SUMMARY OF SAFETY AND CLINICAL PERFORMANCE

ART FILLER

Device without medical purpose

SSCP Reference number: SSCP – ART FILLER - CL

Summary of safety and clinical performance
Healthcare professionals part

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The SSCP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals. Following this information there is a summary intended for patients.

1. Device identification and general information

Considering the Annex XVI of the European Regulation (EU) 2017/745, the products do not claim therapeutic action as they are part of list of groups of products without an intended medical purpose referred to in Article 1 (2) and in Annex XVI - §3." "Substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, excluding those for tattooing".

1.1 Device trade name(s)

ART FILLER Fine Lines
ART FILLER Eyes
ART FILLER Lips Soft
ART FILLER Lips
ART FILLER Universal
ART FILLER Volume

1.2 Manufacturer's name and address

LABORATOIRES FILL-MED
38 Cours Albert 1er
75008 PARIS
France

1.3 Manufacturer's single registration number (SRN)

Organization name	Role	Actor ID/SRN
Laboratoires Fill-Med	Manufacturer	FR-MF-000007907

1.4 Basic UDI-DI

Basic UDI-DI: 3664948ARTFILLERWL

1.5 Medical device nomenclature

CND (EMDN)code: X0303 (Substances, combinations of substances, or items without an intended medical purpose intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, by a prefilled means for introduction, excluding those for tattooing – resorbable Class of device)

ART FILLER products are devices of Class III according to rules 8 and 14 of Annex VIII of Regulation (EU) 2017/745**.**

1.6 Year when the first certificate (CE) was issued covering the device

CE mark according to Regulation (EU)2017/745: 2025

1.7 Authorised representative if applicable, name and the SRN

Not applicable as Laboratoires FILL-MED are established in France.

1.8 NB's name (the NB that will validate the SSCP) and the NB's single identification number

Eurofins product testing Italy s.r.l (NB number 0477)

2. Intended use of the device

2.1 Intended purpose

ART FILLER are products without an intended medical purpose, used for aesthetic purposes, intended to restore changes to skin structure caused by ageing: fill in lines and creases in the facial skin and restore volume. The presence of lidocaine aims to decrease the pain sensation of the patient during treatment.

2.2 Indication(s) and target population(s)

Depending on their degree of crosslinking, ART FILLER devices are indicated for filling of skin depressions of different importance:

- **ART FILLER Fine Lines** is indicated to fill in fine lines, superficial lines and small skin folds of crow's feet, forehead (except glabella zone), upper lip and cheeks by means of an injection into the upper dermis..
- **ART FILLER Eyes** is indicated to correct the periorbital ageing signs including the superficial skin wrinkles of crow's feet, and the tear trough deformity (infraorbital hollow).
- **ART FILLER Lips Soft** is indicated to increase the volume of lip and enhance the lip outline and to fill medium and deep nasolabial folds with or without marionette lines by injection into the middle to deep dermis.
- **ART FILLER Lips** is indicated to increase the volume and/or enhance the lip outline as well as to fill medium and deep nasolabial folds with or without marionette lines by injection into the middle to deep dermis.
- **ART FILLER Universal** is indicated to:
    - fill in medium to deep nasolabial folds with or without marionette lines, and cheeks folds by dermal or subdermal injection,
    - add volume to define the shape of the nose by subdermal or dermal injection and restore volume to the midface by subdermal injection,
    - increase the volume of the lip and enhance the lip outline by submucous, intradermal or subdermal injection.
- **ART FILLER Volume** is indicated to restore volume to the mid-face, jawline, temples and chin, via subcutaneous, supraperiosteal or deep dermis injections.

Target population

Users: Users are trained medical doctors who are qualified or accredited in accordance with national law or professionals authorized according to National laws.

Patients: Adults (according to Regulation, patients have to be older than 18 years), who want to improve their appearance by reducing wrinkles and correcting the signs of ageing.

2.3 Contraindications and/or limitations

All ART FILLER variants must not be injected	**Specifically,**
- Into blood vessels. - Into an area where a non-absorbable filler implant has already been injected. - Do not over-correct. - In patients with known hypersensitivity to hyaluronic acid, lidocaine and amide type local anesthetics. - In patients with a medical history of auto-immune illness or receiving immunotherapy. - In patients who have a medical history of severe multiple allergies or anaphylactic shock. - In patients suffering from epilepsy that is not controlled with treatment. - In patients affected by porphyria. - In patients with a tendency to develop hypertrophic scars. - In patients with medical history of recurring sore throats related to rheumatic fever localised in the heart. - Do not use in conjunction with a medical treatment with inhibitors of cytochrome P450, due to interactions with lidocaine. - In persons who are less than 18 years old. - In pregnant or breastfeeding women. - In areas that are inflamed and/or contagious skin lesions (acne, herpes, etc.) - Immediately after or before laser treatment, deep chemical peeling or dermabrasion	**ART FILLER Fine Lines** must not be injected into eyelids. **ART FILLER Eyes** must not be injected into eyelids. **ART FILLER Lips soft** must not be injected: - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area). **ART FILLER Lips** must not be injected: - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area). - **ART FILLER Universal** must not be injected: - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area). **ART FILLER Volume** must not be injected: - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area), the glabellar area or into the lips. - Into muscles

3. Device description

3.1 Description of the device

ART FILLER products are crosslinked viscoelastic hyaluronic acid gels of non-animal origin, slowly absorbable over time, clear, colorless, sterile, non-pyrogenic, physiological and containing 0.3% by weight of lidocaine hydrochloride for its anesthetic properties.
According to the reference, the amount of hyaluronic acid and gel volume in the syringe varies :

	Sodium hyaluronate	Lidocaine hydrochloride (% w/w)	Gel volume /syringe	Needle supplied with the device
ART FILLER Fine Lines	20 mg/g	0.3%	1.0 ml	30G½"
ART FILLER Eyes	20 mg/g	0.3%	1.0 ml	30G½"
ART FILLER Lips Soft	25 mg/g	0.3%	1.0 ml	30G½"
ART FILLER Lips	25 mg/g	0.3%	1.0 ml	27G½"
ART FILLER Universal	25 mg/g	0.3%	1.2 ml	27G½"
ART FILLER Volume	25 mg/g	0.3%	1.2 ml	27G½"

3.2 A reference to previous generation(s) or variants if such exist, and a description of the differences

Not applicable

3.3 Description of any accessories which are intended to be used in combination with the device

No accessory according to regulatory definition. (Regulation (EU) 2017/745 art. 2).

3.4 Description of any other devices and products which are intended to be used in combination with the device

Sterile single-use needles are supplied with **ART FILLER** as a procedure pack. (Regulation (EU) 2017/745 art.22.4)

ART FILLER can also be used in conjunction with:

- Standard hypodermic needles according to instructions of their manufacturer.
- Sterile single-use canula (22G-25G), sterile, according to instructions of their manufacturer.

4. Risks and warnings

4.1 Residual risks and undesirable effects

According to LABORATOIRES FILL-MED policy, risks are reduced as far as possible, few residual risks (related to patient profile or history) are

- Patient allergy: results of biocompatibility and clinical studies strongly demonstrate that the allergy risk, which may present a potentially high severity, has a very low probability to occurs.
- Concomitant presence of non-resorbable implant in implantation zone or injection of filler on a zone previously injected with another filler are reduced ART FILLER are meant to be used by skilled and adequately trained healthcare professionals aware of those, as highlighted during usability tests.

During clinical investigations, adverse events are collected all over the follow-up period, serious adverse events (SAE) if any and local events are described, relation with the device or the procedure, duration and severity of events are analyzed when information is available. In the 6 Clinical investigations have been conducted with ART FILLER, no Serious Adverse Event related to the devices has been reported, local events are mostly reported after injection, are mostly of mild intensity and do not last long. no difference with the comparator was reported In comparative studies.

ART FILLER safety profile does not show any difference compared to the reference products and data published in literature, most of detected events were noted as slight in most cases and are routinely seen when using HA dermal fillers.

As **ART FILLER** devices were previously CE marked according to Directive 93/42EEC since February 2016 for **ART FILLER Fine Lines**, **ART FILLER Universal**, **ART FILLER Lips** and **ART FILLER Volume**), August 2019 for **ART FILLER Lips Soft**, long market history is available, this confirming that undesirable effects are extremely rare.

Occurrence	ART FILLER Fine Lines ART FILLER Eyes	ART FILLER Lips Soft	ART FILLER Lips	ART FILLER Universal	ART FILLER Volume
< 0.001%	Local Reaction – Induration	Skin inflammation Pain	Nodule Granuloma	Nodule Skin Inflammation	Granuloma Bruise

	Numbness Fever Pain Allergic reaction Fatigue Bruise Itching sensation Necrosis Skin discoloration	Papula Erythema Bruise	Skin Inflammation Itching sensation	Granuloma Local Reaction - Induration Necrosis Pain Thrombosis Burning Sensation Quincke Edema Papula Itching sensation Bruise Eye Injury Muscle Spasm	Paresis Itching sensation Skin disorder Local Reaction - Induration Necrosis Skin infection – Herpes Burning Sensation Pain Blister Skin infection – Crust Ischemia Paresthesia Chills Muscle Spasm Allergic Reaction
≥ 0.001% and < 0.01%	Erythema Granuloma Nodule Papula Swelling	Local reaction – Induration Swelling	Swelling Pain Local Reaction - Induration	Swelling Erythema	Swelling Nodule Skin Inflammation
≥ 0.01%	-	-	-	-	-

The list of potential adverse effects related to implantation of dermal fillers is given in Instructions For Use. If applicable, this list is updated with specific events reported with ART FILLER during Post-Market Surveillance.

Undesirable effects described in IFU:

- *Vascular complications (embolism, ischemia, necrosis, loss of vision, thrombosis, paralysis, paraesthesia, hair loss).*
- *Systemic and local allergic reactions (itching sensation, Quincke edema/angioedema, anaphylactic shock).*
- *Inflammatory reactions (burning sensation, swelling, erythema, nodule, granuloma, fibrosis, skin inflammation, fever, pain, local reaction – induration/pruritus).*
- *Infections (abscess, skin infection).*

Other adverse events (hematoma, bruise, skin discoloration/Tyndall effect, poor filling effectiveness or poor filling effect, ecchymosis, migration, pain).

The healthcare professional must ensure that the patient notifies them of any undesirable effects.

Treatment of AE is also given in IFU:

- *Vascular complications (ischemia, necrosis, loss of vision, embolism, paralysis...) can be treated by: oxygen therapy, antibiotics, analgesics, non-steroidal anti-inflammatory drugs (NSAID).*
- *Systemic and local allergic reactions (itching sensation, Quincke edema/angioedema…) can be treated by: antihistamines and corticosteroids, steroids, and hospitalization in case of angioedema/Quincke edema.*
- *Inflammatory reactions (swelling, erythema, pain, fever, local reaction-induration, nodule, granuloma, skin inflammation…) can be treated by: analgesics, NSAIDs, steroids, antibiotics and hyaluronidase.*
- *Infections (abscess…) can be treated by: antibiotics, analgesics, NSAIDs and surgical intervention.*

Other adverse effects:

- *Bruise, hematoma and ecchymosis can be treated with arnica and local cold compress.*
- *Skin discoloration/Tyndall effect can be treated with hyaluronidase or massage of the involved zone.*

The prolonged use of any medication in treatment of adverse events has to be carefully assessed, since this may carry a risk for the patient.

4.2 Warnings and precautions

Common warnings to All ART FILLER variants	Specific warnings
- Do not inject into blood vessels, bones, tendons, ligaments or beauty spots. - Unintentional injection of soft tissue fillers into blood vessels in the face can result in rare, but serious side effects such as embolization which can cause vision impairment, blindness, stroke and damage and/or skin and underlying facial structures necrosis. These rare cases of blood vessels embolization are mostly reported in glabella, in and around the nose, forehead, and periorbital region. - Check the expiry date. - Do not use if the packaging is opened or damaged. - Check the integrity of the sterile barrier immediately prior to using the product. - Do not use a syringe with opened or shifted tip cap within the blister. - Do not re-use vial, needles and syringes for more than one patient. - The re-use of a product bears a risk (e.g. cross-contamination) for the patient. - Do not re-sterilize. - Dispose of the syringe and the remaining product after use. - After use, the needles must be thrown away in a suitable safe container. Refer to the guidelines in force for their disposal. - Never try to straighten a bent needle. Dispose of it and replace it. - Do not inject excessive volume, it can potentially lead to side effects.	**ART FILLER** Fine Lines is not indicated for injections other than intradermal injections. **ART FILLER Eyes** not indicated for injections other than intradermal injections. **ART FILLER Universal** is not indicated for areas other than intradermal or subdermal areas and the mucous membrane of the lips. **ART FILLER Lips soft** is not indicated for areas other than intradermal areas and the mucous membrane of the lips. **ART FILLER Lips** is not indicated for areas other than intradermal areas and the mucous membrane of the lips. **ART FILLER Volume** is not indicated for injections other than subcutaneous, supraperiosteal or deep dermis injections. The technique and the depth of injection vary according to the treatment area.

