

# An Exploratory Split-Area Pilot Case Series of Two Hyaluronic Acid Skinboosters across Facial and Non-Facial Regions

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## Abstract

**Background:** Hyaluronic acid (HA) skinboosters are widely used to enhance skin hydration, elasticity, and texture. Cost has been identified as a common barrier to accessing aesthetic treatments, underscoring the importance of comparative data across available HA formulations. Hyamira 40 Booster is a high-concentration HA product increasingly used in practice; however, published data remain limited. **Objectives:** This paper aims to evaluate patient-reported outcomes and tolerability of Hyamira 40 Booster and an established HA skinbooster across the face, neck, décolleté, and hands. **Methods:** In this prospective, single-center, split-area exploratory pilot evaluation, adult participants received Hyamira 40 Booster on one side of each treated region and the comparator HA skinbooster on the contralateral side. All injections were performed in the superficial subdermal plane using a 25 G/60 mm cannula. Three sessions were administered at baseline, on Day 15, and on Day 30, with follow-up on Day 45. Outcomes were assessed using patient-reported Global Aesthetic Improvement Scale (GAIS) scores and a 16-item satisfaction questionnaire. Paired t-tests were used for within-side comparisons; between-product comparisons were descriptive given the exploratory sample size. The study included five participants and was not powered for formal comparative analysis. **Results:** Both products were associated with progressive GAIS improvements in radiance, elasticity, hydration, smoothness, and overall skin quality across all anatomical regions. Mean scores for the Hyamira-treated and comparator-treated sides were similar at all time points, with no consistent differences observed between sides, while several within-side improvements reached statistical significance ( $p < 0.05$ ). Satisfaction questionnaire responses were highly similar for both sides, and participants most often selected “Equal” when asked to compare comfort, tolerability, or perceived aesthetic improvement. **Conclusions:** Both treatments were associated with improvements in multiple

patient-reported skin-quality parameters across all evaluated regions, with no consistent differences observed between sides in this exploratory sample. Cost differences may represent a practical consideration in clinical use, although no economic analysis was performed. These findings should be interpreted in light of the small sample size, absence of objective outcome measures, and short follow-up duration. Further studies incorporating larger populations, objective assessments, and longer follow-up are warranted.

### **Keywords**

Hyaluronic Acid, Skinboosters, Skin Rejuvenation, Patient-Reported Outcomes, Aesthetic Dermatology

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## **1. Introduction**

The pursuit of natural-looking and harmonious rejuvenation has expanded considerably in recent years [1] [2]. While the face traditionally received the greatest attention through procedures such as surgical lifting [3]-[5], neuromodulation [6]-[8], and volumizing fillers [9]-[13], limiting treatment to facial structures alone often accentuates age-related changes in adjacent areas. The neck, décolleté, and hands are highly visible, frequently exposed to environmental stressors, and therefore contribute significantly to the overall perception of aging. As aesthetic practice shifts toward a more global approach, improving skin quality in non-facial areas has become an important clinical focus [14] [15].

Cutaneous aging results from the interplay between intrinsic biological mechanisms and extrinsic environmental influences. Intrinsic aging causes progressive reductions in cellular function, extracellular matrix quality, vascular supply, and subcutaneous volume, which weaken the dermis over time. Extrinsic factors such as UV exposure, pollution, smoking, nutritional status, and hormonal changes further accelerate this process. Clinically, these mechanisms manifest as wrinkles, pigmentary alterations, laxity, volume loss, and declines in hydration, elasticity, and texture, all of which contribute to reduced skin quality [16]-[20].

These changes present differently across anatomical regions. In the neck, thinning and segmentation of the platysma muscle, loss of superficial fat, and chronic photodamage contribute to horizontal lines, laxity, and altered contour. The décolleté, particularly susceptible to long-term sun exposure, frequently develops rhytids, dyspigmentation, and textural irregularities. The dorsal hands, the second most exposed area after the face, often exhibit pigmentary changes, dermal thinning, microvascular deterioration, and progressive volume depletion, leading to increased visibility of veins, tendons, and bony structures [15] [21]-[23].

Alongside advances in laser technologies, chemical peels, and energy-based devices, injectable treatments have become central to contemporary skin rejuvenation. Among them, hyaluronic acid (HA)-based skinboosters represent an important option for patients seeking subtle, progressive, and non-surgical improve-

ment in skin quality. Unlike traditional fillers used for structural augmentation, skinboosters are designed to improve hydration, elasticity, smoothness, and overall skin quality. Their lower viscosity and elasticity allow even intradermal distribution and support extracellular matrix repair [24]-[27].

Hyaluronic acid is well-suited for skin-quality treatments because it plays a key role in maintaining dermal homeostasis. As a major glycosaminoglycan in the extracellular matrix, it binds water, interacts with collagen and elastin, and supports the environment needed for normal cellular function. With age, both the amount and molecular weight of endogenous HA decrease, reducing skin hydration and elasticity. Intradermal injection of linear or lightly stabilized HA can help offset these changes, and multiple clinical studies have shown improvements in hydration, elasticity, and fine lines in areas such as the face, neck, décolleté, and hands [28]-[30].

