RHA® 4 is a combination of sodium Hyaluronic Acid (NaHA) with a concentration of 23 mg/g crosslinked with 1,4-butanediol diglycidyl ether (BDDE).

CLINICAL STUDY

The safety and effectiveness of RHA® 4 in the correction of moderate to severe nasolabial folds was evaluated in a pivotal clinical study described below.

1. Fixed Study Design

A controlled, randomized, double-blinded, within-subject, multicenter, split-face study was conducted to evaluate the safety and effectiveness of RHA® 4 versus a control treatment for the correction of moderate to severe nasolabial folds. Subjects were randomly assigned to receive RHA® 4 and a control treatment in deep skin to superficial skin to evaluate the safety and effectiveness of RHA® 4 in the correction of moderate to severe nasolabial folds, or to a non-treatment group. The side of the face for each device injected was assigned randomly. Subjects were allocated to three groups: 30 were allocated to RHA® 4 treatment and 30 to the Control treatment, and 20 were allocated to untreated controls.

2. Adverse Events

The primary efficacy endpoint was the analysis of mean Wrinkle Severity Rating Scale (WSRS) change from injection site to baseline at 24 weeks after injection, as assessed by the BLE (see data in Figure 1). Global Aesthetic Improvement (GAI) was also assessed by the BLE and the investigator by means of a 100-mm visual analog scale (VAS). Secondary efficacy endpoints included rates of subjects rated by the investigator as having “moderate” or “severe” improvement on a 5-point scale (worse, much worse, no change, much improved, improved) compared to pre-injection, as well as rates of subjects rated by the subject as having “improved” compared to pre-injection, as assessed by means of a 100-mm VAS. Subjects were rated at baseline, 1 week after injection, 2 weeks after touch up injection, and 24 weeks after injection. The CTR numbers indicated in the “Last Day” column are also included in the “8-14 Days” column.

3. Demographics

A controlled, randomized, double-blinded, within-subject, multicenter, split-face study was conducted to evaluate the safety and effectiveness of RHA® 4 versus a control treatment for the correction of moderate to severe nasolabial folds. Subjects were randomly assigned to receive RHA® 4 and a control treatment in deep skin to superficial skin to evaluate the safety and effectiveness of RHA® 4 in the correction of moderate to severe nasolabial folds, or to a non-treatment group. The side of the face for each device injected was assigned randomly. Subjects were allocated to three groups: 30 were allocated to RHA® 4 treatment and 30 to the Control treatment, and 20 were allocated to untreated controls.

4. Treatment Characteristics

The study protocol allowed a maximum of 3.0 ml per midfacial filler injection. Subjects were randomized to one of four devices: RHA® 4 and the Control Device – Safety Population or untreated control (C2 M13 J13 N0 and C85 M90 J10 N0). The Control Device has been demonstrated to be safe and effective in multiple clinical studies. The device was selected based on the comparison of pre-injection Wrinkle Severity Rating Scale (WSRS) to the device to be compared. For scoring the severity of nasolabial folds, NLF (the parenthesis) was used for scoring the nasolabial fold severity on the WSRS, on the device without the WSRS. The baseline WSRS score was then subtracted from the WSRS score at each time point to calculate the change in the WSRS score. The final WSRS score was calculated as the average of the WSRS scores at each visit. The side of the face for each device injected was assigned randomly. Subjects were rated at baseline, 1 week after injection, 2 weeks after touch up injection, and 24 weeks after injection. The CTR numbers indicated in the “Last Day” column are also included in the “8-14 Days” column.
The results demonstrated that non-inferiority to the control was achieved for RHA® 4 at 24 weeks for the treatment of NLFs. The results demonstrated that RHA® 4 is safe and effective in the treatment of wrinkles and folds such as NLFs. The safety of injecting greater amounts has been extensively studied.

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• Prior to injection, the patient should be asked if they are taking any medications which may thin the blood (e.g., aspirin, nonsteroidal anti-inflammatory drugs).

• Patients should notify the injector if any of the following occurs:

- Changes in vision.
- Shouldn't put the needle to the syringe.
- Any redness and/or swelling that lasts for more than a week.
- Any electrode or device that they have described above that occurs after injection.

• Expiration date (YYYY-MM-DD)

• The injection should be stopped before pulling the syringe out of the skin, this means that the injection is too superficial. This should be avoided as the results of the correction could be irregular.

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• Before applying the needle to the skin, both the needle and syringe should be gently massaged until it returns to a normal color. Blanching may represent an allergic reaction and must be stopped immediately. A suitable anesthetic treatment for managing these reactions should be used.

• In case of injury to the skin, to prevent the product from leaking out, or product misplacement (too much product), the injection should be stopped immediately and the area treated with alcohol or another suitable antiseptic solution.

• Once the needle is inserted into the deep dermis to superficial subcutaneous tissue, the plunger should be forcefully pushed until a small droplet of the gel is visible at the tip of the needle.

• When the injection is completed, the treated site should be gently massaged until it returns to a normal color. Blanching may represent an allergic reaction and must be stopped immediately. A suitable anesthetic treatment for managing these reactions should be used.

• The injection should be stopped before pulling the syringe out of the skin, this means that the injection is too superficial. This should be avoided as the results of the correction could be irregular.

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