Precautions prior to use:

- There are no clinical data available in terms of efficacy and tolerance of the (ART FILLER variant) injections for an area that has already been treated with another “permanent” (non resorbable) filling product.
- The healthcare professionals must decide about the indication on a case by case basis according to the nature of the allergy and (s)he must specifically monitor patients who present a risk. In particular (s)he may decide to offer a double test or adapted preventive treatment prior to any injection.
- (ART FILLER variant) must be used with precaution in patients with cardiac conduction conditions.
- (ART FILLER variant) must be used with a great deal of precaution in patients suffering from hepatocellular insufficiency with coagulation disorders as well as patients receiving treatment with medicinal products that reduce or inhibit hepatic metabolism, which are prone to result in coagulation disorders.
- (ART FILLER variant) must be used with special care in patients with chronic herpes labialis.

- Patients must receive the following advice:
    - Avoid taking aspirin and vitamin C and/or vitamin E in high doses the week prior to the injection.
    - Patient receiving anticoagulant treatment must be warned of the increased risk of bruising and bleeding during injection.
    - Do not apply any make-up at all for 12 hours after the injection.
    - Avoid exposure to extreme temperatures (extreme cold, sauna, steam room) as well as prolonged sun exposure or ultraviolet light for 2 weeks following the injection.
- If the needle is obstructed, do not increase the pressure on the tip of the plunger. Stop the injection and use a new needle.
- Healthcare professionals are reminded to bear in mind that this product contains lidocaine and they must take this into account.
- Lidocaine should be used with caution in patients receiving other local anaesthetics or other agents structurally related to amide -type local anaesthetics such as certain anti-arrhythmic medication, since the systemic toxic effects can be additive.
- Lidocaine should be used with caution in patients receiving a medical treatment, the patient must refer to the healthcare professional to evaluate the possible interaction with lidocaine.

There are no clinical data available in terms of efficacy and tolerance for Fitzpatrick phototypes V and VI. (All variants).

Hyaluronic acid is incompatible with quaternary ammonium compounds, such as benzalkonium chloride solutions. This is why ART FILLER (all variants) must never come into contact with medical and surgical instruments treated with this type of product.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

No FSCA, No FSN

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)

5.1 Summary of clinical data related to equivalent device, if applicable

No equivalence with competitor products claimed as clinical investigations and marketing experience are available for all variants of the ART FILLER range.

Equivalence between following ART FILLER variants is demonstrated:

- **ART FILLER Lips Soft** is equivalent to **ART FILLER Universal**, sole differences are volume of gel in the syringe (1ml versus 1.2 ml/syringe for UNIVERSAL) and type of needle provided (30G½" versus 27G½").
- **ART FILLER Eyes** is equivalent to **ART FILLER Fine Lines**

5.2 Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

ARTFILLER 1 (AF1), conducted to evaluate safety and efficacy of ART FILLER before initial CE-marking according to Directive 93/42EEC, results were assessed for CE-marking, is a multicenter, prospective, comparative study (split-face design), with blind evaluation of long-term efficacy and safety of **ART FILLER Universal** in the nasolabial folds and **ART FILLER Fine Lines crow's feet**. The aim of this study was to document the non-inferiority of the two variants in terms of their ability to fill moderate and deep wrinkles and superficial

wrinkles, respectively, compared to a product that technically is of the same type and considered as a reference. Concomitantly, this study seeks to verify that local and delayed-onset tolerability of the products is also close to or similar to that known for hyaluronic acid filler agents. This study was conducted in 2 phases : a first phase for 6 months and a second optional phase of 12 months.

The performance of **ART FILLER Universal** and **ART FILLER Fine Lines**, were maintained until at least D180 respectively on nasolabial folds and crow's feet.

Overall, local tolerability of ART FILLER devices did not present any particular difference compared to reference devices. Neither serious adverse events nor unexpected adverse event possibly related to studied devices were detected. Intensity of events was noted as slight in most cases. All detected events are routinely seen when using HA filling procedures to correct facial wrinkles. Incidence of these local, expected and being events were not statistically different between **ART FILLER** variant and Control. High Frequency Dermal Echography was realized at follow-up visits, D30-45, D90 and D180, no inflammatory nodules were detected, allowing to eliminate risk of occurrence of granuloma for subjects treated in this clinical study. ART FILLER safety profile did not show any difference with reference products and data published in literature and no unanticipated risk was identified during this study.

5.3 Summary of clinical data from other sources, if applicable

Not applicable

5.4 An overall summary of the clinical performance and safety

Clinical performance of ART FILLER devices was evaluated through several clinical investigations using whenever possible randomized protocol (split-face), one pre-CE mark (**AF1** – see 5.2) and the others are Post Market Clinical Follow-up (PMCF) studies conducted after initial CE mark according to Directive 93/42EEC. Several ART FILLER variants injected on different zones may be evaluated in a clinical investigation as shown on the below table.

	AF1[1]	AF2[2]	AF3[3]	AF4[4]	AF5[5]	FEM1[6]	Zones
ART FILLER Fine Lines*							Crow's feet – Forehead - Upper lip- Cheek folds - Tear trough - Face combined with NCTF® 135HA
ART FILLER Lips							Lips volume - Very deep Nasolabial folds alone or with marionette lines
ART FILLER Universal**							Nasolabial folds alone or with marionette lines - Lips volume – Nose – Midface - Cheek folds- Face combined with NCTF® 135HA
ART FILLER Volume							temples, mid-face, chin and jawline

* Applicable to equivalent device ART FILLER Eyes
** Applicable to equivalent device ART FILLER Lips Soft

1. **ARTFiller 1,** a multicenter, prospective, comparative study (split-face design), with blind evaluation of long-term efficacy of the two hyaluronic acid filler devices for wrinkles **ART FILLER® Universal** (previously called Filorga Universal Filler) injected in the **nasolabial fold (NL)** versus Juvederm® Ultra 3 and **ART FILLER® Fine Lines** (previously called Filorga Fine Lines Filler) injected in the **crow's feet (CF)** versus First Lines Pure Sense. This study was conducted in 2 phases : a first phase for 6 months and a second optional phase of 12 months.
2. **ARTFiller 2**, a multicenter, prospective, non-comparative study, of long-term efficacy of the two hyaluronic acid filler devices for wrinkles **ART FILLER® Volume** (injected in the **midface** and **ART FILLER® Lips** injected in the **upper and lower lips**. This study was conducted in 2 phases : a first phase for 12 months and a second optional phase of 6 months only for patients injected by at **least ART FILLER Volume.**

3. **ARTFiller 3,** a multicenter, prospective, comparative study (split-face design), with blind evaluation of long-term efficacy of the hyaluronic acid filler device **ART FILLER® Volume** injected in the **midface, temple and jawline** versus Juvederm® Voluma and non-comparative for the **chin** were only **ART FILLER® Volume** was injected.
4. **ARTFiller 4,** a multicenter, prospective, non-comparative study, of long-term efficacy of three hyaluronic acid filler devices **ART FILLER® Fine Lines** injected in the **forehead wrinkles, upper lip wrinkles, cheek folds** and **crow's feet wrinkles**, **ART FILLER® Universal** injected in the **lips** and **nasolabial folds alone or with marionette lines**, and **ART FILLER® Lips** injected in the **lips** and **very deep nasolabial folds alone or with marionette lines**.
5. **ARTFiller 5,** a prospective, comparative, non- randomized, multicenter study of longevity, volume-correcting efficacy and safety of **ART FILLER® Fine Lines** in tear trough, **ART FILLER® Universal** in nose, midface, and cheek folds, **ART FILLER® Lips** in lips and **ART FILLER® Volume** in temples, midface and chin.
6. **FEM1,** a multicenter, prospective, non-comparative study, of long-term efficacy of a new protocol (named Bio NutriLift) combining intradermal injection on the face of NTF135 HA with one or two hyaluronic acid filler devices: **ART FILLER® Fine Lines** alone or in combination with **ART FILLER® Universal**.

The results show that the products provide a visible and rapid improvement in the treated areas, usually within the first few weeks after injection. In most studies, between 80% and 100% of participants showed a measurable improvement of at least one grade on standard clinical aesthetic scales. The aesthetic correction was maintained for several months, and in some cases up to 18 months, depending on the product and the treated area. In comparative studies, the outcomes were comparable to those of reference products.

Clinical visual photographic scales showed significant improvement for filling of :

- forehead, upper lip, cheek folds and crow's feet with **ART FILLER Fine Lines**
- crow's feet and infraorbital (tear trough) with **ART FILLER Eyes (**identical to **ART FILLER Fine Lines)**
- for lips volume and nasolabial folds with or without marionette lines with **ART FILLER Lips**
- nasolabial folds with or without marionette lines, lips volume, cheek folds, nose and mid-face with **ART FILLER Universal**
- Lips volume and nasolabial folds with or without marionette lines with **ART FILLER Lips Soft**
- temples, mid-face, chin and jawline with **ART FILLER Volume**

The lifetime after implantation of the **ART FILLER** devices was determined through the above clinical studies and may be summarized as follows:

		Clinically significant improvement after injection (% of subjects)		
	Zone	**6 months**	**12 months**	**18 months**
ART FILLER Fine Lines **ART FILLER** Eyes	Crow's feet wrinkles	80 – 88%	70 – 74 %	44 – 57 %
	Forehead wrinkles	83%	70%	66%
	Upper lip wrinkles	93%	85%	88%
	Cheek folds	84%	73 %	56 %
ART FILLER Lips	Nasolabial folds	100%	100%	91%
	Marionette lines	100%	94%	88%
	Lips volume	48(**) - 95%	40(**) - 77%	33(**) - 67%
ART FILLER Universal **ART FILLER** Lips Soft	Nasolabial folds	94 - 100%	83 - 100%	74 - 100%
	Marionette lines	95%	100%	82%
	Lips volume	66%	46%	32%
ART FILLER Volume	Medio-facial restoration	80 – 95%	57 - 66%	37 - 55%
	Temple hollows	97%	79%	62%
	Jawlines	74%	61%	53%
	Chin volume	82%	76%	73%

(**) Results related to a maximum injected volume of 1ml without any touch-up nor reinjection.

ART FILLER safety profile does not show any difference compared to the reference products and data published in literature, most of detected events were noted as slight in most cases and are routinely seen when using HA filling procedures to correct facial wrinkles and no unanticipated risk was identified during the

different studies. No serious adverse event related to the devices was reported in the different clinical investigations.

In addition, the combined use of ART FILLER Fine Lines and/or Universal and NCTF 135HA in a specific protocol did not show an impact on safety, most reported reactions remained of light intensity and corresponded to usual adverse effects reported with such treatments (ecchymosis, swelling, erythema, hematoma, oedema).

