the Vancouver scale and POSAS (Patient and Observer Scar Assessment Scale) for the patients' perception assessment. The results reveal an excellent response in all parameters measured from the first application in most patients. The safety results of the treatment show very good performance with mild adverse effects.

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Introduction

Fibrosis is the excessive development of fibrous connective tissue in an organ or tissue. This process arises as a consequence of a reparative or reactive process. It is produced by a chronic inflammatory course, which triggers an increase in the production and deposition of extracellular matrix.

Upon injury to the skin, a series of events aimed at repairing the skin lesion are instantly initiated and are usually divided into three overlapping phases:

1) Inflammatory response.
2) Tissue granulation, re-epithelialization and angiogenesis.
3) Remodeling of the extracellular matrix.

Collagen is the main structural element of the extracellular matrix, as it forms a relaxed network of cross-linked long-chain fibers to give integrity to the skin. Collagen types I and III play the most important role in wound repair mechanisms. These collagens are differentially expressed in various types of fibrotic scar tissue. Due to fibroblasts, type III collagen expression is prominent in the early proliferative phase of wound scarring, but is replaced by stronger type I collagen fibers during the later stages of the proliferative and early remodeling phases. An excessive formation of fibrous scar tissue can lead to hypertrophic scar fibrosis, including the creation of an intermediate raised dermal scar structure and finally a proliferative fibrotic keloid scar structure, which represents a form of pathologic scarring.

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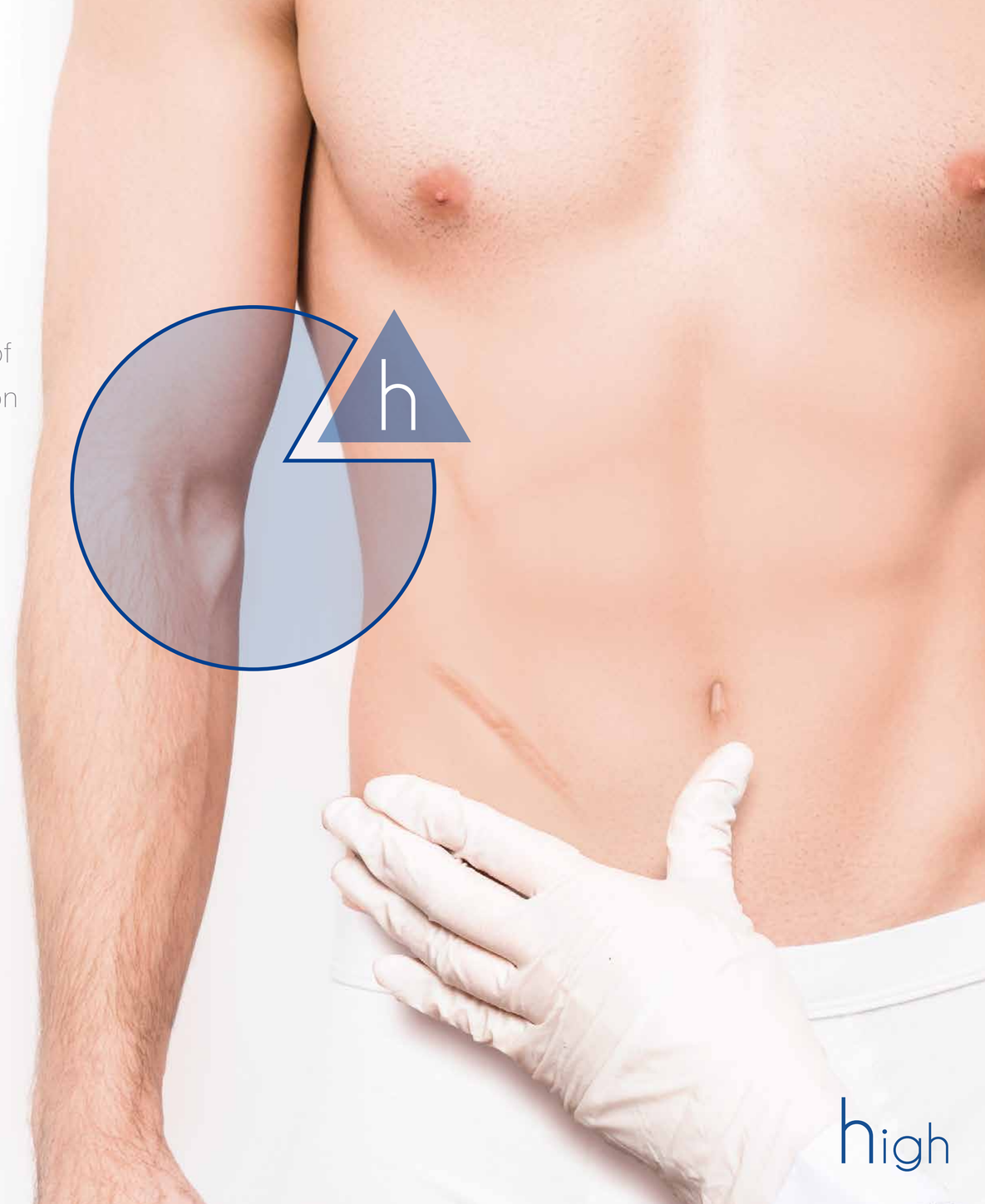
Hyaluronic acid (HA) is a glycosaminoglycan that has a structural function as an important component of the extracellular matrix. This molecule plays an important role in the transmission of intercellular signals during the process of tissue regeneration. It is a hydrophilic molecule, which increases the hydration and structural integrity of the extracellular matrix of tissues, thus contributing to proper cell proliferation, migration and adhesion during the tissue repair process.