A wide range of HA skinboosters is currently available, differing in molecular composition, stabilization, and rheological behavior. Among these, Hyamira 40 Booster (NyumaPharma) is a high-concentration HA formulation that is increasingly used in aesthetic practice. However, despite its growing adoption, clinical evidence supporting its performance, particularly across different anatomical regions, remains limited.

Understanding patient perspectives also remains essential. A recent multinational survey by Fabi *et al.* examined motivations and barriers related to minimally invasive facial aesthetic procedures in more than 14,000 adults and over 1,300 physicians across 18 countries. In this survey, 61% of respondents and 53% of physicians identified cost as a barrier to seeking aesthetic treatments, alongside other concerns such as discomfort, potential side effects, and the risk of unnatural-looking results. Although most individuals expressed a strong interest in maintaining their appearance, these factors influenced willingness to pursue treatment [31]. Such observations underscore the importance of evaluating emerging skin-quality injectables in a structured clinical setting and comparing them with established, widely used options.

Given the growing demand for effective, minimally invasive options to improve skin quality, evaluating newer HA skinboosters is important. This study therefore evaluated patient-reported outcomes and tolerability of Hyamira 40 Booster and an established HA skinbooster across the face, neck, décolleté, and hands.

## 2. Material and Methods

### 2.1. Study Design

This prospective, single-center, split-area exploratory evaluation compared the effects of a high-concentration hyaluronic acid skinbooster (Hyamira 40 Booster®; NyumaPharma) with another hyaluronic acid skinbooster (Prophilo Structura® (IBSA Farmaceutici Italia Srl)) [32] on the skin quality of the face, neck, décolleté, and hands.

Prophilo Structura® was selected as the comparator because it is an established

hyaluronic acid-based injectable used in aesthetic practice for skin-quality improvement. Its use as a comparator allowed Hyamira 40 Booster® to be evaluated alongside a clinically familiar HA-based product within the same broad treatment category.

The evaluation was conducted at PHP Aesthetic-Wellness in the United Kingdom. Participants were followed for approximately 2 - 3 months and completed four scheduled visits.

No formal sample size calculation was performed; the study was designed as an exploratory pilot evaluation.

## 2.2. Participants

Adult volunteers seeking improvement in skin quality in one or more of the targeted anatomical regions were eligible. The evaluation excluded women who were pregnant, breastfeeding, or planning to become pregnant. Women who suspected pregnancy or intended to conceive during the study period were likewise excluded.

At the initial screening/treatment visit (Day -1 to Day 0), written informed consent was obtained before any study-related procedures. Demographic data (age and gender), medical and medication history, including prescription medications, over-the-counter treatments, and dietary or herbal supplements, were recorded. A physical examination, including height and weight, was performed. Eligibility was confirmed by the investigator in accordance with the inclusion and exclusion criteria.

## 2.3. Blinding and Treatment Allocation

A split-area design was employed for all treated anatomical regions. For each region, Hyamira 40 Booster was administered on one side and Prophilos Structura on the contralateral side. Hyamira 40 Booster contains 40 mg/mL of hyaluronic acid.

Participants were blinded to the side allocation, while the investigator was aware of the assignment, resulting in a single-blinded design.

Side assignment was not randomized. Allocation of Hyamira 40 Booster and the comparator to the left or right side was determined by the investigator and remained consistent across treatment sessions for each participant.

## 2.4. Intervention

Participants could receive treatment to the face, neck, décolleté, and hands based on individual presentation and clinical judgment. At each treatment session, 1 mL of each product was administered per side for each treated area (*i.e.*, 1 mL of Hyamira 40 Booster on one side and 1 mL of the comparator on the contralateral side), distributed across multiple injection points. All injections were performed in the superficial subdermal plane using a 25 G/60 mm cannula (Magic Needle®, Needle Concept). Treatments were delivered under standard clinical conditions for superficial subdermal injection.

## 2.5. Study Visits

The study comprised four visits. Visit 1 (Day -1 to Day 0) included screening

assessments followed by the first treatment session. Visit 2 (Day 15  $\pm$  3 days) consisted of the second treatment. Visit 3 (Day 30  $\pm$  3 days) served as a follow-up visit and included a repeat treatment session in accordance with the protocol. Visit 4 (Day 45  $\pm$  3 days) was a follow-up evaluation assessing the progression of treatment outcomes.

## 2.6. Clinical Assessments

Clinical outcomes were assessed using a patient-reported Global Aesthetic Improvement Scale (GAIS, higher scores indicate greater perceived improvement) and a patient satisfaction questionnaire. The GAIS measured the patient's perception of changes for each treated side across several parameters of skin quality, including skin radiance, skin elasticity, skin hydration, skin smoothness, and overall skin quality. Patients completed this evaluation independently at the designated follow-up visits.