5.5 Ongoing or planned post-market clinical follow-up

Study number/ Reference	AF 5bis	
Objectives and indications	To demonstrate objectively the effectiveness of the studied device between baseline and D21 (or D42 for subjects with touch-up injection into the tear trough) on the decrease of the Universal Aesthetic Clinical Score (UACS) evaluated by the investigator in front of the subjects on Tear trough	To measure the improvement of restoration of following zones separately after the injection of Art Filler Fine Lines® (in the Crow's feet), Art Filler Universal® (in the Nasolabial folds), Art Filler Lips® (in the Lips and in the deep Nasolabial) and Art Filler Volume® (in the Temples, the Midface and the Jawline) from baseline (D0) to D21 and other time points till 18 months according to a Universal Aesthetic Scale
Study design / Nº of centers / FPI / Study zones	Study design: 18-months non comparative prospective monocenter Spain Number of subjects: 60 Tear trough	Study design: 18 month prospective, non-randomized, multicenter. Centers: 10 Number of subjects: 210 Study zones: - Crow's feet - Nasolabial folds
Safety assessments	Adverse events Local tolerability	Adverse events Local tolerability
Efficacy assessments (GAIS, SSQ, skin elasticity, skin hydration and skin structure/surface roughness…)	- Universal Aesthetic Scale (UAS) (0 to 5) - Allergan Infraorbital Hollows Scale - Allergan Temple Hollowing Scale - Subject Global Aesthetic Improvement Scale (SGAIS) - Investigator Global Aesthetic Improvement Scale (IGAIS) - Standardized Photographs - Rosenberg Self-esteem Scale (RSE)	- Universal Aesthetic scales (UAS) - Bazin Crow's Feet Scaling - MEDICIS lip fullness Scale (MLFS) - Bazin Nasolabial Folds - Medicis Midface Volume Scale - Allergan temple hollowing scale - Narins and Carruthers Jawline scale - Subject Global Aesthetic Improvement Scale (SGAIS) - Investigator Global Aesthetic Improvement Scale (IGAIS) - Rosenberg Self-esteem Scale (RSE) - Standardized Photographs
Estimated final report date	Q3 2026	Q3 2027

6. Possible diagnostic or therapeutic alternatives

ART FILLERS are devices without an intended medical purpose, they are used for aesthetic purposes, it is important to understand patients' wishes and to orientate them to the treatment modality that will give the most satisfying results before choosing the strategy for the individual case.
Dermal fillers are well known as being effective in reducing wrinkles , filler materials can be classified based on the extent and speed of degradation temporary (degradable), semi-permanent and permanent (not degradable). Examples for temporary fillers include hyaluronic acid, polylactic acid, poly-L-lactic acid, and collagen. Permanent or semi-permanent fillers may contain polymethylmethacrylate, polyacrylamide hydrogels, or polyalkylimide or calcium- hydroxyapatite. Each type of device may have its advantages and disadvantages for the individual consumer so that different fillers cannot be regarded as interchangeable "alternatives" in each case.

As evident from the state-of-the-art literature, the use of temporary HA dermal fillers, due to their favourable safety profile, is preferred in clinical practice, while other alternative modalities, such as permanent and semi-permanent dermal fillers are outdated. Products with a longer duration of effect carry an inherently higher risk of complication, as their adverse effects are longer lasting and more difficult to manage. Another disadvantage is the lack of reversing agents such as hyaluronidase for hyaluronic acid. Due to their favourable benefit/risk profile compared to alternative treatment approaches, HA-based temporary fillers are currently the most popular and most frequently used devices for dermal filling worldwide, they provide a safe and reversible option with temporary results.
Several other minimally invasive cosmetic procedures such as botulinum toxin, laser resurfacing, mechanical resurfacing, dermabrasion and chemical peels are available and decision to use one or another technique has to be taken by the healthcare professional considering the patient profile

7. Suggested profile and training for users

These products must only be administrated by trained healthcare professionals who are qualified by education or accredited in accordance with national law and trained in injection techniques.

8. Reference to any harmonised standards and CS applied

The products are compliant with harmonized standards and common specifications applicable to Art Filler.
“Commission Implementing Regulation (EU) 2022/2346 of 1 December 2022 laying down common specifications for the groups of products without an intended medical purpose listed in Annex XVI to Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices” and more specifically by Annex IV laying down common specifications for *substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, excluding those for tattooing*, as specified in Section 1 of that Annex.”

The following harmonized standards are fully applied: EN ISO 13485:2016/A11:2021, EN ISO 13485 2016, EN 285+A1 2021, EN ISO 11737-1 2018, EN ISO 11737-1/A1 2021, EN ISO 11607-1/A1 2023, EN ISO 11607-2/A1 2023, EN ISO 14971 2019, EN ISO 14971/A11 2021, EN ISO 15223-1 2021, EN ISO 10993-9 2021, EN ISO 10993-10 2023, EN ISO 10993-12 2021, EN ISO 10993-17 2023, EN ISO 10993-18 /A1 2023, EN ISO 10993-23 2021

AF1 **ARTFiller 1,** a multicenter, prospective, comparative study (split-face design), with blind evaluation of long-term efficacy of the two hyaluronic acid filler devices for wrinkles **ART FILLER® Universal** (previously called Filorga Universal Filler) injected in the **nasolabial fold (NL)** versus Juvederm® Ultra 3 and **ART FILLER® Fine Lines** (previously called Filorga Fine Lines Filler) injected in the **crow's feet (CF)** versus First Lines Pure Sense. This study was conducted in 2 phases : a first phase for 6 months and a second optional phase of 12 months.

Performance of ART FILLER Fine Lines in crow's feet and fine lines
Criteria for success: a decrease of at least 1 grade on the Lemperle score
During Phase 1 (comparative 6-months) , a decrease of at least 1 grade on the Lemperle score was reported at D30 in 95.1% and 93.4% of subjects for Fill-Med and control treatments, respectively
During Phase 2 (non-comparative) 12 months further follow-up, compared to baseline value,

- Mean Lemperle CF score decreased on average by -0.61 ± 0.71
- 48.4% (30 out of 62) of CF areas have still a one point decrease.

Longevity of Art Filler FINE LINES without reinjection. A decrease of at least 1 grade on the Lemperle Crow's feet wrinkles score after injection of Art Filler Fine Lines was observed on:

- 30 days or 3 months after injection: all the patients
- 6 months or 9 months after injection: 80% of the patients (N=8 out of 10). 90% with Teosyal PureSense
- 12 months after injection: 70% of the patients (N=7 out of 10). 70% with Teosyal PureSense
- 18 months after injection: 44% of the patients (N=4 out of 9). 56% with Teosyal PureSense

Performance of ART FILLER Universal in nasolabial folds
Criteria for success: A decrease of at least 1 grade on the Lemperle score
During Phase 1 (comparative 6-months) a one-point decrease in Lemperle score was noted in all cases (100% success rate for Fill-Med and Control devices) at D30.
During Phase 2 (non-comparative) 12 months further follow-up

- Changes in nasolabial folds are more substantial with a mean decrease of 2.1 ± 0.73
- 98.4% of NL Folds (61 out of 62) are still meeting the predefined success criterion of one point decrease compared to baseline.

Longevity of Art Filler Universal without reinjection versus Juvéderm Ultra 3. A decrease of at least 1 grade on the Lemperle Nasolabial score was observed:

- 30 days or 3 months after injection: all the patients (same results with Juvéderm Ultra 3)
- 6 months, 9 months, or 12 months after injection: all the patients (same results with Juvéderm Ultra 3)

18 months after injection: all the patients (N=9 out of 9 and 8 out of 9 / 89 % of the patients injected with Juvéderm Ultra 3)

Safety
No serious adverse event was reported
Most events were mild and none was unexpected.
Redness, swelling and pain at palpation were the most frequently reported items.
No relevant difference between treatments was detected.
Erosions were noticed at the crow's feet on both sides (ART FILLER Fine lines and Control) at 72h, at D14, no erosion was observed.
No inflammatory nodules for 18 months post-injection, confirmed by high frequency dermal ultrasound.

	All Adverse Events reported D0 to D45		Adverse Event according to involved treatment							
			Both		Control		Fill-Med		Total	
	N	%	N	%	N	%	N	%	N	%
Bruise	16	25,4%	1	4,5%	6	46,2%	7	41,2%	14	26,9%
Edema	13	20,6%	5	22,7%	2	15,4%	4	23,5%	11	21,2%
Hematoma	6	9,5%	3	13,6%	2	15,4%	1	5,9%	6	11,5%
Pain	6	9,5%	3	13,6%	0	,0%	2	11,8%	5	9,6%
Skin heterogeneity at palpation	5	7,9%	2	9,1%	2	15,4%	1	5,9%	5	9,6%
Erythema	5	7,9%	3	13,6%	0	,0%	1	5,9%	4	7,7%
Dysesthesia	1	1,6%	0	,0%	1	7,7%	0	,0%	1	1,9%
Erosion	2	3,2%	2	9,1%	0	,0%	0	,0%	2	3,8%
Toothache	2	3,2%	2	9,1%	0	,0%	0	,0%	2	3,8%
Malaise	2	3,2%								
Headache	1	1,6%								
Nausea	1	1,6%								
Pruritus	1	1,6%	0	,0%	0	,0%	1	5,9%	1	1,9%
Skin thickness	1	1,6%	1	4,5%	0	,0%	0	,0%	1	1,9%
Whitlow	1	1,6%								
Total	63	100,0%	22	100,0%	13	100,0%	17	100,0%	52	100,0%

		Treatment							
		Both		Control		Fill-Med		Total	
		N	%	N	%	N	%	N	%
Intensity	Slight	23	85,2%	8	72,7%	7	41,2%	38	69,1%
	Moderate	4	14,8%	3	27,3%	7	41,2%	14	25,5%
	Severe	0	,0%	0	,0%	3	17,6%	3	5,5%
	Total	27	100,0%	11	100,0%	17	100,0%	55	100,0%
Duration	Transitory	21	77,8%	9	81,8%	10	71,4%	40	76,9%
	Persistent	6	22,2%	2	18,2%	4	28,6%	12	23,1%
	Total	27	100,0%	11	100,0%	14	100,0%	52	100,0%
Causality	Certain	24	88,9%	10	90,9%	17	100,0%	51	92,7%
	Possible	2	7,4%	1	9,1%	0	,0%	3	5,5%
	Excluded	1	3,7%	0	,0%	0	,0%	1	1,8%
	Total	27	100,0%	11	100,0%	17	100,0%	55	100,0%

AF2 **ARTFiller 2**, a multicenter, prospective, non-comparative study, of long-term efficacy of the two hyaluronic acid filler devices for wrinkles **ART FILLER® Volume** (injected in the **midface** and **ART FILLER® Lips** injected in the **upper and lower lips**. This study was conducted in 2 phases : a first phase for 12 months and a second optional phase of 6 months only for patients injected by at **least ART FILLER Volume.**

AF2 **ART FILLER Lips - Lips volume** **Upper and lower lips (red lips and borders)**

Performance

Criteria for success: Increase of at least 1 point of Medicis Lip Fullness Scale (MLFS) compared to baseline score

- Success obtained in 96% of subjects (N=73 patients- 141 injections), (with a lower limit of the 95% confidence interval of 92.8%).
- A significant increase from 1.7 ± 0.5 at D0 to 3.1 ± 0.7 at DOptimal (D21 or D42 depending on the retouch)

Persistence of the optimal score was reported at D180 in 76% of subjects (N=62 patients – 113 injections) and at D270 in 64% of subjects (N=45 patients for whom at least one area was not reinjected of the PP population / N=76 injections at D270

Results on GAIS: At D90, 84% of patients rated their lips fullness as improved or much or very much improved on the GAIS (N=139), 80% of patients at 6 months (N=123), 77% at D270 (N=124) and 66% at D360 (N=124).

Longevity of the volumizing effect of **Art Filler Lips** over 18 months with or without reinjection.

A decrease of at least 1 grade was observed on (with or without retouch):

- 3 weeks after injection: 94-97% of the patients (N=131 out of 139 / 119 out of 123)
- 3 months after injection: 96% of all the studied patients (N=133 out of 139) and 95% for patients without any retouch (N=117 out 123)
- 6 months after injection: 80% of all the studied patients (N=99 out of 123) and 95% for patients without any retouch (N=109 out 113)
- 9 months after injection: 82% of all the studied patients (N=102 out of 124) and 82% for patients without any retouch (N=62 out 76)
- 12 months after injection: 77% of all the studied patients (N=96 out of 124) and 77% for patients without any retouch (N=56 out 73)
- 15 months after injection: 88% of all the studied patients (N=37 out of 42) and 80% for patients without any retouch (N=12 out of 15)
- 18 months after injection: 79% of all the studied patients (N=33 out of 42) and 67% for patients without any retouch (N=10 out 15)

AF2 **ART FILLER Volume** **mid-face (bilateral)**

Performance

Criteria for success: Decrease of at least 1 point of Medicis Midface Volume Scale (MMVS) compared to baseline score.

- Success obtained for 97% of injections (N=158 injections – 79 subjects) 3 weeks after the first injection OR 6 weeks after the first injection if a touch-up at 3 weeks. (with a lower limit of the 95% confidence interval of 94.3%)
- A significant decrease from 3.2 ± 0.4 at D0 to 1.7 ± 0.6 at DOptimal (D21 or D42 depending on the retouch) has been observed.
- Persistence of optimal score at D540 was observed 22% of injections (N=66).