In our paper we present a multicenter clinical study conducted in 10 dermatological clinics with 42 patients and 44 scars with the aim of demonstrating by quantitative criteria the effect of the enzymatic system together with high molecular weight HA. The recombinant enzymes collagenase PB220, lipase PB500 and lyase PB72K together with the high molecular weight HA have a positive effect on the reduction of fibrosis in tissue repair during healing processes, which opens a new therapeutic alternative to the treatment of this type of fibrotic alterations.



Methodology

The multicenter clinical study involved 10 dermatologists from 10 different clinics, 42 volunteers were selected and 44 scars were treated, all of which met 100% of the inclusion criteria: 1) people over 18 years of age, 2) who had scars in the classification established for the trial, 3) good physical and psychological state of health, as well as complying with the parameters specified in the health questionnaire, 4) not pregnant or breastfeeding.

The scars to be treated were classified into three groups:

1) Hypertrophic
2) Atrophic
3) Keloid

Treatment with High (hyaluronic acid, r-collagenase, r-lipase and r-lyase) was administered to the previously identified groups. 15 minutes prior to the injection of the treatment local anesthesia was applied using an ointment with a topical mixture of 7% tetracaine and 23% lidocaine in the scar area. After that time the treatment was injected using the blanching technique in the scar area; this technique consists of multiple injections in the scar separated by 0.5 cm from each other. The depth of the injection was intradermal to the center of the scar by placement of the needle (30 g 1/2") at an angle of application of 15 degrees to the skin surface. In all applications, whitening of the scar should be observable at the time of insertion of the device.

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Five assessments of the patients' scar condition were performed based on scar classification parameters: 1) before the first treatment application, 2) before each application and 3) 15 days after the last application.
The Vancouver scale for diagnosis was used as a reference for the physician's assessment, whereas the POSAS scale was used for the patient's assessment of the scar to be treated. Each visit by the medical specialist was also accompanied by photographs of the evolution of the scars.

Statistical analysis of the data was performed by evaluating the clinical and subjective variables, which were treated as categorical response variables using generalized linear mixed models (glmm). The models were adjusted to evaluate the effect of treatment day (0, 15, 15, 30, 45, 60) and scar type (atrophic, hypertrophic, keloid) on each of the response variables. The model used was of the predictive type, in which the possible response to the treatment is analyzed over time.
The significance level established for the trial was 0.05 (95% confidence interval).

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Results and discussion

Vancouver scale results

The results obtained on the evolution of scar fibrosis were positive and significant over time after the first or second application in the parameters of pigmentation, vascularity, pliability and scar height.