At Visit 1, the GAIS assessment was completed after the initial treatment session and therefore reflected early post-treatment perception rather than a true pre-treatment baseline. At subsequent visits, GAIS and satisfaction assessments were completed before any additional treatment was administered during that visit.

Participants also completed a structured satisfaction questionnaire that captured their overall impressions of treatment efficacy and tolerance, as well as their side-by-side preference between the two injected products. These patient-reported outcomes were used to characterize subjective aesthetic improvements throughout the evaluation period.

The GAIS was scored on a seven-point ordinal scale ranging from  $-3$  (Very Much Worse) to  $+3$  (Very Much Improved), with  $0$  indicating No Change and higher scores indicating greater perceived improvement. The 16-item satisfaction questionnaire was developed specifically for this evaluation and was not a previously validated instrument. Responses were summarized descriptively, and items requiring direct side-by-side comparison were reported as the proportion of participants selecting each response category.

## 2.7. Participant Restrictions

Participants agreed not to undergo any additional aesthetic procedures involving the face, neck, décolleté, or hands for the duration of their participation. Makeup was not permitted on visit days or for twelve hours after each injection. Participants were instructed to avoid sunlight or ultraviolet exposure throughout the evaluation period and to refrain from exposure to extreme temperatures, including intense cold, saunas, and hammam, for two weeks following each injection. Touch-ups or re-injections outside the protocol-defined treatment sessions were not allowed. All adverse events and any changes in medication were to be reported promptly to the investigator.

## 2.8. Statistical Analysis

Descriptive statistics were used to summarize all outcomes. Paired comparisons

from baseline were performed using a two-tailed paired Student’s t-test and are reported as exploratory, unadjusted analyses. Although GAIS scores are ordinal, they were treated as continuous variables for the purpose of this exploratory analysis. All p-values were considered exploratory and were not adjusted for multiple comparisons.

### 3. Results

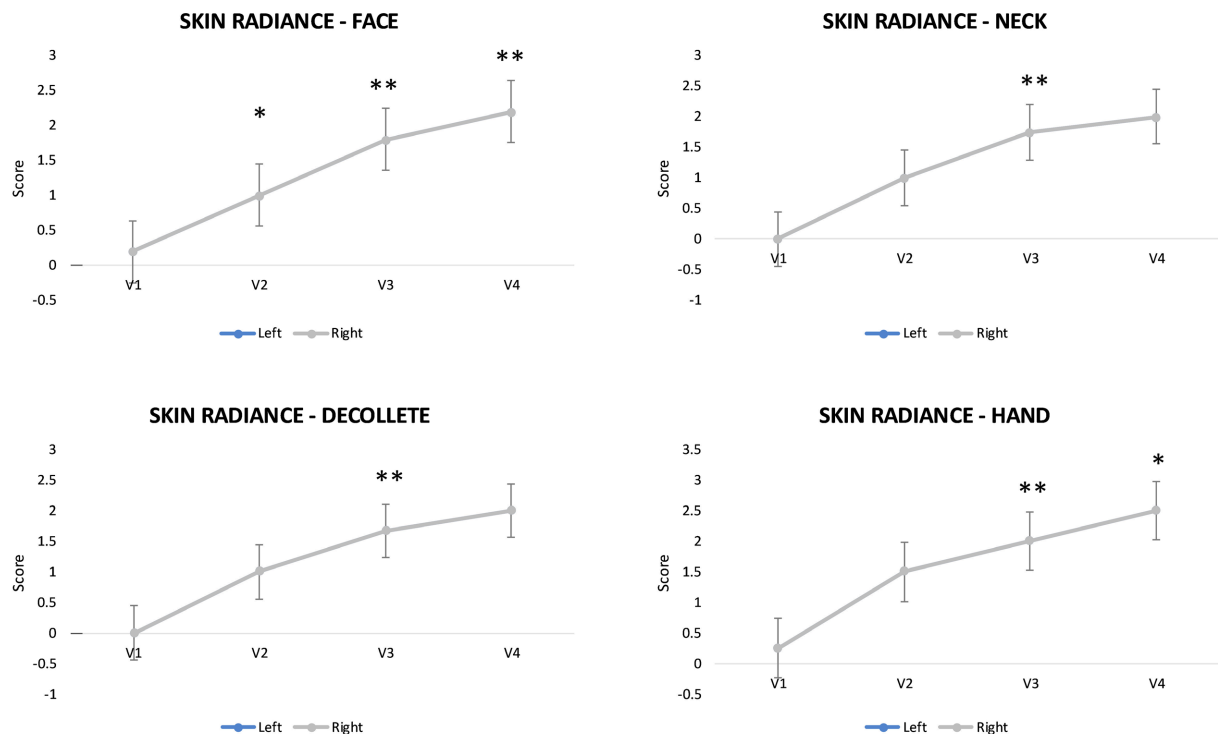
Of the five participants enrolled, all five received treatment to the face and neck. Four participants received treatment to the décolleté and hands. Per-region denominators are indicated where applicable throughout the Results.