At D90, 84% of patients rated their midface volume as improved or much or very much improved on the GAIS (N=154), 86% at 6 months (N=140), 77% at D270 (N=144), 63% at D360 (N=141), 69% at D450 (N=70) and 68% at D540 (N=68).

Longevity of the volumizing effect of Art Filler Volume over 18 months with or without reinjection. A decrease of at least 1 grade was observed:

- 3 weeks after injection: at least 64-97% of the patients (one retouch at D21 allowed to obtain the expected efficacy on all the subjects whose efficacy was not satisfying 3 weeks later)
- 3 months after injection: 98% of the patients without any retouch (N=129 out of 131) and 100% for patients with retouch (N=25 out 25)
- 6 months after injection: 95% of the patients without any retouch (N=109 out of 115) and 100% for patients with retouch (N=25 out 25)
- 9 months after injection: 79% of the patients without any retouch (N=94 out of 119) and 84% for patients with retouch (N=21 out 25)
- 12 months after injection: 66% of the patients without any retouch (N=79 out of 119) and 64% for patients with retouch (N=16 out 25)
- 15 months after injection: 44% of the patients without any retouch (N=24 out of 54) and 50% for patients with retouch (N=8 out 16)
- 18 months after injection: 37% of the patients without any retouch (N=19 out of 51) and 47% for patients with retouch (N=7 out 15)

AF2 Safety

No Serious Adverse Event was reported.
Most frequently reported reactions in lips were swelling, sensitivity and in midface redness, sensitivity and pain.
AE related to injections reported were from mild (N=44 / 62%) to severe intensity (N=1 / 1%) in lips and mild or moderate after injection in the midface with a duration of reaction less than 2 weeks for 85% of them.

ART FILLER Lips Lips injections N=141 injection / 73 patients Number of subjects with at least one TEAE: 32 (45%)		**ART FILLER Volume** Medio-facial injections N=158 injection / 79 patients Number of subjects with at least one TEAE: 49 (47%)	
Dermatological disorders (N)		**Dermatological disorders (N)**	
Dyschromia	2	Erythema	12
Ecchymosis	1	Oedema	10
Hematoma	4	Nodule	7
Induration	2	Pain on palpation	15
Over-correction	5	Spontaneous Pain	2
Oedema	7	Pain on cold	1
Nodule	30	Burning sensations	2
Tyndall effect	3		
Pain on palpation	15		
Spontaneous Pain	1		

Most frequently reported events and longest duration (after pooling all reactions) are shown below:

Type of reaction reported by 1/3 of subjects	ART FILLER® Lips Duration after injection in **lips**	ART FILLER Volume Duration after injection in **midface**
Sensitivity / Tenderness	7 days	8 days
Swelling	5 days	5 days
Bruise	4 days	
Pain	2 days	3 days

AF3 **ARTFiller 3,** a multicenter, prospective, comparative study (split-face design), with blind evaluation of long-term efficacy of the hyaluronic acid filler device **ART FILLER® Volume** injected in the **midface, temple and jawline** versus Juvederm® Voluma and non-comparative for the **chin** were only **ART FILLER® Volume** was injected.

AF3 **ART FILLER Volume** **Midface, jawline, chin and temple**

Performance: Criteria for success: Improvement of at least 1 point according to a global Aesthetic 6-grade scale (further modified to a 7 grade-scale)

- A satisfactory result was observed on all the studied area injected with Art Filler® Volume
- A significant improvement / improvement of at least 1 grade for more than 80% of the subjects, from 90% for the jawline to 100% for the temple).

At least 74% of the subjects were satisfied of the global aesthetic improvement (Subject GAIS) 21 days after injection, and still about at least half of them were satisfied after 12 months and one third after 18 months.

Longevity: An improvement of at least 1 grade of the global score was still observed on:

- 74 to 85% of the subjects after 3 months,
- 71 to 97% after 6 months,
- 57 to 79% after 12 months and
- 53 to 72% after 18 months

Safety for all zones,
No serious adverse events
Most of reported reactions were slight pain during injection, erythema just after or irregularities at palpation and had disappeared at D21.
Adverse events related to injections reported were from mild (N=69 / 41%) to severe intensity (N=17 for N=8 patients / 10.2%).

	Midface			Jawline			Temples			Chin		
Art Filler Volume	D0 (N=56)	D21 (N=54)	D90 (N=53) and later	D0 (N=72)	D21 (N=70)	D90 (N=69) and later	D0 (N=33)	D21 (N=33)	D90 > (N=33)	D0 (N=25)	D21 (N=25)	D90 (N=25)
Erythema	6 (11%)	1 (2%)	0	5 (7%)	0	0	0	0	0	3 (12%)	0	0
Ecchymosis	1 (2%)	0	0	1 (1%)	0	0	0	0	0	0	0	0
Hematoma	1 (2%)	0	0	2 (3%)	0	0	0	0	0	0	0	0
Oedema	0	1 (2%)	1 (2%) at D90	0	0	0	0	0	0	0	0	0
Dyschromia	0	0	0	0	0	0	0	0	0	0	0	0

Irregularity at palpation	1 (2%)	5 (9%)	1 (2%) at D270	0	11 (16%)	2 (3%) at D90, 180 and 270	0	0	0	0	4 (16%)	0
Necrosis	0	0	0	0	0	0	0	0	0	0	0	0
Tyndall effect	0	0	0	0	0	0	0	0	0	0	0	0
Over-correction	0	0	1 (2%)	0	1 (1%)	0	0	0	0	0	0	0
Spontaneous pain*	10 (18%)	0	0	9 (13%)	1 (1%)	0	4 (12%)	0	0	2 (8%)	0	0
Pain at palpation**	0	1 (2%)	0	0	2 (3%)	0	1 (3%)	1 (3%)	0	0	1 (4%)	0

		Midface		Jawline		Temple		Chin		md		Total excluding the chin		Total	
Adverse event Intensity		N	%	N	%	N	%	N	%	N	%	N	%	N	%
ART FILLER	Slight	8	4.8	20	12.0	3	1.8	6	3.6	0	-	31	18.6	37	22.2
	Moderate	13	7.8	13	7.8	3	1.8	5	3.0	1	1%	29	17.4	35	21.0
	Severe	4	2.4	6	3.6	0	-	2	1.2	0	-	10	6.00	12	7.2
	TOTAL	25	15.0	39	23.4	6	3.6	13	7.8	1	0.6	70	42.0	84	50.3
Control	Slight	9	5.4	18	10.8	2	1.2	0	-	0	-	29	17.4		
	Moderate	16	9.6	18	10.8	2	1.2	0	-	0	-	36	21.6		
	Severe	0	-	2	1.2	0	-	0	-	0	-	2	1.2		
	TOTAL	25	15.0	38	22.8	4	2.4	0	-	0	-	67	40.1		
md (missing data)	Slight	0	-	1	0.6	0	-	0	-	2	1.2	1	0.60	3	1.8
	Moderate	3	1.8	1	0.6	0	-	0	-	6	3.6	4	2.40	10	6.
	Severe	0	-	2	1.2	0	-	0	-	1	0.6	2	1.20	3	1.8
	TOTAL	3	1.8	4	2.4	0	-	0	-	9	5.4	7	4.20	16	9.6

AF4 **ARTFiller 4,** a multicenter, prospective, non-comparative study, of long-term efficacy of three hyaluronic acid filler devices **ART FILLER® Fine Lines** injected in the **forehead wrinkles, upper lip wrinkles, cheek folds** and **crow's feet wrinkles**, **ART FILLER® Universal** injected in the **lips** and **nasolabial folds alone or with marionette lines**, and **ART FILLER® Lips** injected in the **lips** and **very deep nasolabial folds alone or with marionette lines**.

ART FILLER Fine Lines **Forehead wrinkles, upper lip wrinkles, cheek folds, crow's feet wrinkles**

Performance:

- A satisfactory result was observed on all the studied area injected with Art Filler Fine Lines
- A significant improvement / improvement of at least 1 grade for more than 80% of the subjects, from 89% for the upper lip to 94% for the cheek.

Longevity: An improvement of at least 1 grade of the global score (-0.5) was still observed on

- 89 to 96% of the subjects after 3 months,
- 84 to 94% after 6 months,
- 73 to 84% after 12 months and
- 56 to 88% after 18 months

best longevity was observed on the upper lip.

Safety:

AE related to injections reported were from slight (N=74 / 21%) to severe intensity (N=2 for N=8 subjects / 2%).
Most of them concerned oedema (N=49 / 26%), Hematoma (N=41 / 21%), Erythema (N=29 / 15%), irregularities at palpation (N=29 / 15%) and Pain (N=20 / 10%).
87% of local reactions (for whom information was available, N=151) had resolved within 14 days after injection.
No reactions were reported from D180 except some slight irregularity at palpation for N=3 subjects on the forehead.

	Forehead			Upper lips			Cheeks			Crows 'feet		
ART FILLER Fine Lines	D0 (N=84)	D21 (N=83)	D90 (N=81) and >	D0 (N=75)	D21 (N=75)	D90 (N=70)	D0 (N=37)	D21 (N=37)	D90 (N=37)	D0 (N=81)	D21 (N=81)	D90 (N=77)
Erythema	59 (70%)	0	0	36 (48%)	1 (1%)	0	18 (49%)	1 (3%)	0	43 (53%)	2 (2%)	0
Ecchymosis	18 (21%)	1 (1%)	0	5 (7%)	2 (3%)	0	7 (19%)	0	0	27 (33%)	1 (1%)	0
Hematoma	9 (11%)	0	0	5 (7%)	2 (3%)	0	2 (5%)	0	0	9 (11%)	0	0
Oedema	38 (45%)	0	0	33 (44%)	4 (5%)	0	5 (14%)	1 (3%)	0	29 (36%)	2 (2%)	0
Dyschromia	0	0	0	1 (1%)	0	0	0	0	0	0	0	0

Irregularity at palpation	15 (18%)	7 (8%)	5 (6%) at D90 3 (4%) at D180	2 (3%)	2 (3%)	1 (1%)	3 (8%)	3 (8%)	0	9 (11%)	1 (1%)	0
Necrosis	0	0	0	0	0	0	0	0	0	0	0	0
Tyndall effect	0	2 (2%)	0	0	0	0	0	0	0	0	0	0
Over-correction	3 (4%)	3 (4%)	0	0	0	0	0	0	0	4 (5%)	2 (2%)	0
Spontaneous pain*	40 (48%)	2 (2%)	0	35(47%)	1 (1%)	0	14 (38%)	0	0	23 (28%)	0	0
Pain at palpation**	7 (8%)	1 (1%)	0	5 (7%)	0	0	4 (11%)	0	0	3 (4%)	1 (1%)	0

Adverse event Intensity	Forehead		Upper lip		Jawline		Crow's feet		md		na		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Slight	26	7%	9	3%	4	1%	21	6%	13	4%	1	0%	74	21%
Moderate	15	8%	10	6%	7	4%	13	7%	26	15%	3	2%	74	42%
Important	16	13%	11	9%	4	3%	3	3%	5	4%	3	3%	42	36%
Severe	0	-	0	-	0	-	0	-	0	-	2	2%	2	2%
TOTAL	57	29%	30	17%	15	8%	37	16%	44	22%	9	7%	192	100%

ART FILLER Universal Lips volume , nasolabial folds alone or with marionette wrinkles

Performance:

- Immediate clinical results (3 weeks after injection) revealed a satisfactory result on all the studied area
- a significant improvement "improvement of at least 1 grade" observed for more than 80% of the subjects, from 86% for the lips to 96% for the marionette lines.
- At least 88% of the subjects were satisfied of the global aesthetic improvement 21 days after injection, at least 63% after 12 months and 49% after 18 months.

Longevity: An improvement of at least 1 grade of the global score (delta of 0.5 point) was still observed on

- 82 to 98% of the subjects after 3 months,
- 69 to 94% after 6 months,
- 45 to 95% after 12 months and,
- 32 to 82% after 18 months.

Best longevity was observed for Marionette lines then Nasolabial folds

Safety:

Most of reported reactions were slight pain during injection, erythema or oedema or pain just after injection.
Most of them had disappeared at D21. No reactions were still reported after except few slight irregularities at palpation or erythema.
Adverse events related to injections reported were from slight (N=46 / 18%) to severe intensity (N=1 / 1%).
Most of local reactions (82% of adverse events for whom information was available (N=99)) were resolved within 14 days after injection.

