AESTHETIC CORRECTION OF LIPS

MEDICAL DEVICE. ALEXA MEDIUM

- Alexa Medium is a sterile, pyrogen-free, physiological solution made from cross-linked hyaluronic acid (HA), which is not of animal origin (device is produced by bacterial fermentation using a *Streptococcus zooepidemicus* bacterial strain).
- The gel is presented in a pre-filled disposable syringe.
- One syringe contains 1 mL of Alexa Medium: cross-linked hyaluronic acid gel - 17.5 mg; phosphate-buffered saline pH 7.2
- Indication - correction of the lip volume loss within accepted cosmetological practice.

Post-marketing, prospective, multicentre, single-arm, open-label Investigation of subjects who will receive an injection of medical device ‘Alexa Medium’ manufactured by Diaco Biofarmaceutici S.r.l.., Italy for cor rection of the lips volume loss within accepted cosmetological practice.

PURPOSE OF THE CLINICAL INVESTIGATION

Investigation purpose - To confirm the safety, tolerability and effectiveness of the injectable medical device based on cross-linked hyaluronic acid ‘Alexa Medium’ manufactured by Diaco Biofarmaceutici S.r.l.., Italy for correction of the lips volume loss within accepted cosmetological practice.

STUDY CHARACTERISTICS

- **Sites** – 3 in Poland, 1 in Ukraine

- **Subjects number** - 69 subjects aged 25 to70

1. ITT population – all subjects, included to clinical investigation (69)
2. PP population – all subjects that completed the study without major protocol deviations (48)

- **Duration of the study for each subject** - 180±5 days

CLINICAL INVESTIGATION METHODOLOGY

The enrolled subjects of the final analysis population received 1 or 2 injections (second injection might be repeated at the visit 2 at the discretion of the Investigator) of the medical device ‘Alexa Medium’ for correction of the lips volume loss. The first procedure was performed to all subjects at visit 1 (day 0) and the second procedure was performed at visit 2 (day 30±5 days) at the discretion of the Investigator (to 48 patients).

STUDY STRUCTURE

№ CALL	PROCEDURE
Visit 0 (V0)	Outpatient visit, screening, verification of inclusion/exclusion criteria.
Visit 1 (V1)	Outpatient visit, IMD application. Safety data collection. Day 0.
Visit 2 (V2)	Outpatient visit, IMD repeated application (optional). Safety data collection. Effectiveness assessment. Day 30 ± 5 days.
Visit 3 (V3)	Outpatient visit. Effectiveness assessment. Safety data collection. Day 60 ± 5 days
Visit 4 (V4)	Telephone visit. Safety data collection. Day 90 ± 5 days.
Visit 5 (V5)	Telephone visit. Safety data collection. Day 135 ± 5 days.
Visit 6 (V6)	Close-out outpatient visit. Effectiveness assessment. Day 180 ± 5 days.

INCLUSION CRITERIA

- Subject’s age 25 to 70.
- Subject will receive an injection of the medical device ‘Alexa Medium’ manufactured by Diaco Biofarmaceutici S.r.l.., Italy for correction of the lips volume loss within accepted cosmetological practice.
- Subject’s lips requiring correction of the lips volume loss according to the Investigator's judgement.
- The subject has established a realistic aesthetic improvement goal that the Investigator agrees is achievable, i.e., have realistic expectations of aesthetic results.
- Subject willing to have photographs of the face taken.
- Subject psychologically able to understand the Investigation related information and to give a written informed consent.
- Subject able and agreeing to follow Investigation procedures, instructions and likely to complete all required visits.
- The subject agreed to participate in the Investigation and signed the Informed Consent Form.

ASSESSMENT CRITERIA

1. Effectiveness assessment by MLFS (investigator, evaluating investigator) and GAIS (subject, investigator and evaluating investigator) scales on different time periods of the study.
2. Achieving personal correction goal of overall lip fullness (subject).
3. Safety assessment – AE/ADE

The Medicis Lip Fullness Scale

Grade	Lips
1	Very thin
2	Thin
3	Medium
4	Full
5	Very Full

The Global Aesthetic Improvement Scale

	Degree	Description
1	Exceptional improvement	Excellent corrective result
2	Very improved subject	Marked improvement of the appearance, but not completely optimal
3	Improved subject	Improvement of the appearance, better compared with the initial condition, but a touch-up is advised
4	Unaltered subject	The appearance substantially remains the same compared with the original condition
5	Worsened subject	The appearance has worsened compared with the original condition

Primary effectiveness endpoint:

- Global Aesthetic Improvement Scale (GAIS) evaluated by the Investigator on visit 3, day 60±5 days.
- Change in Medicis Lip Fullness Scale (MLFS) evaluated by the Investigator on visit 3, day 60±5 days.

