Management of HIV includes use of antiretroviral therapy, which may be associated with lipodystrophy syndrome. Lipodystrophy of the buttocks may cause both functional (eg, pain when sitting) and aesthetic problems. In France, 294 of 33,206 subjects with active files at HIV-clinics had severe problems with buttock lipoatrophy in 2006. Volumizing treatments for buttock lipoatrophy include silicone implants and injectables (eg, fat, polyalkylimide gel, and poly-1-lactic acid). However, there is no gold standard.

We describe a French 18-month prospective, open-label, baseline-controlled study performed on HIV-infected subjects with buttock lipoatrophy who were unable to sit for more than 30 minutes because of pain. The objectives were to explore effectiveness and safety of Macrolane VRF30 for treatment of buttock lipoatrophy in HIV-infected subjects. Ten subjects who were unable to sit for more than 30 minutes because of pain were injected with a mean of 276 mL and followed for 18 months. The pain score was reduced, and the time that subjects could sit was increased at least up to 9 months post treatment. There was no local displacement of gel. Five mild adverse events occurred; all related to the injection procedure. This pilot study indicates that Macrolane treatment of buttock lipoatrophy is a promising, well-tolerated method that reduces pain at sitting and improves buttock appearance.

**PATIENTS AND METHODS**

The study was approved by an independent ethics committee and the regulatory authority. Eligible subjects were 18–80 years, had buttock lipoatrophy, were unable to sit for more than 30 minutes because of pain, had undergone HIV treatment for more than 2 years, and had less than 50 RNA copies/mL and greater than 200 CD4 cells/mm³. Main exclusion criteria are included in Supplemental Digital Content 1 (http://links.lww.com/PRSGO/A113).

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All subjects received prophylactic oral antibiotics. The procedure was performed in an operating theatre. After cleaning the skin with an antiseptic, local anesthesia was used at the discretion of the investigator. A maximum of 400 mL Macrolane per subject was injected in small aliquots into the subcutaneous tissue (supramuscularly) using a 15-cm blunt-tip 12-gauge cannula.

Pain was evaluated by a 100-mm visual analogue scale (0 mm, “no pain”; 100 mm, “worst possible pain”) after 15 minutes of sitting, and by time to when subjects could no longer stay sitting. The primary outcome assessment was to compare the 6-month pain score with baseline. Esthetic improvement was assessed using standardized photographs and the 5-point Global Esthetic Improvement Scale. A heavily T2-weighted 3D spin echo image was acquired for the pelvis, combined with selective fat suppression to provide isotropic voxels and enable optimal multiplanar reconstruction on a 1.5-T magnetic resonance imaging system (Avanto, Siemens Healthcare, Germany). F.P. manually segmented gel volume for all patients using visual thresholding. Quality of life (QoL) was assessed using a 35-item questionnaire (based on the validated Medical Outcomes Study-HIV questionnaire). Safety was assessed through collection of adverse events. Follow-up extended 18 months.

Pain analyses were performed with SAS system version 9.2 (SAS Institute Inc., Cary, N.C.), using two-sided paired t tests (significance level: 0.05), two-sided 95% confidence intervals (CIs), and descriptive statistics. Global Esthetic Improvement Scale and safety data were summarized descriptively.

RESULTS

Subject disposition is included in Supplemental Digital Content 1 (http://links.lww.com/PRSGO/A113) and demographic and baseline data in Supplemental Digital Content 2 (http://links.lww.com/PRSGO/A114).

The mean injected volume was 276 mL/subject (range: 220–320 mL), equally distributed between the left and right buttocks. Approximately half of the volume was injected in the lower third and ischial tuberosity area, and the other half in the mid third of the buttocks.

Mean pain after 15 minutes of sitting was reduced compared with baseline for up to (and including) 9 months (Fig. 1A). The mean time that subjects could remain seated was longer compared with baseline for up to (and including) 12 months (Fig. 1B).

