

TREATING LIPOATROPHY WITH A NEW FILLER

A look at successful patient cases.

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Later in 2004, we can expect the release of a soft tissue filler — or in this case, revolumizer — to add to the already growing arsenal of products available to our patients.

New Fill, or Sculptra (the new name it will be marketed under), is presently before the FDA and was granted PMA acceptance as of January 2004. In March of this year, the FDA's Reconstructive Plastic Surgical Devices panel voted unanimously (9 to 0) that New Fill is safe and effective for treatment of lipoatrophy. This means this product may be available as early as late summer 2004. The intended use will be in the treatment of facial lipoatrophy, with other cosmetic uses falling under the "off-label" umbrella.

THE MAIN INGREDIENT

New Fill/Sculptra's primary ingredient is polylactic acid, which was first synthesized by a French chemist in 1954. Because polylactic acid is of synthetic origin, no animal sensitivity is involved. In addition, the acid is biodegradable, biocompatible and immunologically inert. Polylactic acid has been used since the early 1960s in products such as non-absorbable sutures (Vicryl). It has also been used in fixation devices in orthopedic surgery, in urethral and tracheal stents, in dental implants and as a vehicle for vaccines. More than 7,000 published articles exist on uses of polylactic acid in humans.

New Fill/Sculptra consists of microspheres of polylactic acid 40 to 60 microns in size. Each kit of Sculptra comes as a powder (lysophilate), and once reconstituted with 5 cc of sterile water, the amount of polylactic acid is 150 mg per 5 cc.

MECHANISM OF ACTION

Sculptra has a dual mechanism of action. Initially there is a volume effect, secondary to the hydrogel volume injected. This effect lasts up to 1 week. The sec-

ondary delayed mechanism of action involves collagen synthesis. At 1 month, histology shows micro particle capsulization with an increase in vascularity. At 6 months, capsule thickness has decreased and the surrounding areas are composed entirely of collagen fibers. At 18 months, the micro particles have been shown to still exist with collagen neogenesis and no signs of inflammation. New Fill may be one of the few soft tissue fillers that can be termed a biocatalyst.

Metabolism involves bioabsorption and gradual degradation. Polylactic acid is gradually hydrolyzed into mono or oligomers (C₃H₆O₃). These fragments are then phagocytized by macrophages before being eliminated in the form of CO₂ to the lactic acid monomer. This is a naturally occurring molecule, and after further degradation through hydration, phagocytosis and the Krebs cycle it is eliminated as CO₂.

PROMISING CLINICAL RESULTS

Many of the European studies, as well as the current U.S. studies, have involved the clinical trial of New Fill as a therapeutic treatment of lipoatrophy. Lipoatrophy is the progressive facial wasting seen in HIV positive patients. In the beginning, lipoatrophy was thought to be caused by the class of drugs known as protease inhibitors; however, it's now theorized that lipoatrophy is a multifaceted process involving the medication taken for HIV, the disease process itself and normal aging.

New Fill was originally synthesized in Biotech Industries in Luxemburg. It's now owned and distributed by Dermik. Several studies around the world have shown promising results with this volumizer. Consider the following data:

- The first European data were submitted by Arnaud and Saint Marc in September 2000, which included results from 26 lipoatrophy patients who were treated with New Fill. Ultrasound meas-

urement was used to gauge dermal thickness. Researchers found a 151% increase in dermal thickness at 3 months, 196% at 6 months, and 131% at 54 weeks.