Five female participants were included in the evaluation. The median age was 50 years. The mean weight was 60.6 kg, and the mean height was 160 cm. All participants completed the planned treatment sessions and follow-up visits.

#### 3.1. Skin Radiance

Skin radiance increased progressively from baseline in all treated regions (Figure 1). For the face, mean GAIS radiance scores improved from 0.2 at Visit 1 to 1.0 at Visit 2 ( $p = 0.0161$ ), 1.8 at Visit 3 ( $p = 0.00284$ ), and 2.2 at Visit 4 ( $p = 0.00320$ ).

For the neck, radiance increased from 0 at Visit 1 to 1.0 at Visit 2, 1.75 at Visit 3 ( $p = 0.00599$ ), and 2.0 at Visit 4.



Changes in skin radiance scores measured on the face, neck, décolleté, and hands at the different study visits (V1 - V4). Data are presented as mean  $\pm$  standard deviation for the left and right sides. Asterisks indicate within-side statistically significant differences compared with baseline (\* $p < 0.05$ ; \*\* $p < 0.01$ ).

**Figure 1.** Skin radiance assessment over time.

For the décolleté, scores rose from 0 at baseline to 1.0 at Visit 2 and 1.67 at Visit 3 ( $p = 0.03775$ ), reaching 2.0 at Visit 4.

For the hands, radiance increased from 0.25 at Visit 1 to 1.5 at Visit 2 ( $p = 0.07960$ ), 2.0 at Visit 3 ( $p = 0.00599$ ), and 2.5 at Visit 4 ( $p = 0.01822$ ).

Across all regions, the left and right sides showed similar mean scores at every visit, with no consistent differences observed between Hyamira 40 Booster and the comparator. The p-values provided reflect within-side improvement over time, and several timepoints reached statistical significance ( $p < 0.05$ ).

### 3.2. Skin Elasticity

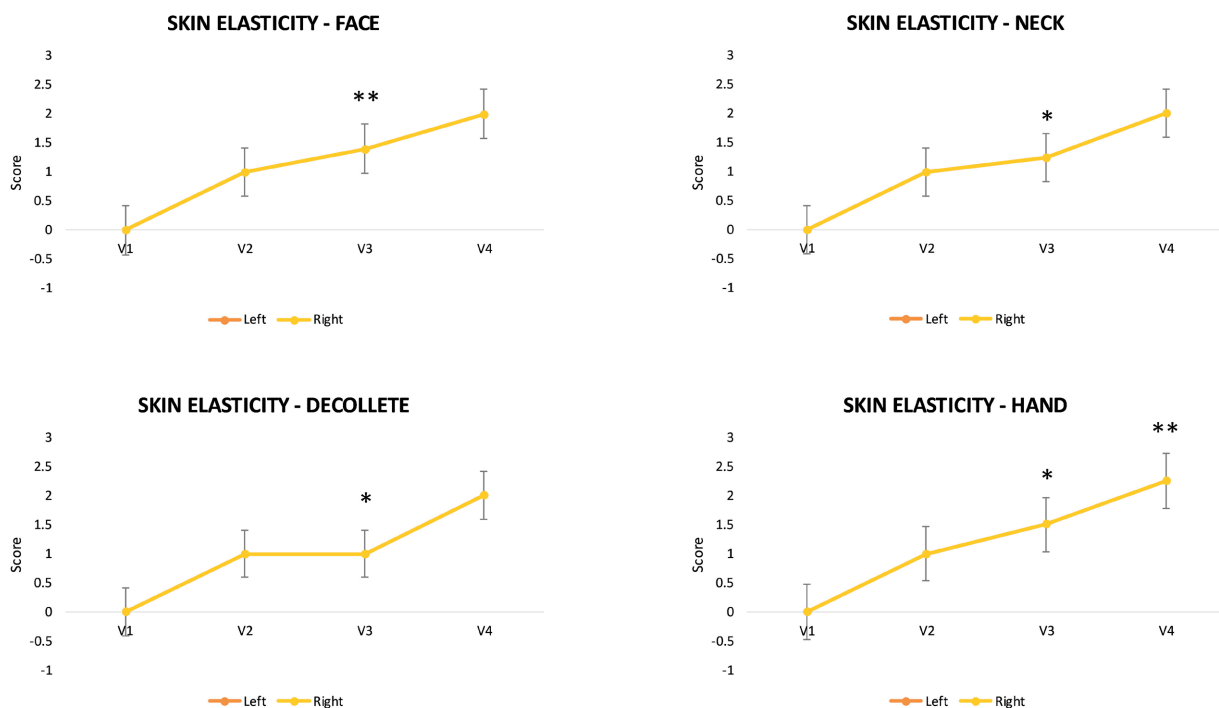
Skin elasticity improved progressively from baseline across all anatomical regions (Figure 2). For the face, mean elasticity increased from 0 at Visit 1 to 1.0 at Visit 2 and 1.4 at Visit 3 ( $p = 0.00464$ ), reaching 2.0 at Visit 4.