	Lips			Nasolabial folds			Marionette lines		
ART FILLER Universal	D0 (N=50)	D21 (N=50)	D90 (N=50)	D0 (N=130)	D21 (N=129)	D90 (N=123)	D0 (N=62)	D21 (N=60)	D90 (N=59)
Erythema	9 (18%)	3 (6%)	0	44 (34%)	3 (2%)	0	27 (44%)	0	0
Ecchymosis	4 (8%)	4 (8%)	0	7 (5%)	4 (3%)	0	5 (8%)	0	0
Hematoma	6 (12%)	0	0	3 (2%)	0	0	3 (5%)	0	0
Oedema	18 (36%)	4 (8%)	0	26 (20%)	0	0	22 (35%)	2 (3%)	0
Dyschromia	0	0	0	0	0	0	0	0	0
Irregularity at palpation	0	5 (10%)	2 (4%) at D90 1 (2%) at D180	1 (1%)	7 (5%)	1 (1%) at D90 and 450	1 (2%)	5 (8%)	0 at D90 1 (2%) at D270
Necrosis	0	0	0	0	0	0	0	0	0
Tyndall effect	0	0	0	0	0	0	0	0	0
Over-correction	0	0	0	0	1 (1%)	0	0	0	0
Spontaneous pain*	28 (56%)	3 (6%)	0	44 (34%)	4 (3%)	0	26 (42%)	0	0
Pain at palpation**	1 (2%)	1 (2%)	0	3 (2%)	2 (2%)	0	2 (3%)	1 (2%)	0

Adverse event Intensity	Lips		Nasolabial folds		Marionette Lines		md		na		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
Slight	9	4%	10	4%	3	1%	23	9%	1	0%	46	18%
Moderate	10	8%	8	6%	5	4%	17	13%	2	2%	42	33%
Important	8	9%	16	19%	10	12%	5	6%	1	1%	41	48%
Severe	0	-	0	-	0	-	0	-	1	2%	1	2%
TOTAL	27	21%	34	29%	18	17%	45	28%	5	5%	130	100%

ART FILLER Lips **Lips volume, very deep nasolabial folds alone or with marionette lines**

Performance:

- A satisfactory result was observed on nasolabial folds and marionette lines injected with Art Filler Lips
- A significant improvement / improvement of at least 1 grade for more than 94% of the subjects.

- Results from lips were slightly lower with a success rate of about 73% 21 days after injection

Longevity: An improvement of at least 1 grade of the global score (delta of 0.5) was still observed on these areas for

- at least 95% of the subjects after 3 months,
- 100% after 6 months or 12 months and
- 88% after 18 months (for subjects whose scores were available)

The best longevity was observed on the nasolabial folds).

For lips volume, a significant improvement was observed until 15 months with an improvement of at least 1 grade on 25% of the subjects.

Subjects were globally satisfied by the treatment with at least 88% of the subjects that were satisfied of the global aesthetic improvement 21 days after injection, whatever the concerned area, at least 50% after 12 months and 30% after 18 months.

Safety:
Most of reported reactions were slight pain during injection, erythema or oedema or pain just after injection.
Adverse events related to injections reported were from slight (N=20 / 14%) to severe intensity (N=1 / 3%).
Most of them had disappeared at D21.
Most of local reactions (75% of adverse events for whom information was available (N=38)) were resolved within 14 days after injection.
No reactions were still reported after except few slight irregularities at palpation or over-correction.

	Lips			Nasolabial folds			Marionette lines		
ART FILLER Lips	D0 (N=34)	D21 (N=34)	D90 (N=32) and later	D0 (N=67)	D21 (N=65)	D90 (N=62)	D0 (N=49)	D21 (N=49)	D90 (N=44)
Erythema	8 (24%)	1 (3%)	0	30 (45%)	2 (3%)	0	16 (33%)	3 (6%)	0
Ecchymosis	0	0	0	6 (9%)	1 (2%)	0	6 (12%)	3 (6%)	0
Hematoma	4 (12%)	0	0	3 (4%)	0	0	0	1 (2%)	0
Oedema	20 (59%)	4 (12%)	0	15 (22%)	1 (2%)	0	10 (20%)	1 (2%)	0
Dyschromia	0	1 (3%)	0	0	0	0	0	0	0
Irregularity at palpation	2 (6%)	7 (21%)	3 (9%) at D90 and D180	0	1 (2%)	1 (2%) at D360	0	0	1 (2%) at D180
Necrosis	0	0	0	0	0	0	0	0	0
Tyndall effect	0	0	0	0	1 (2%)	0	0	0	0
Over-correction	1 (3%)	1 (3%)	1 (3%)	0	0	0	0	0	0

Spontaneous pain*	15 (44%)	1 (3%)	0	24 (36%)	1 (2%)	0	14 (29%)	3 (6%)	0
Pain at palpation**	0	1 (3%)	0	2 (3%)	1 (2%)	0	0	0	0

Adverse event	Lips		Nasolabial folds		Marionette Lines		md		na		Total	
Intensity	N	%	N	%	N	%	N	%	N	%	N	%
Slight	4	3%	9	6%	3	2%	4	3%	-	-	20	13.51%
Moderate	1	1%	11	15%	8	11%	9	12%	-	-	29	39.19%
Important	4	8%	7	14%	4	8%	5	10%	2	4%	22	44.59%
Severe	0	-	0	-	0	-	0	-	1	3%	1	2.70%
TOTAL	9	12%	27	35%	15	21%	18	25%	3	7%	72	100%

AF5	**ARTFiller 5,** a prospective, comparative, non- randomized, multicenter study of longevity, volume-correcting efficacy and safety of **ART FILLER® Fine Lines** in tear trough, **ART FILLER® Universal** in nose, midface, and cheek folds, **ART FILLER® Lips** in lips and **ART FILLER® Volume** in temples, midface and chin.

AF5 **ART FILLER Fine Lines** **Tear trough (55 subjects)**

Performance: (98.18% of subjects – 54/55 injected with cannula)

- Significant evolution (p<0.0001) of the clinical score was observed, with a satisfactory correction on 98% of the subjects after one or two injections.
- Significant decrease of the Universal Clinical score was still observed on patients injected with either one or two injections of Art Filler Fine Lines in the tear trough, with a satisfactory correction on at least 86% of the patients at D180.
- % in success on evolution of the Allergan Infra-Orbital Score was 100% at D28 and 98% at D90 and D180
- Satisfaction of investigators and subjects was respectively 98% at D28, 100% at D49, 98% at D90 and 96% at D180 and 92% at D28, 89% at D49, 88% at D90 and 82% at D180

Longevity:

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 86% of patients with only one injection and 90% including patients with second injection or touch up.
- Persistence of effect on Allergan Infra-Orbital Score was 86% at D90 and 80% at D180

Safety:

No Serious Adverse event related to the medical device or procedure
N=62 adverse Events were reported on 34 patients. Within these Adverse Events, N=48 could be related to the medical device or the procedure (23 to the medical device), that corresponds to 28 patients (50.8 % of the patients injected).
Most of Adverse Events concern Hematoma, swelling/edema or ecchymosis or erythema.
Most of Adverse Events were of mild (79.2%) to moderate intensity (18.8%) and last less than 3 days (duration of 3.4 ± 4.8 / max of 19 days).

ART FILLER Fine Lines	All related to the medical device and/or the procedure								Device only	Procedure only
AE in Tear trough	N. subjects (%)	N. AE (%)	1-3 days	4-7 days	8-14 days	15-30 days	>30 days	ND**	N. AE (%)	N. AE (%)
Hematoma	16 (29.1%)	18 38.3%	19.20%	14.9%	0	0	0	4.3%		18 38.3%
Swelling/ Edema	14 25.5%	15 31.9%	6.40%	2.1%	0	2.10%	0	21.3%	15 31.9%	15 31.9%
Ecchymosis	7 12.7%	8 17.0%	12.80%	0	0	4.30%	0	0	8 17.0%	8 17.0%
Erythema	4 7.3%	4 8.5%	8.50%	0	0	0	0	0		4 8.5%

ART FILLER Universal **nose (59 subjects)**

Performance ;

- Significant evolution (p<0.0001) of the Universal Aesthetic score was observed, with a satisfactory correction on 100 % of the subjects after one or two injections
- Significant decrease of the Universal Aesthetic score was still observed on patients injected with either one or two injections, with a satisfactory correction on at least 90% of the patients at D180
- % in success on evolution of Modified Nose Treatment Goal Attainment Score was 100 % at D21 and at Dopt (D21 or D42 depending of touch up), 94% at D90 and at D180
- Satisfaction of investigators and subjects was respectively 100% at D21 and D42, 96% at D90 and 94% D180 and 91% at D21, 93% at D42, 80% at D90 and 83% at D180

Longevity of ART FILLER Universal in the nose :

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 90 % of patients with or without touch up.
- Persistence of effect on Modified Nose Treatment Goal Attainment Score was 90% at D90 and 92% at D180

Safety:

One Serious Adverse event was reported that was not related to the medical device or procedure

N=95 adverse Events were reported on 38 patients. N=67 could be related to the medical device or the procedure (47 to the medical device), that corresponds to 37 patients (62.7 % of the patients injected).

Most of them concern Erythema, Hematoma, pain or swelling/edema. were of mild (68.7%) to moderate intensity (29.9%) and last less than 10 days (duration of 8.6 ± 15.7 / max of 92 days).

ART FILLER Universal	All related to the medical device and/or the procedure								Device only	Procedure only
AE in	N. subjects (%)	N. AE (%)	1-3 days	4-7 days	8-14 days	15-30 days	>30 days	ND**	N. AE (%)	N. AE (%)
Nose										
Erythema	21 35.6%	23 34.3%	25.4%	4.5%	0	1.5%	3.0%	0	23 34.3%	0 0%
Hematoma	17 28.8%	18 26.9%	9.0%	9.0%	7.5%	1.5%	0	0	0 0%	18 26.9%
Pain	11 18.6%	11 16.4%	4.5%	9.0%	0	0	1.5%	1.5%	11 16.4%	11 16.4%
Swelling/ Edema	5 8.5%	7 7.5%	3.0%	0	0	0	3.0%	1.5%	5 7.5%	5 7.5%

ART FILLER Universal **mid-face (68 subjects)**

Performance:

- Significant evolution (p<0.0001) of the Universal Aesthetic score was observed, with a satisfactory correction on 99 % of the subjects after one or two injections
- Significant decrease of the Universal Aesthetic score was still observed on patients injected with either one or two injections, with a satisfactory correction on at least 94% of the patients at D180
- % in success on evolution of the Medicis Midface Volume Loss Clinical Score was 78% at D21, 84% at D21 or D42 depending of touch up, 84% at D90 and 76% at D180
- Satisfaction of investigators and subjects was respectively 100% at all timepoints and 97% at D21, 80% at D42, 97% at D90 and 94% at D180

Longevity:

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 94 % of patients with or without touch up.
- Persistence of effect on the Medicis Midface Volume Loss Clinical Score was 94% at D90 and 96% at D180

Safety:

One Serious Adverse event was reported that was not related to the medical device or procedure

N=65 adverse Events were reported on 33 patients. N=42 could be related to the medical device or the procedure (29 to the medical device), that corresponds to 28 patients (41.2 % of the patients injected).

Most of them concern Hematoma, swelling/edema or ecchymosis or erythema, were of mild (83.3%) to moderate intensity (16.7%) and last less than 15 days.

ART FILLER Universal	All related to the medical device and/or the procedure								Device only	Procedure only
AE in	N. subjects (%)	N. AE (%)	1-3 days	4-7 days	8-14 days	15-30 days	>30 days	ND**	N. AE (%)	N. AE (%)
Midface										
Erythema	10 14.7%	11 26.2%	2.4%	0	0	16.7%	4.8%	2.4%	11 26.2%	0 0%
Ecchymosis	8 11.8%	8 19.0%	0	7.1%	2.4%	4.8%	2.4%	2.4%	0 0%	8 19.0%
Pain	8 11.8%	8 19.0%	2.4%	9.5%	7.1%	0	0	0	8 19.0%	8 19.0%
Swelling/ Edema	7 10.3%	8 19.0%	0	7.1%	0	9.5%	0	2.4%	8 19.0%	8 19.0%
Hematoma	5 7.4%	5 11.9%	2.4%	7.1%	2.4%	0	0	0	0 0%	5 11.9%

AF5 ARTFILLER Universal **Cheek folds (46 subjects)**

Performance

- Significant evolution (p<0.0001) of the Universal Aesthetic score was observed, with a satisfactory correction on 89 % of the subjects after one or two injections
- Significant decrease of the Universal Aesthetic score was still observed on patients injected with either one or two injections of Art Filler Universal, with a satisfactory correction by 84% of patients with only one injection and 85% including patients with second injection or touch up at D180
- % in success on evolution of the Flament Clinical Score was 86% at D21, 86% at D21 or D42 depending of touch up, 95% at D90 and 92% at D180
- Satisfaction of investigators and subjects was respectively 100% at D21 and D42, 97% at D90 and 100% at D180 and 93% at D21, 100% at D42, 90% at D90 and 80% at D180

Longevity:

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 84 % of patients with or without touch up.
- Persistence of effect on the Flament Clinical Score was 82% at D90 and 88% at D180

Safety:

One Serious Adverse event was reported that was not related to the medical device or procedure

N=58 adverse Events were reported on 27 patients. N=50 could be related to the medical device or the procedure (32 to the medical device), that corresponds to 25 patients (54.3 % of the patients injected).