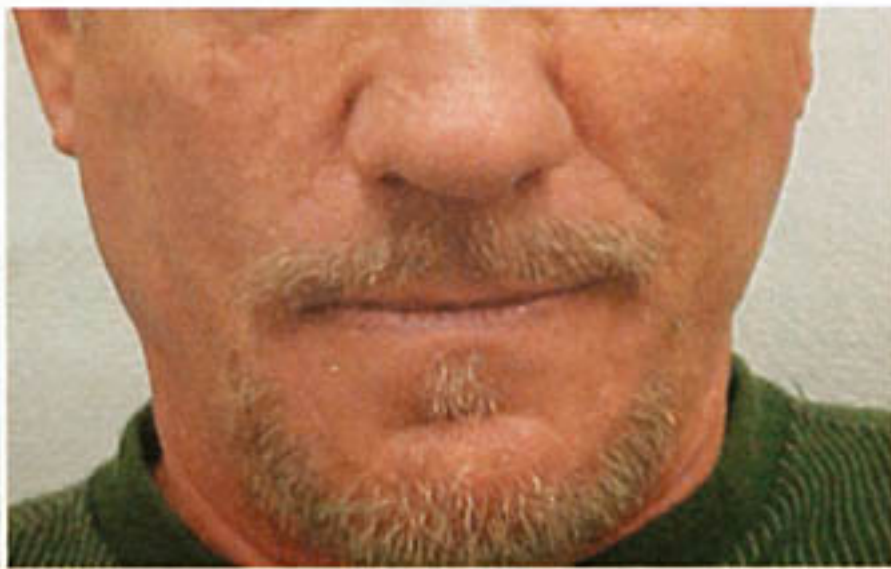
- A 96-week study was presented at the 10th Conference for Retroviral and Opportunistic Infection in Boston in February of 2003. Researchers from this VEGA study presented the results of 50 HIV-positive patients after receiving New Fill for correction of facial lipoatrophy. Change in dermal thickness was evaluated using ultrasound and color Doppler performed by the same trained radiologists. They found a three-fold increase in dermal thickness that was sustained at 72 and 96 weeks.

- Another study presented by Laaurie from St. Louis Hospital in Paris, France, involved 40 patients who had lipodystrophy. In this study, patients were treated with 150 mg per cheek every 15 days. Efficacy was evaluated at 2 months, and after 6 months, photographs were analyzed by digital surface photogrammetry software. The results showed a mean increase of dermal thickness of 2.4 mm after two injections. Results were maintained at 2 and 6 months.

OUR OWN STUDIES

In July 2002, an IDE was submitted and accepted from Blue Pacific Aesthetic Medical Group in Hermosa Beach, CA. We enrolled 100 patients who received one to six treatments spaced 3 weeks apart. Caliper skin thickness was used to measure changes in transcutaneous thickness. Baseline labs were taken and repeated every 3, 6 and 12 months to verify no change in lactic acid level. Patients completed a well-being questionnaire prior to treatment, at the end of treatment and at 6 and 12 months.

As of January 2004, 100 patients were enrolled in the study, and 92 had completed treatment; 35 had completed the 6-month follow-up, and 15 completed the 12-month follow-up.



These patients all underwent treatment with the revolumizer agent New Fill/Sculptra, which was recommended for approval for the treatment of lipatrophy by an FDA advisory panel in March.

The product is expected to receive FDA approval by late summer of this year.

An average 58.2% increase in transcutaneous thickness was noted at the end of the study. At 6 months, the increase in transcutaneous thickness was 53.3%, and this was maintained at 1 year with a 54.3% increase in thickness. Actual measurements were:

- initially (prior to treatment) 6.5 mm
- end of treatment, 10.16 mm
- 6-month follow-up, 10.78 mm
- at 1 year, 10.85 mm.

These results showed that augmentation not only held at 1 year but actually increased. There were no serious adverse results. Bruising occurred in 31%, nodule formation in 9.2%, and there were no significant changes in lactate level.

In October of 2003, we began the second protocol. The same 100 patients will be retreated as necessary with up to 12 treatments and followed-up after the final treatment. The only difference in the second protocol is that each vial will be mixed with 5 cc of sterile water and treatment intervals will be 5 weeks apart. The reason for the later change is that it had been surmised there may be less nodule formation with a more dilute solution.

The results in supplementation facial volume loss have been quite impressive. Up until now, fat has been the only option for large areas of revolumization. Artecoll/Artefill and silicone have been used to treat lipoatrophy but have not been used with as much success in these other areas. When Sculptra is approved, it will be useful for the lipoatrophy we see in our aging patients. The average volume loss in the face per year may be up to 4 cc to 5 cc. Although fat grafting and implants are available to camouflage this volume loss, these options don't have the ease of New Fill injections. In our study, our patients received up to six treatments. For cosmetic purposes, most patients require only two to three treatments.