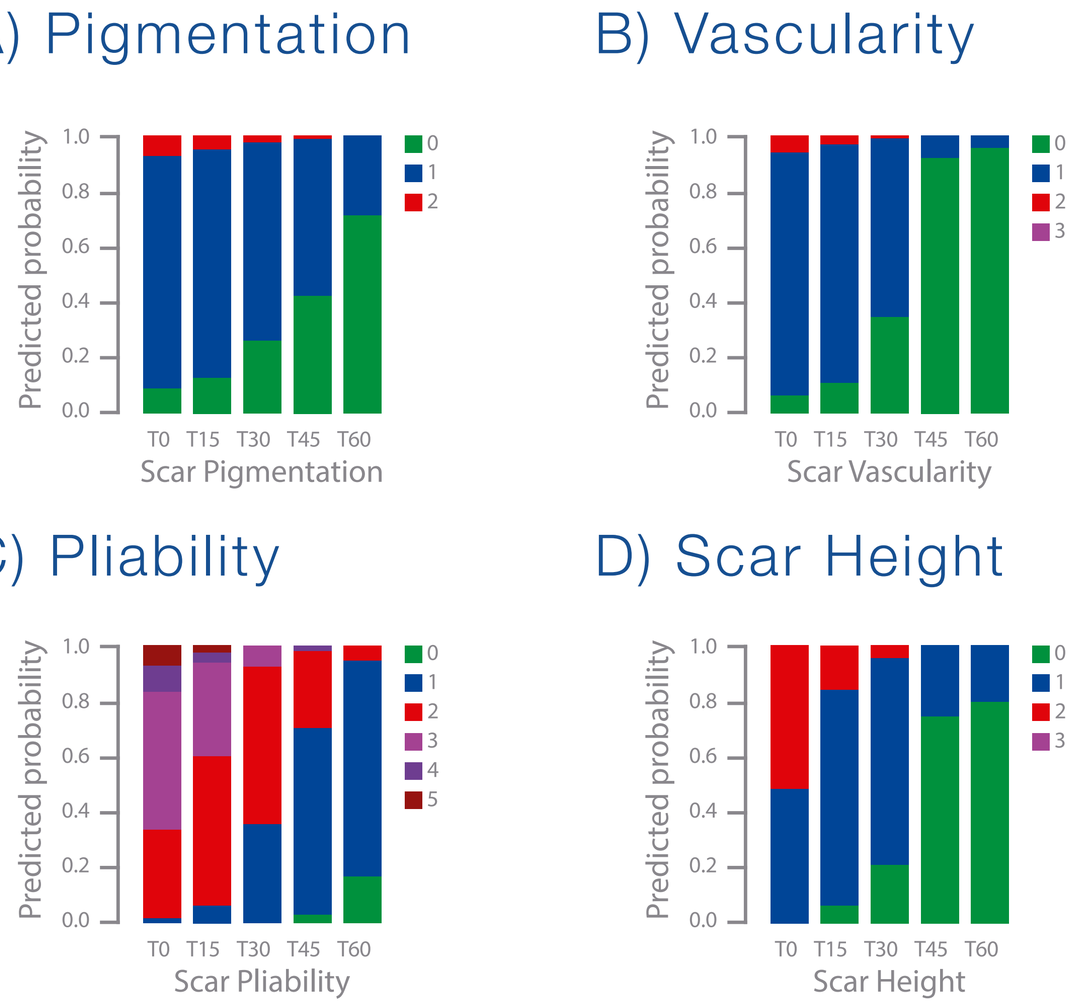


Figure 1.Evolution of parameters according to the Vancouver scale. A) Pigmentation was valued as follows: Normal pigmentation (resembling body color). Value = 0 (green); Hypopigmentation. Value = 1 (blue); Hyperpigmentation. Value = 2 (red); B) Vascularity was assessed as follows: Normal vascularity (resembling body color). Value = 0 (green); Pink scar. Value = 1 (blue); Red scar. Value = 2 (red); Purple scar. Value = 3 (purple); C) Pliability was assessed as follows: Normal pliability. Value = 0 (green color); Pliable with minimal resistance. Value = 1 (blue); Yielding (yields to pressure). Value = 2 (red); Firm (inflexible, does not move easily, resistant to manual pressure). Value = 3 (pink); Cord (rope-like fabric that whitens upon extension). Value = 4 (purple); Contracture (permanent shortening of the wound resulting in deformity or distortion). Value = 5 (maroon); D) The scar height is evaluated as follows: Normal. Value = 0 (green); < 2mm. Value = 1 (blue); > 2mm < 5mm. Value = 2 (red); > 5mm. Value = 3 (purple).