Most of them concern Pain, Hematoma, erythema, subcutaneous nodule, swelling/edema or ecchymosis were of mild (84.0%) to moderate intensity (11.0%) and last less than 7 days.

ART FILLER Universal	All related to the medical device and/or the procedure								Device only	Procedure only
AE in	N. subjects (%)	N. AE (%)	1-3 days	4-7 days	8-14 days	15-30 days	>30 days	ND**	N. AE (%)	N. AE (%)
Pain	11 23.9%	12 24.0%	20.0%	4.0%	0%	0%	0%	0%	12 24.0%	12 24.0%
Hematoma	11 23.9%	11 22.0%	16.0%	4.0%	0%	2.0%	0%	0%	0 0%	11 22.0%
Erythema	6 13.0%	6 12.0%	4.0%	2.0%	0%	0%	0%	6.0%	6 12.0%	0 0%
Subcutaneous nodule	6 13.0%	6 12.0%	2.0%	2.0%	2.0%	2.0%	0%	4.0%	6 12.0%	0 0%
Ecchymosis	4 8.7%	4 8.0%	0%	4.0%	4.0%	0%	0%	0%	0 0%	4 8.0%
Swelling/ Edema	3 6.5%	3 6.0%	4.0%	0%	2.0%	0%	0%	0%	3 6.0%	3 6.0%
Burning sensations	3 6.5%	3 6.0%	6.0%	0%	0%	0%	0%	0%	0 0%	3 6.0%

AF5 ART FILLER Lips ***Lips*** *(62 subjects)*

Performance:

- Significant evolution (p<0.0001) of the Universal Aesthetic score was observed, with a satisfactory correction on 74% of the subjects after one injection or after touch-up
- Significant decrease of the Universal Aesthetic score was still observed on patients injected with either one or two injections of Art Filler Lips, with a satisfactory correction on at least 64% of the patients at D180 with or without touch up
- % of success on evolution of the Medicis Lips Fullness Score was 63% at D21 and 61% at D90 and 58% at D180
- Satisfaction of investigators and subjects was respectively 100% at D21, D42, D90 and D180 and 97% at D21, 100% at D42, 96% at D90 and 90% at D180

Longevity:

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 64 % of patients with or without touch up.
- Persistence of effect on Medicis Lips Fullness Score was 95% at D90 and 95% at D180

Safety

No Serious Adverse event was reported
N=108 adverse Events were reported on 36 patients. N=98 could be related to the medical device or the procedure (70 to the medical device), that corresponds to 34 patients (54.8 % of the patients injected)
Most of them concern Swelling/edema, Pain, Subcutaneous nodule, ecchymosis, pain or swelling/edema.
Most of them were of mild (85.1%) or moderate intensity (11.9%) and last less than 530 days (duration of 22.9 ± 23.3 / max of 165 days).

ART FILLER Lips	All related to the medical device and/or the procedure								Device only	Procedure only
AE in lips	N. subjects (%)	N. AE (%)	1-3 days	4-7 days	8-14 days	15-30 days	>30 days	ND**	N. AE (%)	N. AE (%)
Swelling/Edema	31 50.0%	31 31.60%	1.0%	4.1%	1.0%	22.4%	1.0%	2.0%	31 31.6	31 31.6%
Erythema	23 37.1%	23 23.5%	1.0%	0%	1.0%	19.4%	0%	2.0%	23 23.5%	- 0%
Ecchymosis	19 30.6%	20 20.4%	0%	3.1%	1.0%	14.3%	0%	2.0%	- 0%	20 20.4%
Subcutaneous nodule	7 11.3%	7 7.1%	0%	0%	0%	1.0%	5.1%	1.0%	7 7.1%	- 0%

AF5 ART FILLER Volume **Temples (61 subjects)**

Performance:

- Significant evolution (p<0.0001) of the Universal Aesthetic score was observed, with a satisfactory correction on 92% of the subjects one injection or after touch-up
- Significant decrease of the Universal Aesthetic score was still observed on patients injected with either one or two injections, with a satisfactory correction on at least 98% of the patients at D180
- % of success on evolution of the Allergan/ Carruthers temple hollowing Score was 90% at D21, 92% at D21 or D42 depending of touch up, 98% at D90 and 98% at D180
- Satisfaction of investigators and subjects was respectively 97% at D21, 100% at D42, D90 and D180 and 86% at D21, 100% at D42, 82% at D90 and 79% at D180

Longevity:

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 98 % of patients with or without touch up.
- Persistence of effect on the Allergan/ Carruthers temple hollowing Score was 81% at D90 and 79% at D180

Safety:

No Serious Adverse event was reported

N=79 adverse Events were reported on 38 patients.

N=53 could be related to the medical device or the procedure (46 to the medical device), that corresponds to 30 patients (49.2 % of the patients injected).

Most of them concern pain, subcutaneous nodule, swelling/edema, Hematoma, or paresthesia, were of mild (69.8%) to moderate intensity (26.4%) and last less than 15 days (duration of 12.8 ± 29.0 / max of 187 days).

ART FILLER Volume	All related to the medical device and/or the procedure								Device only	Procedure only
AE in Temples	N. subjects (%)	N. AE (%)	1-3 days	4-7 days	8-14 days	15-30 days	>30 days	ND**	N. AE (%)	N. AE (%)
Pain	19 31.1%	22 41.5%	22.6%	5.7%	5.7%	5.7%	1.9%	0	22 41.5%	22 41.5%
Subcutaneous nodule	8 13.1%	9 17.0%	7.5%	0	1.9%	1.9%	5.7%	0	9 17.0%	0 0%
Swelling/ Edema	7 11.5%	7 13.2%	7.5%	0	3.8%	1 .9%	0	0	7 13.2%	7 13.2%
Hematoma	4 6.6%	4 7.5%	3.8%	1.9%	0	0	1.9%	0	0 0%	4 6.9%
Paresthesia	4 6.6%	4 7.5%	5.7%	0	1.9%	0	0	0	4 6.6%	0 0%
Ecchymosis	3 4.9%	3 5.7%	3.8%	0	1.9%	0	0	0	0 0%	3 5.7%

AF5 **ART FILLER Volume** **Midface (55 subjects)**

Performance:

- Significant evolution (p<0.0001) of the Universal Aesthetic score was observed, with a satisfactory correction on 60% of the subjects after with or without touch up
- Significant decrease of the Universal Aesthetic score was still observed on patients, with a satisfactory correction on at least 92% of the patients at D180
- % of success on evolution of the Medicis Midface Volume Loss Clinical Score was 52% at D21, 52% at D21 or D42 depending of touch up, 67% at D90 and 67% at D180
- Satisfaction of investigators and subjects was respectively 100% at D21, D42, D90 and 98% at D180 and 98% at D21, 100% at D42, 98% at D90 and 94% at D180

Longevity:

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 92 % of patients with or without touch up.
- Persistence of effect on Medicis Midface Volume Loss Clinical Score was 78% at D90 and 82% at D180

Safety

No Serious Adverse event was reported

N=102 adverse Events were reported on 43 patients. N=62 could be related to the medical device or the procedure (43 to the medical device), that corresponds to 38 patients (69.1 % of the patients injected).

Most of them concern Erythema, ecchymosis, pain or swelling/edema, were of mild (82.3%) or moderate intensity (14.5%) and persisted less than 5 days (mean duration of 3.8 ± 5.7 / max of 33 days).

ART FILLER Volume	All related to the medical device and/or the procedure								Device only	Procedure only
AE in Midface	N. subjects (%)	N. AE (%)	1-3 days	4-7 days	8-14 days	15-30 days	>30 days	ND**	N. AE (%)	N. AE (%)
Erythema	17 30.9%	17 27.4%	25.8%	0	0	0	0	1.6%	17 27.4%	0 0%
Ecchymosis	13 23.6%	13 21.0%	6.5%	8.1%	3.2%	0	0	3.2%	0 0%	13 21.0%
Pain	11 20.0%	11 17.7%	11.3%	1.6%	3.2%	0	1.6%	0	11 17.7%	11 17.7%
Swelling/ Edema	5 9.1%	5 8.1%	1.6%	6.5%	0	0	0	0	5 8.1%	5 8.1%
Subcutaneous nodule	4 7.3%	4 6.4%	1.6%%	0%	0%	1.6%	1.6%	1.6%	4 6.4%	0 0%

AF5 ART FILLER Volume **Chin (67 subjects)**

Performance:

- Significant evolution (p<0.0001) of the Universal Aesthetic score was observed, with a satisfactory correction on 70% of the subjects after one injection with or without touch up
- Significant decrease of the Universal Aesthetic score was still observed on patients with or without touch-up, with a satisfactory correction on at least 79% of the patients at D180
- % of success on evolution of the Allergan/Sykes Chin Retrusion Score was 66% at D21, 66% at D21 or D42 depending of touch up, 73% at D90 and 86% at D180
- Satisfaction of investigators and subjects was respectively 98% at D21, 100% at D42, D90 and D180and 89% at D21, 100% at D42, 93% at D90 and 88% at D180

Longevity:

- Satisfactory result on Universal Aesthetic Score maintained at 6 months by 79 % of patients with or without touch up.
- Persistence of effect on Allergan/Sykes Chin Retrusion Score was 83% at D90 and 71% at D180

Safety:

No Serious Adverse event was reported
N=106 adverse Events were reported on 41 patients.
N=60 could be related to the medical device or the procedure (47 to the medical device), that corresponds to 37 patients (55.2 % of the patients injected).
Most of them concern pain, subcutaneous nodule, or swelling/edema, were of mild (85.5%) or moderate intensity (8.3%) and last less than 7 days (duration of 4.7 ± 9.4 / max of 63 days).

ART FILLER Volume	All related to the medical device and/or the procedure								Device only	Procedure only
AE in Chin	**N. subjects (%)**	**N. AE (%)**	**1-3 days**	**4-7 days**	**8-14 days**	**15-30 days**	**>30 days**	**ND****	**N. AE (%)**	**N. AE (%)**
Erythema	25 37.3%	26 43.3%	41.7%	0%	0%	0%	0%	1.7%	26 43.3%	0 0%
Ecchymosis	10 14.9%	10 16.7%	5.0%	6.7%	3.3%	0%	0%	1.7%	0 0%	10 16.7%
Pain	8 11.9%	9 15.0%	10.0%	1.7%	1.7%	1.7%	0%	0%	9 15.0%	9 15.0%
Subcutaneous Nodule	5 7.5%	5 8.3%	0%	0%	1.7%	3.3%	3.3%	1.7%	5 8.3%	0 0%
Hematoma	3 4.5%	3 5.0%	1.7%	1.7%	1.7%	0.0%	0%	0%	0 0%	3 5.0%
Local Reaction	3 4.5%	3 5.0%	1.7%	1.7%	1.7%	0.0%	0%	0%	3 5.0%	0 0%
Nodule	3 4.5%	3 5.0%	0.0%	1.7%	0.0%	0.0%	1.7%	1.7%	3 5.0%	3 5.0%

FEM1 **FEM1,** a multicenter, prospective, non-comparative study, of long-term efficacy of a new protocol (named Bio NutriLift) combining intradermal injection on the face of NTF135 HA with one or two hyaluronic acid filler devices: **ART FILLER® Fine Lines** alone or in combination with **ART FILLER® Universal**.