Esthetic improvement is shown in Supplemental Digital Content 3 (http://links.lww.com/PRSGO/A115).

Gradual decrease in volume of remaining gel (with no local displacement of gel) is illustrated in Figure 2.

Fig. 1. A, Mean change from baseline in pain after 15 minutes of sitting (measured using a VAS), intention to treat (ITT) population (n = 10). The lowest mean pain score was noted 3 months after treatment (mean change from baseline: −40 mm [95% CI, −47.7 to −32.8]). At 6 months, mean change from baseline was −28 mm (95% CI, −44.0 to −12.2). At this time point, 9 subjects (90%) experienced decreased pain. Significant difference from baseline: *P < 0.05, **P < 0.01, ***P < 0.001. VAS, visual analogue scale. B, Mean change from baseline in time to when subjects could no longer stay in the sitting position, ITT population (n = 10). Six months after treatment, the mean time that subjects could remain seated was increased with 35 minutes (95% CI, 31.0–39.4). The longest mean time that subjects could remain seated was noted 12 months after the treatment. By then, all subjects for whom data were recorded (n = 5) were able to remain seated for more than 60 minutes (mean change from baseline: 37 minutes [95% CI, 31.2–43.7]). Significant difference from baseline: ***P < 0.001.
The mean physical health Medical Outcomes Study-HIV score increased from baseline to 3 and 6 months [mean changes from baseline: 5 (95% CI, 1.8–8.2) and 9 (95% CI, 3.9–14.2), respectively (P < 0.05)]. The mean mental health score increased from baseline to 9 months [mean change from baseline: 5 (95% CI, 0.3–9.7; P < 0.05)]. Scores were not significantly different from baseline at other time points.

Three subjects (30%) had 5 adverse events [implant-site effusion (n = 2); implant-site inflammation (n = 3)]. These were nonserious and of mild intensity and related to the injection procedure but not the study product.

**DISCUSSION**

The mean pain score reduction and increase in mean time that subjects could remain seated were maintained at least until 9 months post treatment, showing the clinical relevance of the results and that the gel functioned as intended. Moreover, esthetic aspects of the buttocks were successfully addressed, and treatment was well tolerated.

This was a pilot study with limited long-term data because of subjects being lost to follow-up. Nevertheless, all subjects completed the primary 6-month assessment. There was no local displacement of the gel, which degraded over time. However, at 1 month, the mean estimated volume of remaining gel was higher than the mean injected volume. Potential reasons may include water absorption by the gel or relate to the method used to estimate remaining volume. At 12 months, the estimated mean percentage of remaining gel (31%) was comparable with that (36%) reported previously for healthy subjects seeking esthetic buttocks treatment.

Treatment had a minor impact on overall QoL in this study. However, QoL is a complex measure that is influenced by several parameters. The subjects may also have become accustomed to having fuller buttocks and the associated benefits of less pain and ability to sit for a longer time, which to some extent, could explain the limited effect on QoL measures.

Obvious limitations with Macrolane treatment of buttock lipoatrophy relate to product degradation and that repeated treatments likely would be needed to maintain the effect. Benefits include that the treatment is minimally invasive, can be administered without general anesthesia, requires no-to-minimal downtime, and can easily be adapted if the lipoatrophy progresses. Additionally, Macrolane can be removed by aspiration or with hyaluronidase. This is advantageous compared with permanent/semipermanent treatments, for which adjustment generally...
requires invasive procedures. Although fat injections seem to give long-lasting results, drawbacks include difficulty to obtain required volumes from thin subjects, donor-site morbidity, and fat necrosis. We, therefore, believe that Macrolane is a useful option for treatment of buttock lipoatrophy.

CONCLUSION

This pilot study indicates that Macrolane treatment of buttock lipoatrophy is a promising and well-tolerated method, which reduces pain while sitting and improves esthetic aspects of buttock appearance.

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