In the neck, scores increased from 0 at Visit 1 to 1.0 at Visit 2 and 1.25 at Visit 3 ( $p = 0.01539$ ), with further improvement to 2.0 at Visit 4.

For the décolleté, elasticity progressed from 0 at baseline to 1.0 at Visit 2 and remained at 1.0 at Visit 3 ( $p = 0.03775$ ), increasing to 2.0 at Visit 4.

For the hands, scores rose from 0 at Visit 1 to 1.0 at Visit 2 and 1.5 at Visit 3 ( $p = 0.01385$ ), with further improvement to 2.25 at Visit 4 ( $p = 0.00290$ ).

Across all regions, the left and right sides exhibited similar mean scores, with no consistent differences observed between sides.



Evolution of skin elasticity scores on the face, neck, décolleté, and hands from baseline (V1) to the final visit (V4). Values represent mean  $\pm$  standard deviation for left and right sides. Asterisks indicate within-side statistically significant differences compared with baseline (\* $p < 0.05$ ; \*\* $p < 0.01$ ).

Figure 2. Skin elasticity assessment over time.

### 3.3. Skin Hydration

Skin hydration improved consistently across all anatomical regions following treatment (Figure 3). For the face, mean hydration scores increased from 0.6 at Visit 1 to 1.4 at Visit 2 ( $p = 0.01613$ ), 2.0 at Visit 3 ( $p = 0.00464$ ), and 2.4 at Visit 4 ( $p = 0.00858$ ).

In the neck, hydration increased from 0 at baseline to 1.25 at Visit 2 ( $p = 0.01539$ ), reaching 2.0 at Visit 3 and 2.5 at Visit 4 ( $p = 0.00324$ ).

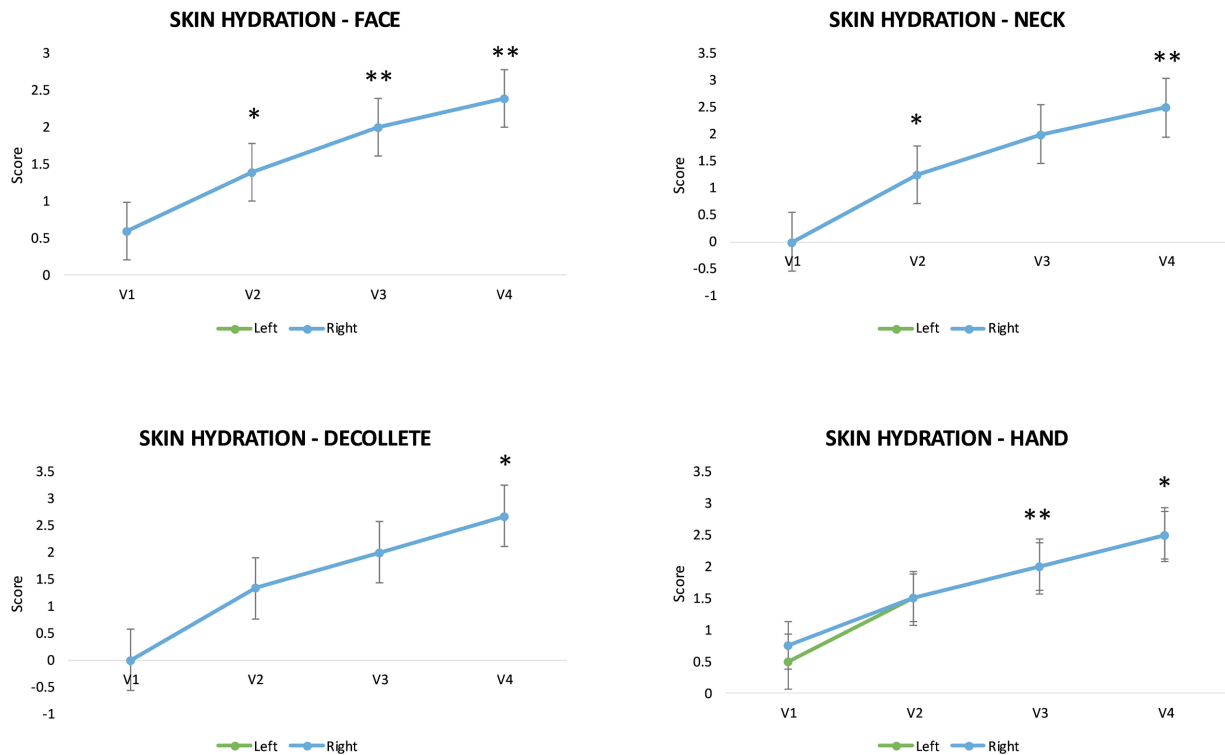
For the décolleté, scores progressed from 0 at Visit 1 to 1.33 at Visit 2 ( $p = 0.05719$ ), 2.0 at Visit 3, and 2.67 at Visit 4 ( $p = 0.01527$ ).