Performance:

- A significant evolution of the clinical score (Bazin Cheek folds Scoring) was observed after treatment, with a success on 77% of the patient assessed at both D0 and D30.
- Best results were observed on the skin radiance.
- Satisfaction of both patients and investigators allow to summary this efficacy of a global treatment on the face better than localized scores.

Longevity:

Improvement of Bazin Cheek folds Scoring remained significant even 120 days after injections.

Safety

No serious Adverse Event was reported.

Most reported reactions corresponded to usual adverse effects reported with such treatments (ecchymosis, swelling, erythema, hematoma, oedema)**.**These events occurred on the first 7 days following injections and last about 5 ± 1 days (from 1 to 17 days).

Slight irregularity at palpation was reported in one (1) subject at D30, no reaction were still reported at D60 nor D120 among the data collected for the N=69 (D60) or N=93 (D120) subjects concerned.

Aspect of treated areas	D0 (N=99)	D30 (N=87)	D60 (N=60)	D120 (N=93)
Erythema	49 (49%)	0	0	0
Ecchymosis	28 (28%)	0	0	0
Hematoma	17 (17%)	0	0	0
Oedema	29 (29%)	0	0	0
Dyschromia	0	0	0	0
Nodule	0	0	0	0
Irregularity at palpation	0	1 (1%)	0	0
Necrosis	0	0	0	0
Tyndall effect	0	0	0	0
Others (heating sensations)	1 (1%)	0	0	0
Spontaneous Pain	2 (2%)	0	0	0
Pain at palpation	2 (2%)	0	0	0
Pruritus	1 (1%)	0	0	0

Most reported reactions remained of slight intensity

	Total		Slight		Moderate		Intense	
Signs	N	%	N	%	N	%	N	%
Ecchymosis	27	44%	11	18%	12	20%	4	7%
Swelling	11	18%	5	8%	6	10%		
Erythema	5	8%	2	3%	2	3%	1	2%
Pain	4	7%	4	7%				
Irregularities at palpation	4	7%	2	3%	1	2%	1	2%
Pain at palpation	2	3%	2	3%				
Pruritus	2	3%	2	3%				
Stinging	2	3%	2	3%				
Dryness / Eyes	1	2%	1	2%				
Stinging / Eyes	1	2%	1	2%				
Nodule	1	2%	1	2%				
Pigmentation	1	2%	1	2%				
TOTAL	61	100%	34		21		6	10%

9. Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
V01	01/12/2023	Creation of the document	☐Yes ☒No Validation language: English
V02	17/10/2024	Update of the document: - Add a summary of the safety and clinical performance of the device, intended for patients - Update of the content in section "1.6 Class of device" and "1.7 Year when the first certificate (CE) was issued covering the device" - Update of section "6. Possible diagnostic or therapeutic alternatives"	☐Yes ☒No Validation language: English
V03	20/11/2024	Update of the document to: - Correct the SSCP reference number - Add the details of harmonized standards in section 8	☐Yes ☒No Validation language: English
V04	05/02/2025	Update of the section "§1.3 Manufacturer's single registration number (SRN)" - Remove system/pack procedure	☐Yes ☒No Validation language: English
V05	15/10/2025	Update of the document to: - Add the variant ART FILLER Eyes, equivalent to ART FILLER Fine Lines - Add injection zones for ART FILLER Universal	☐Yes ☒No Validation language: English

A summary of the safety and clinical performance of the device, intended for patients, is given below.

Summary of safety and clinical performance
Patient part

Document revision: V05

Date issued: 15.10/2025

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant card or the Instructions For Use to provide information on the safe use of the device.

1. Device identification and general information

1.1 Device trade name

ART FILLER Fine Lines
ART FILLER Eyes
ART FILLER Lips Soft
ART FILLER Lips
ART FILLER Universal
ART FILLER Volume

1.2 Manufacturer; name and address

LABORATOIRES FILL-MED
38 Cours Albert 1er
75008 PARIS
France

1.3 Basic UDI-DI

Basic UDI-DI[1]: 3664948ARTFILLERWL

1.4 Year when the device was first CE-marked

CE mark according to Regulation (EU)2017/745: 2025

[1] The Basic UDI-DI is the primary identifier of a device model. It is the device identifier assigned at the level of the device unit of use. It is the main key for records in the UDI database and is referenced in relevant certificates and EU declarations of conformity.

2. Intended use of the device

2.1 Intended purpose

ART FILLER are products without an intended medical purpose, they are used for aesthetic purposes.

ART FILLER range is intended to restore changes to skin structure caused by ageing: fill in lines and creases in the facial skin and restore volume. The presence of lidocaine aims to decrease the pain sensation of the patient during treatment.

2.2 Indications and intended patient groups

ART FILLER Fine Lines is indicated to fill in fine lines, superficial lines and small skin folds of crow's feet, forehead (except glabella zone), upper lip and cheeks by means of an injection into the upper dermis..
ART FILLER Eyes is indicated to correct the periorbital ageing signs including the superficial skin wrinkles of crow's feet, and the tear trough deformity (infraorbital hollow).
ART FILLER Lips Soft is indicated to increase the volume of lip and enhance the lip outline and to fill medium and deep nasolabial folds with or without marionette lines by injection into the middle to deep dermis.
ART FILLER Lips is indicated to increase the volume and/or enhance the lip outline as well as to fill medium and deep nasolabial folds with or without marionette lines by injection into the middle to deep dermis.
ART FILLER Universal is indicated to:

- fill in medium to deep nasolabial folds with or without marionette lines, and cheeks folds by dermal or subdermal injection,
- add volume to define the shape of the nose by subdermal or dermal injection and restore volume to the midface by subdermal injection,
- increase the volume of the lip and enhance the lip outline by submucous, intradermal or subdermal injection.

ART FILLER Volume is indicated to restore volume to the mid-face, jawline, temples and chin, via subcutaneous, supraperiosteal or deep dermis injections.

ART FILLER devices are used for aesthetic purposes, as such intended patients do not present any specific pathology. According to Regulation, patients have to be older than 18 years.

2.3 Contraindications

All ART FILLER variants cannot be injected	**Specifically,**
- Into blood vessels. - Into an area where a non-absorbable filler implant has already been injected. - Do not over-correct. **And if** - You have a known hypersensitivity to hyaluronic acid, lidocaine and amide type local anesthetics. - You have a medical history of auto-immune illness[2] or receiving immunotherapy[3].	**ART FILLER Fine Lines** cannot be injected into eyelids. **ART FILLER Eyes** cannot be injected into eyelids. **ART FILLER Lips soft** cannot be injected: - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area).

[2] Condition in which the body's immune system mistakes its own healthy tissues as foreign and attacks them.
[3] Prevention or treatment of disease with substances that stimulate the immune response

All ART FILLER variants cannot be injected	**Specifically,**
- You have a medical history of severe multiple allergies or anaphylactic shock[4]. - You suffer from epilepsy that is not controlled with treatment. - You have been affected by porphyria[5]. - You have a tendency to develop hypertrophic scars. - You have a medical history of recurring sore throats related to rheumatic fever localised in the heart. - You have a medical treatment with inhibitors of cytochrome P450, due to interactions with lidocaine. - You are less than 18 years old. - You are a pregnant or breastfeeding woman. - You have inflamed areas and/or contagious skin lesions (acne, herpes, etc.). - You receive just before or after a laser treatment, a deep chemical peeling, a dermabrasion.	**ART FILLER Lips** cannot be injected: - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area). **UNIVERSAL** cannot be injected: - For injection other than intradermal injections. - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area). **VOLUME** cannot be injected: - For correction of superficial and fine lines. - Into the eye area (eyelids, crows' feet, under eye area), the glabellar area or into the lips. - Into muscles.

3. Device description

3.1 Device description and material/substances in contact with patient tissues

ART FILLER products are crosslinked viscoelastic hyaluronic acid gels of non-animal origin, slowly absorbable over time, clear, colorless, sterile, non-pyrogenic, physiological and containing 0.3% by weight of lidocaine hydrochloride for its anesthetic properties.
According to the reference, the amount of hyaluronic acid and gel volume in the syringe varies :

	Sodium hyaluronate	Lidocaine hydrochloride (% w/w)	Gel volume /syringe	Needle supplied with the device
ART FILLER Fine Lines	20 mg/g	0.3%	1.0 ml	30G½"
ART FILLER Eyes	20 mg/g	0.3%	1.0 ml	30G½"
ART FILLER Lips Soft	25 mg/g	0.3%	1.0 ml	30G½"
ART FILLER Lips	25 mg/g	0.3%	1.0 ml	27G½"
ART FILLER Universal	25 mg/g	0.3%	1.2 ml	27G½"
ART FILLER Volume	25 mg/g	0.3%	1.2 ml	27G½"

ART FILLER products are intended to be used in conjunction with sterile single-use hypodermic needles or canula (22G-25G) in accordance with their original destination.

3.2 Information about medicinal substances in the device, if any

ART FILLER devices contain 0.3% of lidocaine hydrochloride. Lidocaine is an amide local anesthetic whose effect is of rapid onset (after one minute) and of long duration (about one hour). Its mechanism of action is

[4] Serious, potentially fatal allergic reaction
[5] Group of disorders in which substances called porphyrins build up in the body, adversely affecting the skin or nervous system.

based on inhibition of nerve influx by binding of the activated molecule to a specific receptor in the sodium channel in the membrane surrounding the nerve fiber.
Lidocaine is frequently used to anesthetize the skin before invasive procedures. It is also incorporated in most of dermal fillers.
The presence of lidocaine aims to decrease the pain sensation during the injections.

3.3 Description of how the device is achieving its intended mode of action

ART FILLER devices are cross-linked HA dermal fillers. Cross-linked HA injected into the dermis hydrates the skin and mechanically fills wrinkles through a higher water-binding capacity. Because of its half-life of a few days in natural form, hyaluronic acid is chemically stabilized by a crosslinking process; the crosslinking agent most commonly used is BDDE (1, 4-butanediol diglycidyl ester). Depending on molecular weight of HA, the process and degree of crosslinking, the HA molecule thus modified comes in the form of a highly viscose, insoluble gel, usable as a dermal filler. The clinical effect and duration of presence in the skin are directly associated with the rheological characteristics of the HA gel its cohesiveness and its elasticity, the injected amount and the area treated.

3.4 Description of accessories, if any

ART FILLER devices do not include any accessories.

4. Risks and warnings

Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

4.1 How potential risks have been controlled or managed

According to LABORATOIRES FILL-MED policy, the residual risks have been identified and reduced as far as possible. The actions taken by the manufacturer to mitigate any identified risks do not impact the patient safety. The main method of mitigation is the design control of the device, validation of usability of the device to the foreseeable use errors, manufacturing controls and then the information provided to the user (labelling, instruction for use, …).

The residual risks are consistent with a high level of protection for the safety and health of persons. This is in accordance with the state of science and medical knowledge.

4.2 Remaining risks and undesirable effects

Few residual risks have been identified and evaluated

- Patient allergy, this residual risk is due to the high severity of the initial risk. The results of the clinical evaluation and the biocompatibility studies strongly demonstrate that the allergy risk during the use of ART Filler products has a very low probability to occurs.
- Concomitant presence of non-resorbable implant in implantation zone and injection of filler on a previously injected zone with other filler. ART Filler products are meant to be used by healthcare professionals, that have the appropriate skills and the adequate training for filler injection. They are aware of risks related to the injection of a filler in a zone where another implant is present.

The healthcare professional must inform you that the following potential adverse effects related to implantation of this device exist:

- Vascular complications (embolism, ischemia, necrosis, loss of vision, thrombosis, paralysis, paraesthesia, hair loss).
- Systemic and local allergic reactions (itching sensation, Quincke edema/angioedema, anaphylactic shock).
- Inflammatory reactions (burning sensation, swelling, erythema, nodule, granuloma, fibrosis, skin inflammation, fever, pain, local reaction – induration/pruritus).
- Infections (abscess, skin infection).
- Other adverse events (hematoma, bruise, skin discoloration/Tyndall effect, poor filling effectiveness or poor filling effect, ecchymosis, migration, pain).

In the event of adverse effects, contact your healthcare professional.

Experience shows that the adverse events related to **ART FILLER devices** are rare and similar to other similar devices available on the market.