POSAS results

(Patient and Observer Scar Assessment Scale)

The POSAS scale is one of the few, if not the only one, that allows subjective evaluation of pain, itching, color, stiffness, thickness and irregularities through the patient's perception on a numerical scale. The results obtained were positive and significant in relation to the evaluated parameters after the first or second application.

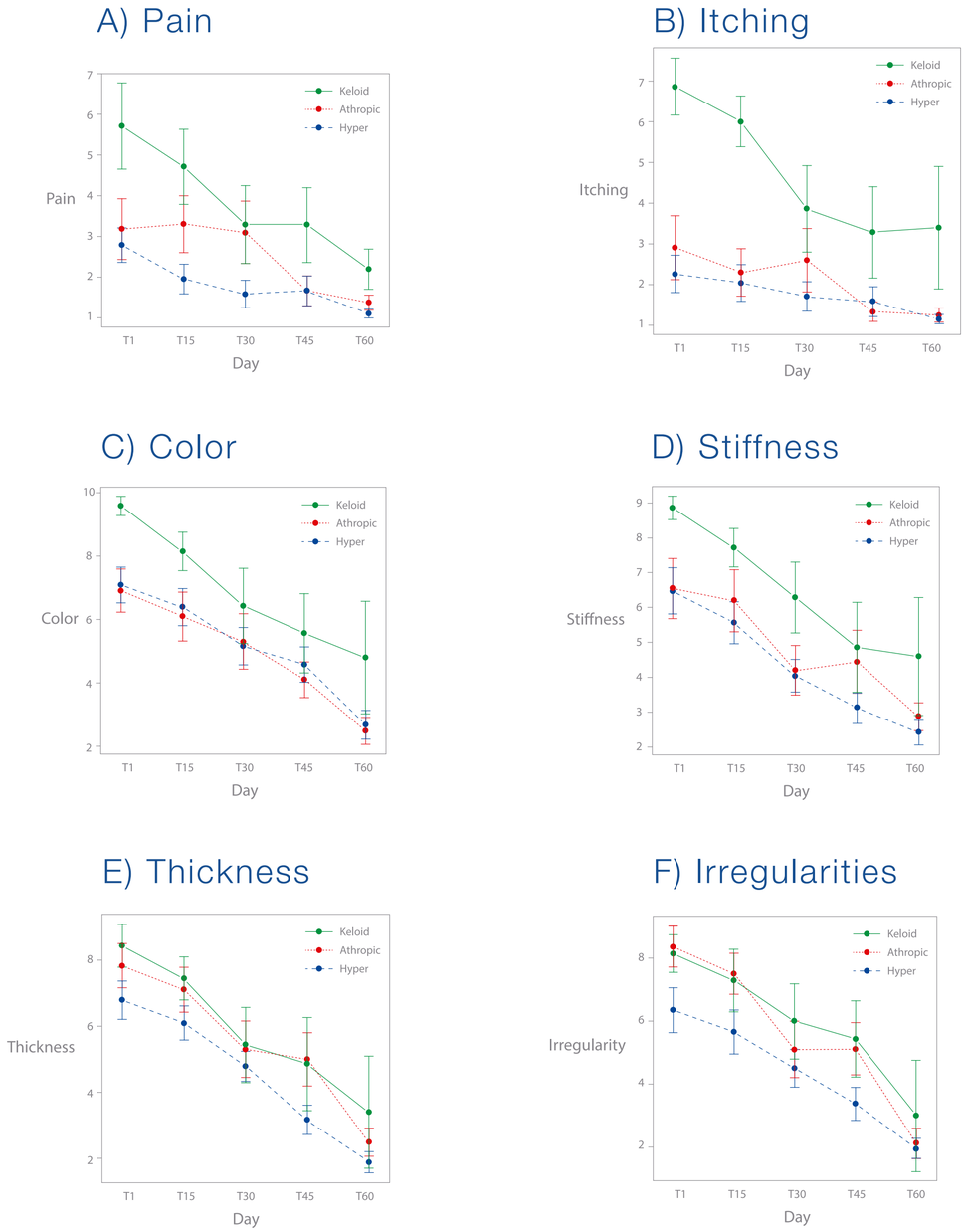
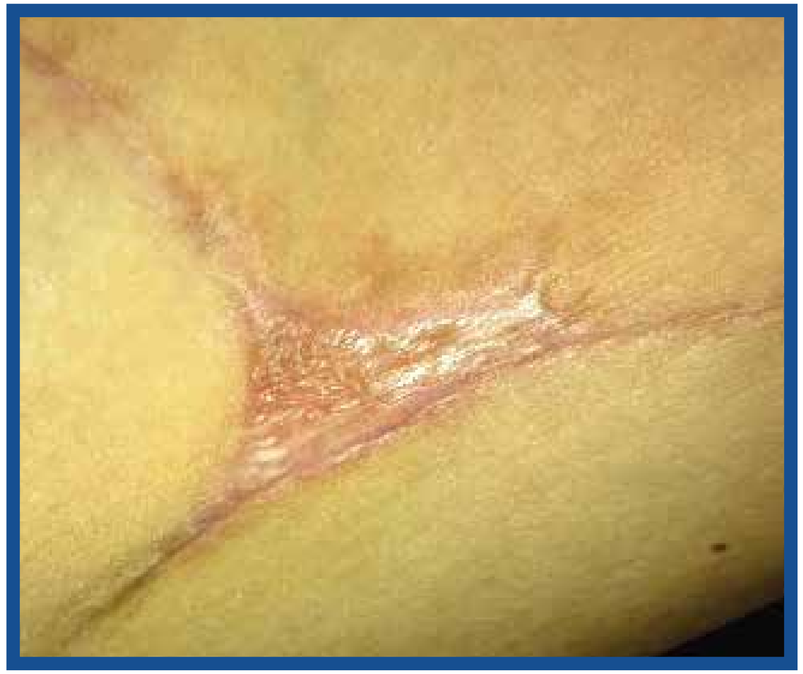
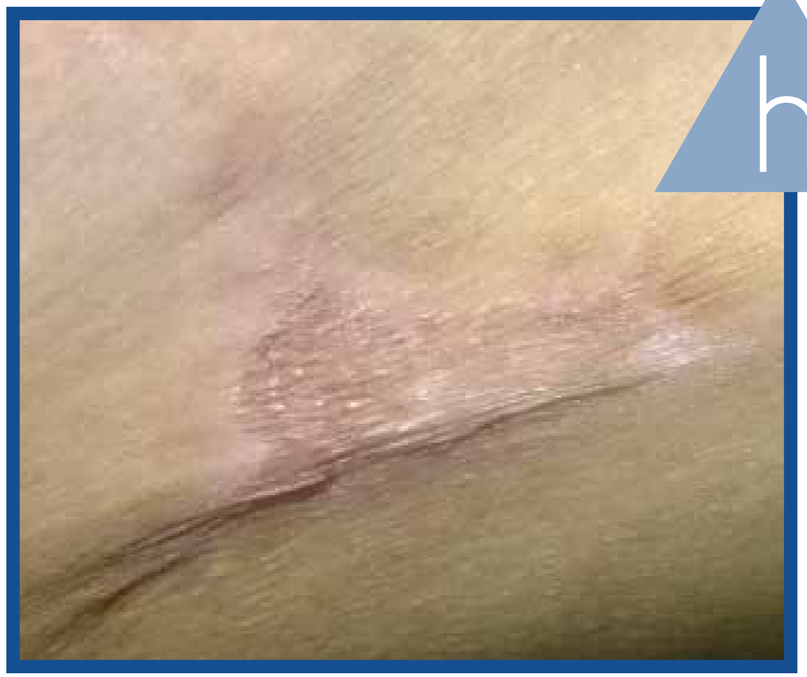


Figure 2. Evolution of the parameters according to the POSAS.