For the hands, hydration increased from 0.5 (left) and 0.75 (right) at Visit 1 to 1.5 at Visit 2 (right-side  $p = 0.05767$ ), then to 2.0 at Visit 3 ( $p = 0.01385$  for left;  $p = 0.01539$  for right), and 2.5 at Visit 4 ( $p = 0.04052$  for left;  $p = 0.03535$  for right).

Across all four regions, mean hydration values were equal on both treated sides at nearly all visits, indicating similar hydration trends.

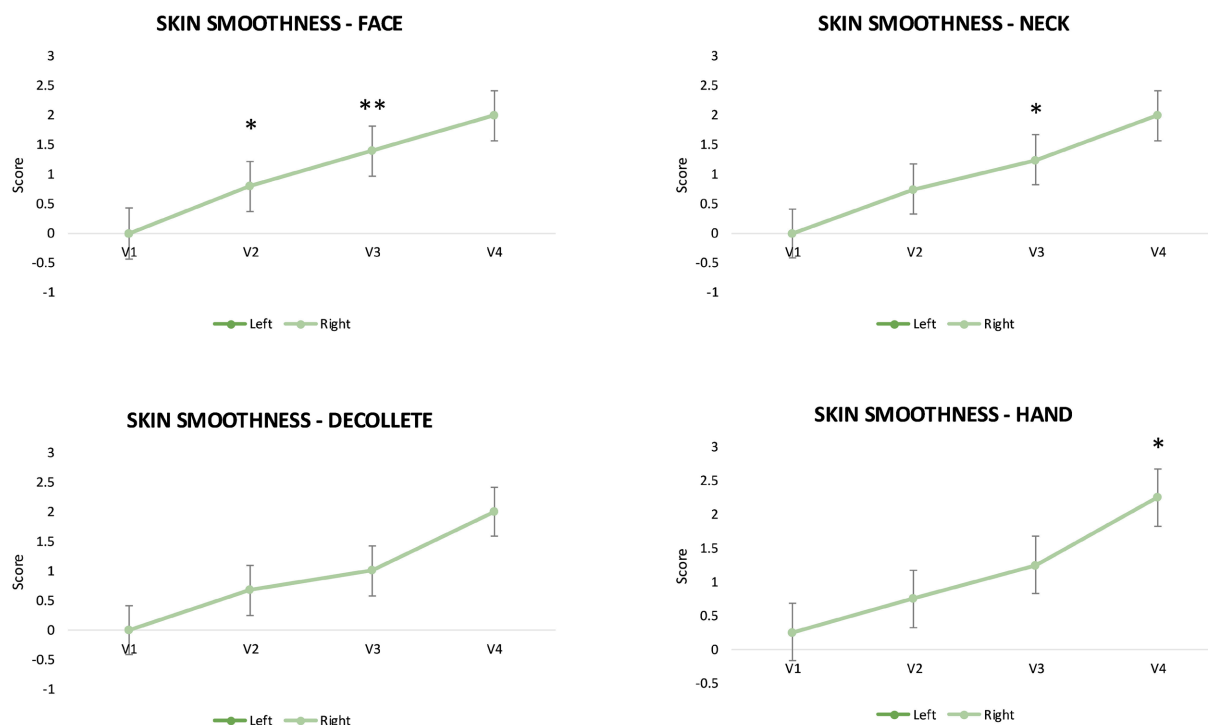
### 3.4. Skin Smoothness

Skin smoothness improved progressively across all anatomical regions following treatment (Figure 4). For the face, mean smoothness increased from 0 at Visit 1 to 0.8 at Visit 2 ( $p = 0.01613$ ), 1.4 at Visit 3 ( $p = 0.00464$ ), and 2.0 at Visit 4.



Skin hydration scores assessed on the face, neck, décolleté, and hands at each visit (V1 - V4). Results are expressed as mean  $\pm$  standard deviation for left and right sides. Asterisks indicate within-side statistically significant differences compared with baseline (\* $p < 0.05$ ; \*\* $p < 0.01$ ).

Figure 3. Skin hydration assessment over time.



Progression of skin smoothness scores on the face, neck, décolleté, and hands throughout the study visits (V1 - V4). Data are shown as mean  $\pm$  standard deviation for left and right sides. Significant within-side differences versus baseline are marked (\* $p < 0.05$ ; \*\* $p < 0.01$ ).

**Figure 4.** Skin smoothness assessment over time.

In the neck, smoothness increased from 0 at baseline to 0.75 at Visit 2 ( $p = 0.05767$ ), 1.25 at Visit 3 ( $p = 0.01539$ ), and reached 2.0 at Visit 4.

For the décolleté, scores rose from 0 at Visit 1 to 0.67 at Visit 2 ( $p = 0.18350$ ), then to 1.0 at Visit 3, and 2.0 at Visit 4.