Inevitably, we'll want to know how long Sculptra will last. While the quick answer is 18 months, in reality, none of our patients has ever gone back to "ground zero."

INJECTION TECHNIQUE

An 18-gauge needle is suggested in the reconstitution of Sculptra, and 5 cc of sterile water is used. After the reconstitution, the product must stand for

20 minutes and is then placed in an agitator. A 25- or 26-gauge needle is then used for the actual injection process. We find it easiest to draw the reconstituted Sculptra into individual 1-cc syringes with a Luer lock top.

The procedure itself is quite painless with the patient receiving an infraorbital block either intraorally or transcutaneously. Some peripheral infiltration is done with 1% lidocaine in the area not anesthetized with the block. Initially, we primarily treated the malar and temple area. Now we inject the neck, infraorbital area, chin, perioral area and hands, in appropriate patients.

In all areas, there's a distinct difference in injection technique. Primarily, this is based on the depth and vascularity of the individual area. However, certain rules of thumb govern most areas.

Sculptra should be injected in the deep dermis or subcutaneous layers, and in some areas between the periosteum and muscle. The injections are done at about a 30- to 45-degree angle with the bevel up. In some areas, massage can be used to move the product around. The product is meant to be laid deep, and if blanching occurs, infiltration must stop.

INJECTION TECHNIQUES FOR DIFFERENT AREAS OF THE BODY

Malar area. The injection is done at a 30- to 45-degree angle. A crosshatching technique is utilized, and injection is done on withdrawal. A fan-like motion is used, and 5 cc is appropriate for each cheek area.

Temple area. In the temple area, the product is laid as deeply as possible, close to the periosteum with the depot technique. The injection is done from a lateral to medial direction. Because of the vascular nature of this area, reflux may be checked for bloody aspirate. The finger technique can be used to push the product around. Pressure, post-injection, is recommended to reduce eccymoses.

Under-eye area. Just as the temples are, this is another highly vascular area. The product is laid close to the bone, reflux may be checked and massage may be used to mobilize the product. Treatment volume is less in this area — 1 cc or less. It's best to stay out of the region below the inner canthus. Patients will need two

to three sessions, and post-pressure application is also recommended.

Glabella. Frown lines are treated with injections made in the direction of the wrinkle for mid-depth rhytids. For deeper wrinkles, crosshatching can be used. This treatment is usually combined with a prior Botox treatment.

Chin. The chin is done with short crosshatching injections. Volume is variable, depending on how far into the lateral contour of the face the injections are carried. These results are improved with a prior Botox treatment.

Neck. The neck necessitates a larger volume — two entire vials are needed. In addition, it's important to note that it's difficult to perform a block in this area, yet patients report minimal pain. Eccymoses is almost certain, so we prep our patients for this. Crosshatching is used over the entire area. This area as well can be treated beforehand with Botox to lessen phantasmal bands.

Hands. We combine this with prior sclerotherapy. A radial nerve block is used by placing a ring block of 1% lidocaine in the snuff box. Once anesthesia has been established, one reconstituted vial is used per hand. We place it between the veins, and use finger massage afterward to mobilize it.

Perioral. Sculptra isn't a good choice for lip augmentation, but it may be used for support of the aging perioral area. Injections are done at the dermis-subcutis and not in the lip mucosa. Injections are made superior to the vermilion border, and two to three sessions are required

WHAT WE'VE LEARNED

Patient and physician satisfaction are very high with this product. Presently, we're reconstituting with 5 cc of sterile water and not the original 3 cc. Also, each injection session is spaced 5 weeks apart from the next. We have clinical results that suggest that many of our patients not only don't lose results at a year, but they actually improve as has been indicated by transcutaneous thickness. ■

Drs. Humble and Mest practice in Hermosa Beach, CA, and were clinical investigators for Sculptra.