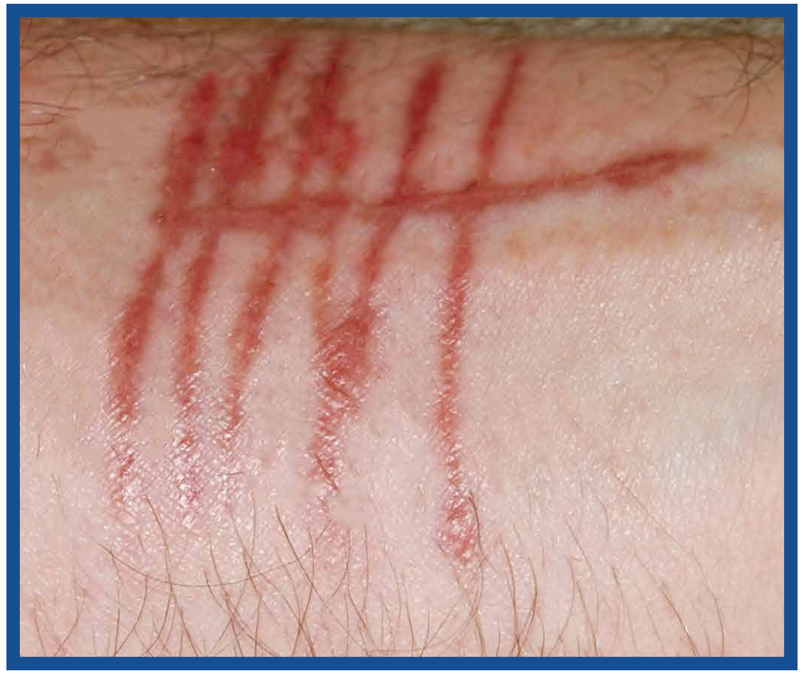
Day 0



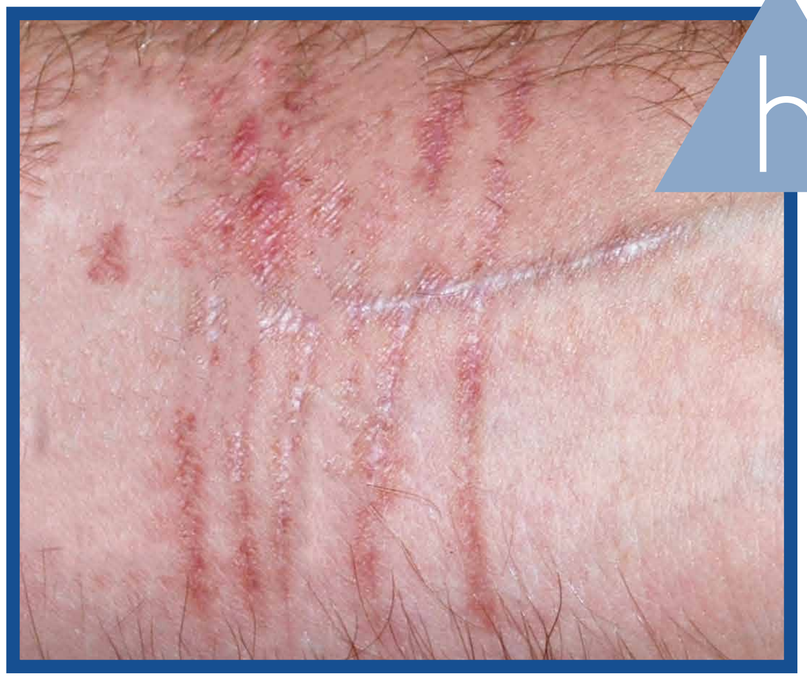
Day 75

Dra. Korkunda (Ukraine).

high



Day 0



Day 30

Dra. Natalia Alijanidi Odessa (Ukraine).