For the hands, smoothness improved from 0.25 at Visit 1 to 0.75 at Visit 2 ( $p = 0.18169$ ), 1.25 at Visit 3, and 2.25 at Visit 4 ( $p = 0.01628$ ).

Across all regions, the left and right sides demonstrated equivalent mean values at every time point, showing similar trends in skin smoothness on both treated sides.

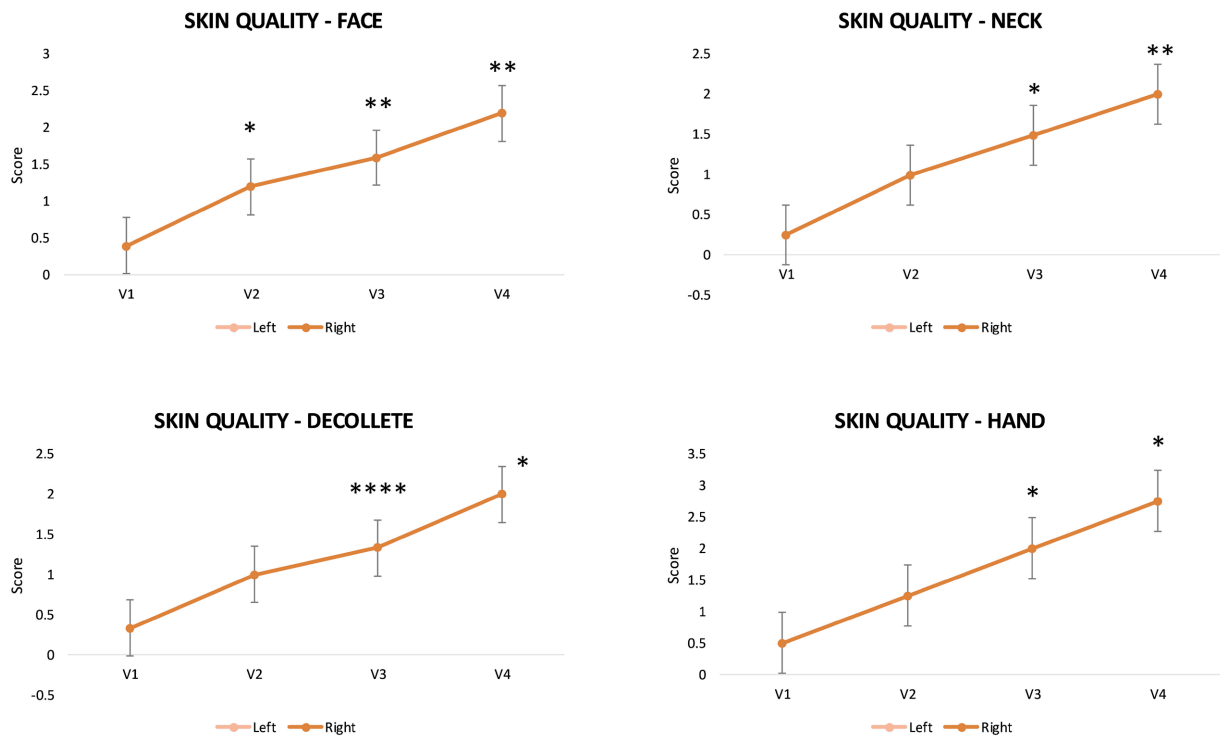
### 3.5. Overall Skin Quality

Overall skin quality improved consistently across all anatomical regions during the evaluation period (Figure 5). For the face, mean GAIS scores increased from 0.4 at Visit 1 to 1.2 at Visit 2 ( $p = 0.01613$ ), 1.6 at Visit 3 ( $p = 0.00388$ ), and 2.2 at Visit 4 ( $p = 0.00858$ ).

In the neck, overall quality improved from 0.25 at Visit 1 to 1.0 at Visit 2 ( $p = 0.05767$ ), 1.5 at Visit 3 ( $p = 0.01539$ ), and 2.0 at Visit 4 ( $p = 0.00599$ ).

For the décolleté, overall skin quality increased from 0.33 at baseline to 1.0 at Visit 2 ( $p = 0.18350$ ), 1.33 at Visit 3, and 2.0 at Visit 4 ( $p = 0.03775$ ).

For the hands, scores progressed from 0.5 at Visit 1 to 1.25 at Visit 2 ( $p = 0.05767$ ), 2.0 at Visit 3 ( $p = 0.01385$ ), and 2.75 at Visit 4 ( $p = 0.01822$ ).



Changes in global skin quality scores evaluated on the face, neck, décolleté, and hands from V1 to V4. Results are presented as mean ± standard deviation for left and right sides. Asterisks indicate within-side statistically significant improvements compared with baseline (\*p < 0.05; \*\*p < 0.01; \*\*\*\*p < 0.0001).

**Figure 5.** Overall skin quality improvement over time.

Across all regions, the left and right sides demonstrated similar mean scores at all visits, showing similar trends in overall skin quality on both treated sides.