Secondary effectiveness endpoints:

- Global Aesthetic Improvement Scale (GAIS) evaluated by the Investigator on visit 2, day 30±5 days.
- Change in Medicis Lip Fullness Scale (MLFS) evaluated by the Investigator on visit 2, day 30±5 days.
- Global Aesthetic Improvement Scale (GAIS) evaluated by the subject on visit 2, day 30±5days.
- Achieving personal correction goal of overall lip fullness evaluated by the subject on visit 2, day 30±5 days.
- Global Aesthetic Improvement Scale (GAIS) evaluated by the Evaluating Investigator on visit 2, day 30±5 days
- Change in Medicis Lip Fullness Scale (MLFS) evaluated by the Evaluating Investigator on visit 2, day 30±5 days
- Achieving personal correction goal of overall lip fullness evaluated by the subject on visit 3,
- Global Aesthetic Improvement Scale (GAIS) evaluated by the subject on visit 3, day 30±5days.
- Global Aesthetic Improvement Scale (GAIS) evaluated by the Evaluating Investigator on visit 3, day 60±5 days.
- Change in Medicis Lip Fullness Scale (MLFS) evaluated by the Evaluating Investigator on visit 3, day 60±5 days.
- Global Aesthetic Improvement Scale (GAIS) evaluated by the Investigator on visit 6, day 180±5 days.
- Change in Medicis Lip Fullness Scale (MLFS) evaluated by the Investigator on visit 6, day 180±5 days.
- Global Aesthetic Improvement Scale (GAIS) evaluated by the subject on visit 6, day 180±5 days.
- Achieving personal correction goal of overall lip fullness evaluated by the subject on visit 6, day 180±5 days.
- Global Aesthetic Improvement Scale (GAIS) evaluated by the Evaluating Investigator on visit 6, day 180±5 days.
- Change in Medicis Lip Fullness Scale (MLFS) evaluated by the Evaluating Investigator on visit 6, day 180±5 days.

SAFETY EVALUATION: AE/ADE

- Number, frequency, predictability, duration, severity, seriousness of all AE*s, which were identified during the Investigation;
- Number, frequency, predictability, duration, severity, seriousness of all ADE**s, which were identified during the Investigation;
- Number, frequency, predictability, duration, severity, seriousness of all ADEs and AEs, leading to the withdrawal of the subject from the Investigation
- All device deficiencies observed during the Investigation will be registered and duly reported.

- AE* – adverse event
- ADE**– adverse device effect

SAFETY CRITERIA

- The levels of discomfort on a scale of 0 (no discomfort) to 10 (extreme discomfort) assessed by the subjects in 15 minutes after the IMD application visit 1 and 2 respectively...
- Bruising of the lips in 15 minutes after the IMD application at visit 1 as assessed by the Investigator.
- Bruising of the lips in 15 minutes after the IMD application at visit 2 as assessed by the Investigator.
- Some swelling of the lips in 15 minutes after the IMD application at visit 1 as assessed by the Investigator.
- Some swelling of the lips in 15 minutes after the IMD application at visit 2 as assessed by the Investigator.
- Mean time to return to normal daily after IMD application at visit 1 and 2, respectively

PRIMARY ENDPOINTS. RESULTS.

	GAIS		MLFS					
	ITT population	PP population	ITT population			PP population		
			Upper lip	Lower lip	Worst result	Upper lip	Lower lip	Worst result
Mean difference of V3 with baseline	-2.64	-2.54	1.08	0.89	1.1	1.06	0.92	1.08
p*	p=0.000	p=0.000	p=0.000	p=0.000	p=0.000	p=0.000	p=0.000	p=0.000
p* - It was statistically significant (p<0,05)								

PRIMARY ENDPOINT EFFECTIVENESS ASSESSMENT

Towards the primary effectiveness endpoint, **in the ITT and PP population the mean GAIS score evaluated by the Investigator at visit 3** corresponded to "Very improved subject" to "Exeptional improvement" condition. The difference with baseline (baseline GAIS score = 4) was statistically significant (p=0.000).

The results of **improvement in MLFS score in all populations** were statistically significant. In the ITT and PP population the mean MLFS score evaluated by the Investigator for upper lip, the lower lip and for worst result at visit 3 corresponded to "Medium" to "Full" lip fullness. The difference with baseline for the upper, lower lips and worst result was statistically significant (p=0.000).

SECONDARY ENDPOINTS EFFECTIVENESS ASSESSMENT

- Towards all secondary endpoints, **in the ITT and PP population the mail GAIS score** at visits 2, 3, 6 corresponded to "Very improved subject" to "Exeptional improvement" condition. The difference with baseline (baseline GAIS score =4) was statistically significant (p=0.000)

- The results of **improvement in MLFS score in all populations** were statistically significant (P=0.000). The mean score evaluated by Investigator and Evaluating Investigator for upper lip and lower lip corresponded to "Medium" to "Full" lip fullness. The worst result evaluated by Investigator and Evaluating Investigator corresponded to 'Medium" to "Full" lip fullness. The difference with baseline for the upper, lower lips and worst result was statistically significant (p=0.000).

SAFETY RESULTS: AE/ADE

The final analysis showed high safety of the IMD as only two adverse events (COVID-19 and Flu), no adverse device effects and no device deficiencies were registered per 117 IMD applications. (69 subjects).

CONCLUSIONS

IMD demonstrated a high level of the safety and clinical effectiveness within accepted cosmetological practice.

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