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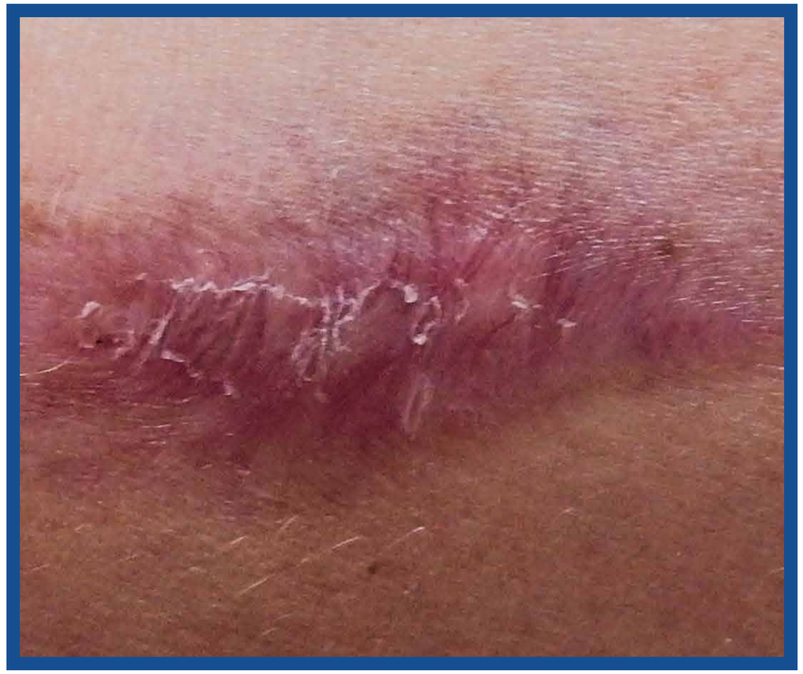
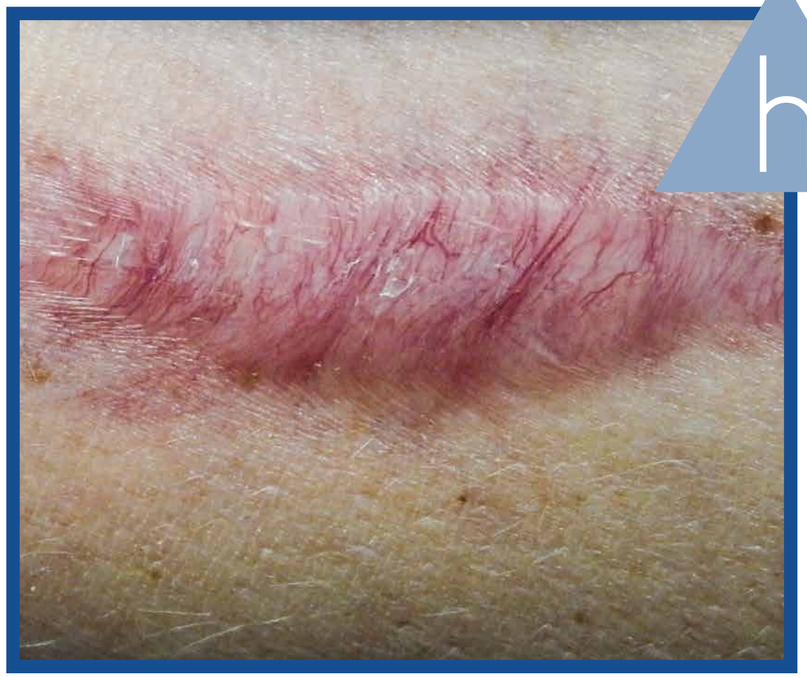


Day 0



Day 30

Dr. Alexey Maladiy (Ukraine).

high

Day 0

Day 75

Dra. Korkunda (Ukraine).

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Conclusions

The results obtained from the assessment using the Vancouver and POSAS scales reveal great success in the treatment of scar fibrosis, regardless of the nature of the fibrosis. Hyaluronic acid supported with the enzymatic system has had an excellent performance in all measured parameters, where a very significant improvement can be observed from the first treatment session and measured in the first 15 days.

The results indicated that the product is safe and no severe adverse effects were observed in any case. All adverse events reported were mild, as well as normal events in injections applied in scar fibrosis.

Therefore, the clinical study report concludes that High has performed excellently in the treatment of scar fibrosis, both in terms of efficacy and safety.

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