### 3.6. Patient Satisfaction

A structured 16-item patient satisfaction questionnaire was administered at each visit beginning at Visit 2 to assess subjective treatment experience and perceived aesthetic improvements for each treated side. Patient-reported satisfaction was consistently high throughout the study and showed no appreciable differences between the two treated sides. For all 16 questionnaire items, participants selected the same response for both the Hyamira-treated and comparator-treated sides. Agreement ratings predominantly fell within the “Totally agree” or “Somewhat agree” categories for all evaluated parameters, including injection comfort, skin tolerance, overall satisfaction, rested appearance, complexion freshness, wrinkle reduction, skin tone, fatigue, firmness, hydration, smoothness, texture, plumpness, brightness, and overall skin quality. For all questions requiring side-by-side comparison, patients uniformly selected “Equal”, indicating no subjective preference for either product. All participants reported that the three-session protocol was not inconvenient.

### 3.7. Safety and Tolerability

Treatment was well tolerated overall. Reported injection-site reactions were mild

and transient and resolved without intervention. No serious adverse events, nodules, persistent induration, or delayed complications were reported. No participant discontinued treatment or follow-up because of tolerability concerns.

#### 4. Discussion

In this prospective, split-area exploratory evaluation, Hyamira 40 Booster showed improvements in skin radiance, elasticity, hydration, smoothness, and overall skin quality that were similar to those observed with an established hyaluronic acid skinbooster. Patient-reported GAIS scores were similar for both sides across all regions and visits.

Patient satisfaction results also supported the similarity between treatments. The 16-item questionnaire, completed at each follow-up visit, consistently showed high satisfaction for both sides, with participants providing the same responses for the Hyamira-treated and comparator-treated areas. For most direct comparison items, patients selected “Equal,” indicating no preference regarding comfort, tolerability, or aesthetic outcome. These findings align with the GAIS scores and support the observation of similar patient-reported outcomes between products.

Although injectability was not formally assessed, informal observations during routine use suggested potential differences when using a 25 G/60 mm cannula. As these observations were not collected through a standardized evaluation, no conclusions can be drawn. Injectability may nonetheless be relevant in clinical practice and warrants formal assessment in future studies.

Cost considerations also remain relevant in clinical decision-making. While economic evaluation was not part of the study design, the substantial price difference between the two products (47.88 euros for Hyamira 40 Booster versus 89 euros for the comparator, per equivalent volume) may be a consideration in clinical practice, particularly in light of evidence identifying cost as a common barrier to aesthetic treatments [31]. In the absence of observed differences in this exploratory sample, affordability may be a relevant reflection; however, these implications lie outside the scope of the present analysis and require formal cost-effectiveness studies.

The findings of the present study are consistent with the established evidence supporting injectable HA formulations for improving skin quality. Numerous clinical studies have shown that intradermal HA injections enhance hydration, elasticity, luminosity, and overall skin appearance, regardless of whether the HA is cross-linked or non-cross-linked. Systematic reviews of HA treatment likewise report improvements in firmness, radiance, and texture [26] [30]. Biometric assessments further confirm measurable gains in hydration and viscoelasticity, with some studies noting that these effects persist for several months [28] [33].

The similar patient-perceived outcomes observed between Hyamira 40 Booster and an established HA skinbooster align with this literature. The split-area design of the present study provides a direct intra-individual comparison, reflecting typical clinical decision-making in aesthetic practice.

Although HA boosters vary in concentration, degree of cross-linking, rheological behaviour, and recommended injection depth, existing data indicate that formulations in this category generally produce similar improvements in skin hydration and overall skin quality.

This study has several limitations. First, the evaluation relied on patient-reported outcomes rather than instrumental measurements. While subjective evaluation is central to aesthetic practice, incorporating objective measures in future work would provide additional depth. Second, the sample size and short follow-up duration limit the interpretation and generalizability of the findings. Third, impressions regarding ease of administration were based on routine clinical experience rather than predefined evaluation criteria. Fourth, the side assignment was not randomized, which may have introduced allocation bias and should be considered when interpreting the split-area comparisons.

Despite these limitations, this study provides preliminary prospective evidence supporting the clinical performance of Hyamira 40 Booster across multiple anatomical regions. The findings suggest that Hyamira 40 Booster showed similar patient-reported outcomes in this exploratory sample. Future research should include larger randomized studies with objective measurements, longer follow-up, and formal assessment of injectability and cost-effectiveness to more comprehensively define the role of Hyamira 40 Booster within the growing category of HA-based skin quality treatments.

### **Ethics Statement**

This study was conducted in accordance with the principles of the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects. All procedures were performed within the intended purpose and normal conditions of use of the Hyamira 40 Booster product.

### **Consent**

Informed consent was obtained from all participants before inclusion in the study.

### **Conflicts of Interest**

Dr Philippe Hamida-Pisal and Dr Jihyun Byun declare that they have no conflicts of interest.

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