

Background: Facial lipotrophy (LA) commonly complicates combination antiretroviral therapy and may stigmatise patients. This 48-week, randomised, double-blind, placebo-controlled trial investigated the impact of rosiglitazone (RSG) therapy on peripheral LA in HIV+ subjects receiving combination antiretroviral therapy. Subjects were able to co-enrol in a malar sub-study (MSS), which aimed to investigate the utility of ultrasonography for quantifying facial LA.

Methods: Subjects had a single ultrasonographic assessment of the maximal subcutaneous fat depth (MFD) over the right malar bone performed at three time points (weeks 0, 24, 48) on one scanner. Bivariate association analysis was completed. Changes from baseline to week 48 in primary and secondary endpoints were compared by randomised treatment group using descriptive statistics. Differences between treatment groups were formally tested using non-parametric methods. Bivariate associations between facial fat changes and other body composition parameters were examined using Spearman's correlation coefficient.

Results: Of the 108 subjects recruited to the main RSG trial, 56 (52%) enrolled in the ultrasonoid study of which 51 (91%) completed all 3 scans. At week 48 MFD had decreased in both arms by 0.14 mm in the RSG arm (n=27) and by 0.16 mm in the placebo arm (n=29); mean difference: 0.04 mm [95% CI: -0.09, 0.10]; $p=0.43$. No significant associations were observed between change from baseline to week 48 in MFD and the following body composition parameters: limb fat by DEXA (rho=0.11; $p=ns$), mid thigh subcutaneous fat by CT (rho=0.13; $p=ns$), Lipodystrophy Case Definition (LCD) score (rho=0.11; $p=ns$) or change in patient self-assessed facial lipotrophy (rho=1.1; $p=ns$).

Conclusions: Ultrasonography did not correlate significantly with more established measures of lipotrophy severity. Nevertheless, RSG may not aid in improving facial LA using this technique. Based on these data measurement of malar fat using ultrasonography is not recommended.



Evaluation of Ultrasound for Assessing Facial Lipotrophy in a Randomised, Placebo-controlled Trial

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Introduction

Facial lipotrophy (LA) commonly complicates combination antiretroviral therapy and may stigmatise patients. This 48-week, randomised, double-blind, placebo-controlled trial investigated the impact of rosiglitazone (RSG) therapy on peripheral LA in HIV+ subjects receiving combination antiretroviral therapy. Subjects were able to co-enrol in a malar sub-study (MSS) which aimed to investigate the utility of ultrasonography for quantifying facial LA.

Methods

Participating subjects had a single ultrasonographic assessment of the maximal subcutaneous fat depth (MFD) over the right malar bone performed on one scanner at three time points (weeks 0, 24 and 48) during the study.

Data were analysed using an intent to treat analysis. Changes from baseline to week 48 in primary and secondary endpoints were summarised by randomised treatment group using descriptive statistics. Differences between the treatment groups were formally tested using non-parametric methods, Wilcoxon rank test. Bivariate associations between facial fat changes and other body composition parameters were analysed using the Spearman correlation coefficient test.

Results

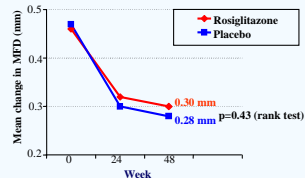
Of the 108 subjects recruited to the main RSG trial, 56 (52%) enrolled in the MSS. Twenty-five subjects (45%) received RSG, the remaining 31 placebo. During the study 2 subjects (1 in each treatment arm) withdrew consent for personal reasons and 3 (all placebo) either did not attend for the week 0 (1) or 48 (2) ultrasound. Fifty-one subjects (91%) completed all 3 scans.

Table 1. Baseline Characteristics of MSS Participants versus Non-participants

Baseline Characteristic	MSS n=56	Non-MSS n=52	p-value (rank test)
PI regimen (%)	59	63	0.63
Severe lipotrophy (%)	64	44	0.04
Age (years), mean	45.7	45.2	0.72
BMI (kg/m ²), mean	23.4	22.6	0.09
Waist : hip ratio	0.97	0.95	0.16
DEXA limb fat mass (kg)	3.04	2.32	0.0006

At week 48 the mean MFD had decreased in both arms; from 0.46 mm (range 0.14-0.85 mm) to 0.30 mm in the RSG arm and from 0.47 mm (range 0.20-0.99 mm) to 0.28 mm in the placebo arm (mean difference 0.04 mm [95% CI -0.09, 0.16] mm; $p=0.43$ (rank test). See Figure 1.

Figure 1. Change from baseline to week 48 in MFD



Changes in MFD from baseline to week 48 were compared with the changes from baseline to week 48 in the following body composition parameters:

- limb fat as measured by DEXA (Figure 2),
- mid-thigh subcutaneous fat measured by CT (Figure 3),
- Lipodystrophy Case Definition (LCD) score (Figure 4).

All showed non-significant associations ($\rho=0.1-0.11$; $p=ns$).

Figure 2. Bivariate Association of MFD & Limb Fat Changes

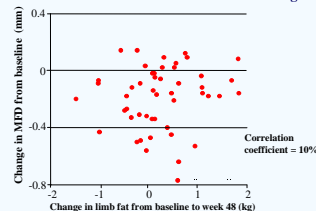


Figure 3. Bivariate Association of MFD & Mid-thigh Subcut Fat Changes

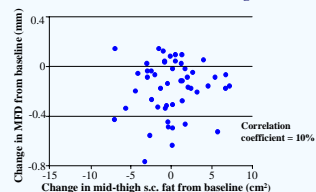
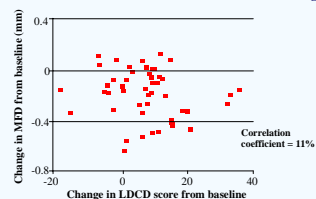
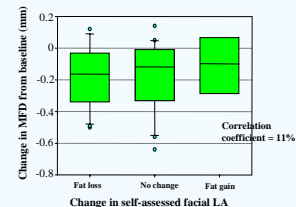


Figure 4. Bivariate Association of MFD & LCD Score Changes



The association between change in MFD from baseline to week 48 and the change in patient self-assessment of facial lipotrophy over the study duration was investigated. These data are presented in Figure 5. No significant association was observed ($\rho=1.1$; $p=ns$).

Figure 5. Association of MFD & Self-assessed Facial LA Changes



Conclusions

- Ultrasonography did not correlate significantly with more established measures of lipotrophy severity.
- Nevertheless, RSG 4mg bid did not appear to improve facial LA using this technique.
- Based on these data, measurement of malar fat using ultrasonography is not recommended.

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