HIV-related Facial Lipoatrophy

Facial lipoatrophy is a condition characterized by localized loss of facial fat tissue. HIV-related lipoatrophy often occurs in HIV-infected individuals being treated with antiretroviral therapy (ART). In these patients, the resulting facial wasting ages the individual's appearance prematurely and, along with a thinning of the skin, allows musculature and vasculature to be easily seen, resulting in what is commonly known as “the face of AIDS” [1]. For the HIV patient, facial lipoatrophy associated with the chronic stage of the disease can be particularly stigmatizing, affects their self-esteem and quality of life, and is often cited as a reason for non-compliance with or delay of ART.

While the use of highly active ART (such as protease inhibitors and nucleoside analogs) in the treatment of HIV-positive patients has greatly increased longevity, the reported incidence of HIV-associated lipoatrophy has correspondingly risen [2]. According to statistics published by AVERT (www.avert.org), worldwide there were 34 million people living with HIV/AIDS in 2011. The number of people receiving ART is reported to be approximately 10 million, and a substantial effort is underway to reach a global target of 15 million people receiving ART by the end of 2015. It has been estimated that 35-50% of patients on antiretroviral therapy have lipoatrophy.

Current Treatment Options

Due to the substantial psychosocial impact of HIV-related facial lipoatrophy, there is a clinical need for an effective product to treat mid-face volume deficiencies. However, current treatments for facial lipoatrophy are limited, expensive, and predominantly short term. Treatment options range from recombinant growth hormone to surgery using various implants both synthetic and natural.

Dermal Fillers

Approved Treatments

There are currently two injectable medical devices approved in the EU and US to treat HIV-related facial lipoatrophy: Sculptra® and Radiesse®. Both products cause a fibrotic reaction that is intended to fill the subcutaneous defect caused by the lipoatrophy. Sculptra (aka New-Fill) is a biocompatible synthetic polymer [poly-L-lactic acid] from the alpha-hydroxy-acid family suspended in carboxymethylcellulose. Radiesse (aka Radiance) is a sterile, semi-solid implant consisting of synthetic calcium hydroxyapatite suspended in a carboxymethylcellulose carrier.

Clinical studies of Sculptra and Radiesse have reported positive outcomes [correcting facial contour defects] using objective and/or subjective measures including skin
thickness, cheek fat volume, and the Global Aesthetic Improvement Scale [3-6]. However, a drawback of these products is that a typical treatment regimen involves multiple injections over several months. In addition, while these implants provide short-term improvement, as the facial lipoatrophy progresses, the implant edges may become apparent and the implants often have a rigid feel.

**Unapproved (off-label) treatments**
Additionally, there are numerous reports in the medical literature of the unapproved (off-label) use of **hyaluronan- and collagen-based dermal fillers** to treat HIV-related facial lipoatrophy showing successful outcomes [7]. It has been reported that hyaluronan- and collagen-based dermal fillers are not permanent and resorb over time. Retreatment is often necessary to maintain appearance.

**Surgical Techniques**
**Autologous Fat Transfer (AFT)** and **Cell Assisted Lipotransfer (CAL)** have been used to resolve HIV-related facial lipoatrophies [7, 8]. Both surgical techniques use autologous fat, obtained via liposuction, as the bulking agent to resolve the lipoatrophy; however, in CAL procedures the whole fat is mixed with additional autologous adipose derived cells (stromal vascular fraction, SVF) and injected subcutaneously to resolve contour defects. While AFT and CAL procedures have proven successful in certain instances [8, 9], the processing and preserving of whole adipose tissue is not without challenges and results can be variable. Moreover, subcutaneous injection of whole fat requires the use of large gauge needles (14-17 gauge) which is not optimal for use in the facial area.

**Renevia as an Alternative Treatment Option for Lipoatrophy**
**Renevia™** is an implantable, resorbable delivery matrix developed as a replacement for autologous fat in CAL procedures by recreating many aspects of the adipose tissue extracellular matrix. **Renevia**’s hydrogel polymer network provides the requisite amino acid sequences for attachment of adipose stromal vascular cells (SVF) and supports proliferation and differentiation of these cells into adipocytes. Over time this matrix is resorbed and replaced with natural extracellular matrix. Once implanted, the three-dimensional matrix that **Renevia** provides has a pliability comparable to that of native adipose tissue, restoring texture in the short term while promoting soft tissue regeneration in the long term.

By contrast, typical dermal fillers cannot be used as cell delivery vehicles, since they are pre-gelled or cross-linked, and thus there is no practical way to mix them with cells. In addition, currently available dermal fillers do not contain the requisite physical and chemical structure for cell attachment and proliferation. The ability to mix and deliver cells with Renevia, coupled with the subsequent gelation occurring **in situ** differentiates Renevia from other available treatment options.

The risk associated with delivery of Renevia/adipose derived cells is comparable to
that of CAL and of other dermal fillers. Since Renevia is a more consistently uniform carrier than autologous fat, the use of this matrix to deliver autologous SVF may yield more reproducible results, and may reduce the need for multiple treatments seen with both AFT and with the approved devices, Sculptra and Radiesse. Additionally, the use of smaller gauge (21-30) needles to deliver Renevia containing autologous SVF may potentially lead to a more natural, smoother appearance.

References