	ART FILLER Fine Lines ART FILLER Eyes	**ART FILLER Universal**	**ART FILLER Lips**	**ART FILLER Lips Soft**	**ART FILLER Volume**
Swelling	≥ 0.001% and < 0.01%	≥ 0.001% and < 0.01%	≥ 0.001% and < 0.01%	≥ 0.001% and < 0.01%	≥ 0.001% and < 0.01%
Erythema[6]	≥ 0.001% and < 0.01%	≥ 0.001% and < 0.01%		< 0.001%	
Bruise[7]	< 0.001%	< 0.001%		< 0.001%	< 0.001%
Nodule[8]	≥ 0.001% and < 0.01%	< 0.001%	< 0.001%		≥ 0.001% and < 0.01%
Granuloma[9]	≥ 0.001% and < 0.01%	< 0.001%	< 0.001%		< 0.001%
Local Reaction – Induration	< 0.001%	< 0.001%	≥ 0.001% and < 0.01%	≥ 0.001% and < 0.01%	< 0.001%
Skin Inflammation		< 0.001%	< 0.001%	< 0.001%	≥ 0.001% and < 0.01%
Skin discoloration	< 0.001%				
Necrosis	< 0.001%	< 0.001%			< 0.001%
Itching sensation	< 0.001%	< 0.001%	< 0.001%		< 0.001%
Burning Sensation		< 0.001%			< 0.001%
Pain	< 0.001%	< 0.001%	≥ 0.001% and < 0.01%	< 0.001%	< 0.001%
Ischemia[10]					< 0.001%
Thrombosis		< 0.001%			< 0.001%
Allergic Reaction	< 0.001%				< 0.001%
Quincke Edema		< 0.001%			
Paresthesia11					< 0.001%
Fever	< 0.001%				

4.3 Warnings and precautions

[6] Redness
[7] Also known as a contusion, is a type of hematoma of tissue
[8] Small firm lumps, usually greater than 1 cm in diameter
[9] Aggregation of cells in response to chronic inflammation
[10] Restriction in blood supply to tissue
[11] Feeling of tingling, numbness or “pins and needles.”

Precautions before use, common to all variants	Specifically,
The use of **ART FILLER** is reserved for healthcare professionals trained in injection techniques. **ART FILLER** must be used with precaution in patients with cardiac conduction conditions. **ART FILLER** must be used with a great deal of precaution in patients suffering from hepatocellular insufficiency with coagulation disorders as well as patients receiving treatment with medicinal products that reduce or inhibit hepatic metabolism which are prone to result in coagulation disorders. **ART FILLER** must be used with special care in patients with chronic herpes labialis. Patients must receive the following advice: - Avoid taking aspirin and vitamin C and/or vitamin E in high doses the week prior to the injection. - Patient receiving anticoagulant treatment must be warned of the increased risk of bruising and bleeding during injection. - Do not apply any make-up at all for 12 hours after the injection. - Avoid exposure to extreme temperatures (extreme cold, sauna, steam room) as well as prolonged sun exposure or ultraviolet light for 2 weeks following the injection. The injection volume depends on the correction required and is under the discretion of the healthcare professional. The recommended maximal dose per year is 15 mL. It is recommended to wait until side effects are resolved (with a minimal interval of 3 weeks) between two injections.	For **ART FILLER Fine Lines;** The recommended dose per treatment site is 1 mL (except for the forehead, the recommended dose is 2 mL). A maximum of two treatment sessions per year is recommended. Possible touch-up sessions enable the sought-after degree of correction to be maintained. For **ART FILLER Eyes.** The recommended dose per treatment site is 0.5 mL for the tear trough and 1 mL for the crow's feet. A maximum of two treatment sessions per year is recommended. Possible touch-up sessions enable the sought-after degree of correction to be maintained except for the tear trough zone. For **ART FILLER Lips soft.** The recommended dose per treatment site is 1 mL per lip, the recommended dose for lips is 2 mL. A maximum of two treatment sessions per year is recommended. Possible touch-up sessions enable the sought-after degree of correction to be maintained. For **ART FILLER Lips** . The recommended dose per treatment site is 1 mL, the recommended dose for lips is 2 mL. A maximum of two treatment sessions per year is recommended. Possible touch-up sessions enable the sought-after degree of correction to be maintained. For **ART FILLER Universal .** The recommended dose per treatment site is 1.0mL per lip, 2.4 mL for the mid face and 1.2mL for the other sites. A maximum of two treatment sessions per year is recommended. Possible touch-up sessions enable the sought-after degree of correction to be maintained. For **ART FILLER Volume** . The recommended dose per treatment site is 1.2 mL for jawlines and temples and 2.4 mL for mid-face and chin. A maximum of two treatment sessions per year is recommended. Possible touch-up sessions enable the sought-after degree of correction to be maintained.

4.4 Summary of any field safety corrective action, (FSCA including FSN) if applicable

No other relevant aspects of safety are applicable. No Field Safety corrective action (FSCA)[12], no Field Safety Notice (FSN)[13] have been implemented.

5. Summary of clinical evaluation and post-market clinical follow-up

5.1 Clinical background of the device

Since launch in Europe in 1996, hyaluronic acid-based fillers have become the "gold standard" in fillers for treating wrinkles, hydrating skin, and increasing volume. During the early years of HAs patients were treated only for wrinkles, nasolabial folds, and lip augmentation, but, progressively, combined restoration of volumes became a standard procedure. The range of HAs available is wide, from slightly to highly viscous products.
As one of the main concerns of patients about injections of fillers is pain and discomfort, lidocaine hydrochloride is added to the filler to reduce pain at injection, currently most commonly used HA-based dermal fillers contain 0.3% lidocaine.

ART FILLER devices were specially designed for the correction of structural defects of the skin. These changes can be associated with aging or other causes with the goal being the reduction of wrinkles and skin folds, restoration of volume loss. Intended use of ART FILLER devices was identical to already marketed dermal fillers both in Europe and USA. The development strategy for ART FILLER range was to develop new products similar to existing and well-established products. Thus ART FILLER would have the same composition, ingredients and origin which would allow the demonstration of non-inferiority (based upon the performance and safety).

5.2 The clinical evidence for the CE-marking

As **ART FILLER** devices were put on the market in 2016, clinical evidence (performance and safety) is based on several clinical studies. Clinical performance of ART FILLER devices was evaluated through several clinical investigations, one pre-CE mark (**AF1**) and five others corresponding to Post Market Clinical Follow-up (PMCF) studies (**AF2, AF3,AF4,AF5 and FEM1**).

	AF1[1]	AF2[2]	AF3[3]	AF4[4]	AF5[5]	FEM1[6]	Zones
ART FILLER Fine Lines*							Crow's feet – Forehead - Upper lip- Cheek folds - Tear trough - Face combined with NCTF® 135HA
ART FILLER Lips							Lips volume - Very deep Nasolabial folds alone or with marionette lines
ART FILLER Universal**							Nasolabial folds alone or with marionette lines - Lips volume – Nose – Midface - Cheek folds- Face combined with NCTF® 135HA
ART FILLER Volume							temples, mid-face, chin and jawline

* Applicable to equivalent device ART FILLER Eyes
** Applicable to equivalent device ART FILLER Lips Soft

Several clinical studies have been carried out to evaluate the efficacy and safety of ART FILLER injectable fillers. The studies included adult volunteers seeking facial rejuvenation and were conducted with different variants on several injections zone as shown here above.

[12] Action is used to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market.
[13] Means of communicating a field safety corrective action (FSCA)

The results show that the products provide a visible and rapid improvement in the treated areas, usually within the first few weeks after injection. In most studies, between 80% and 100% of participants showed a measurable improvement of at least one grade on standard clinical aesthetic scales. The aesthetic correction was maintained for several months, and in some cases up to 18 months, depending on the product and the treated area. In comparative studies, the outcomes were comparable to those of reference products.

Clinical visual photographic scales showed significant improvement for filling of :

- forehead, upper lip, cheek folds and crow's feet with **ART FILLER Fine Lines**
- for lips volume and nasolabial folds with or without marionette lines with **ART FILLER Lips**
- nasolabial folds with or without marionette lines and lips volume with **ART FILLER Universal**
- Lips volume and nasolabial folds with or without marionette lines with **ART FILLER Lips Soft**
- temples, mid-face, chin and jawline with **ART FILLER Volume**

A specific study (FEM) was conducted to evaluate long-term efficacy of a new protocol (named Bio NutriLift) combining intradermal injection on the face of a biorevitalizing solution on face rejuvenation NTF135 HA with one or two hyaluronic acid filler devices: **ART FILLER® Fine Lines** alone or in combination with **ART FILLER® Universal**. A significant improvement of Bazin Cheek folds score was observed with regard to time and this improvement remained significant even 120 days after injections. Best results were observed on the skin radiance.

In terms of **durability of the effect**, the lifetime after implantation of the ART FILLER devices was determined through the above clinical studies , depending on the ART FILLER variant used and on the injection zone, the duration of the results meaning a clinically significant improvement is reported for a certain percentage of patients, for example

*For the correction of crow's feet wrinkles with **ART FILLER Fine Lines,** 80 – 88% of the patients maintained a clinically significant improvement 6 months after injection, 70 – 74 % after 12 months, and 44 – 57 % after 18 months.*

		Clinically significant improvement after injection (% of subjects)		
Product	**Injection zone**	**6 months**	**12 months**	**18 months**
ART FILLER Fine Lines **ART FILLER** Eyes	Crow's feet wrinkles	80 – 88%	70 – 74 %	44 – 57 %
	Forehead wrinkles	83%	70%	66%
	Upper lip wrinkles	93%	85%	88%
	Cheek folds	84%	73 %	56 %
ART FILLER Lips	Nasolabial folds	100%	100%	91%
	Marionette lines	100%	94%	88%
	Lips volume	48(**) - 95%	40(**) - 77%	33(**) - 67%
ART FILLER Universal **ART FILLER** Lips Soft	Nasolabial folds	94 - 100%	83 - 100%	74 - 100%
	Marionette lines	95%	100%	82%
	Lips volume	66%	46%	32%
ART FILLER Volume	Medio-facial restoration	80 – 95%	57 - 66%	37 - 55%
	Temple hollows	97%	79%	62%
	Jawlines	74%	61%	53%
	Chin volume	82%	76%	73%

(**) Results related to a maximum injected volume of 1ml without any touch-up nor reinjection.

These results demonstrate the long-lasting and stable performance of the fillers over time.

Patient satisfaction was consistently high across all studies, with around 90% of subjects being satisfied or very satisfied three weeks after treatment, more than half remained satisfied after 12 months and up to one-third still reported satisfaction after 18 months, depending on the treated area.

5.3 Safety

During clinical investigations, adverse events are collected all over the follow-up period, serious adverse events (SAE) if any and local events are described, relation with the device or the procedure, duration and severity of events are analyzed when information is available.

In the 6 Clinical investigations conducted with **ART FILLER**, no Serious Adverse Event related to the devices has been reported, local events are mostly reported after injection, are mostly of mild intensity and do not last long. No difference with the comparator was reported In comparative studies. In the pre-CE mark study (AF1), high frequency dermal ultrasound control was done at follow-up visits, D30-45, D90 and D180, this very sensitive technique being able to detect nodules much earlier before occurrence of clinical signs. No inflammatory nodules were detected.

All products were found to be well tolerated. Reported side effects were mild and transient, mainly small bruises, redness, or swelling at the injection site, resolving in less than 2 weeks in most of cases. No serious adverse events were recorded in any of the studies.

In FEM1, which corresponds to a combined treatment protocol, most reported reactions remained of light intensity and corresponded to usual adverse effects reported with such treatments (ecchymosis, swelling, erythema, hematoma, oedema, pain and pruritus). At D30, there was only one case reported some irregularity on palpation which has been disappeared later. No reaction were still reported at D60 nor D120 among the data collected. These events occurred on the first 7 days following injections and last about 5 ± 1 days (from 1 to 17 days).

To summarize,
Overall, local tolerability of ART FILLER devices was satisfactory , detected events were noted as slight in most cases and are routinely seen when using HA filling procedures to correct facial wrinkles . **ART FILLER** devices' safety profile does not show any difference compared to the reference products and data published in literature and no unanticipated risk was identified during the different studies.

6. Possible diagnostic or therapeutic alternatives

6.1 General description of therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

Several minimally invasive cosmetic procedures such as botulinum toxin, laser resurfacing, mechanical resurfacing, dermabrasion, chemical peels and injectable products are available for skin ageing and decision to use one or another technique has to be taken by the healthcare professional considering your profile.

7. Suggested training for users

ART FILLER devices are not intended to be handled directly by the subject. These products must only be administrated by trained healthcare professionals who are qualified by education or accredited in accordance with national law and trained in injection techniques.