



A Randomized Placebo Controlled Trial of Rosiglitazone for the Treatment of HIV Lipodystrophy

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OBJECTIVES

To evaluate whether treatment with rosiglitazone would slow peripheral fat loss in patients treated with protease inhibitors (PI) with established HIV lipodystrophy.

METHODS

- HIV+ patients treated on stable, PI-containing highly active anti-retroviral therapy (HAART) and affected by HIV LD were randomized to receive rosiglitazone 4mg po od or matching placebo in a prospective, double blind trial.
- The primary endpoint was an absolute decrease of 5% or greater in arm fat by DEXA over a 24-week period. All scans were performed using a Hologic QDR 4500A (Hologic, Waltham, MA) fan-beam densitometer in the array mode. Pts with diabetes were excluded.
- Clinical and anthropometric evaluations, fasting lipid parameters, oral glucose tolerance testing (OGTT) and DEXA scanning were performed at baseline and week 24.
- HOMA, QUICKI and McAuley indices of insulin resistance were calculated from baseline OGTT results.
- Median changes in DEXA fat mass, lipid profile and insulin resistance measures were compared using the Wilcoxon rank sum test.

Table 1: Characteristics of Patients at Baseline

	Rosiglitazone (n=39)	Placebo (n=39)
Patient		
Age (years)*	47 (9)	46 (14)
Sex (male) †	38 (97%)	38 (97%)
AIDS †	12 (31%)	11 (28%)
CD4 Count (cells/mm ³)*	458 (171)	571 (297)
HIV RNA < 50 copies/ml †	33 (85%)	26 (67%)
d4T use during study †	15 (38%)	20 (51%)
Body Composition		
Arm fat (kg)*	1.47 (0.71)	1.21 (0.57)
Arm fat (%)*	15.7 (6.1)	13.2 (5.7)

* Values are mean (SD).
† Values are n (%).

Table 2: Changes in Primary and Secondary Endpoints

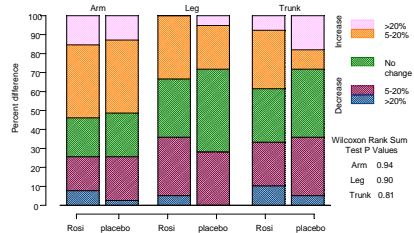
	Week 0		Change at Week 24 from Baseline		Between Group Difference p value
	Rosiglitazone	Placebo	Rosiglitazone	Placebo	
# of pts with 5% or greater decrease in arm fat	--	--	10 (26%)	10 (26%)	0.99
Body Composition					
Weight (kg)	76.1 (64.0, 83.0)	75.7 (69.8, 82.5)	0.5 (-0.8, 2.9)	-0.4 (-1.7, 1.8)	0.12
Body-mass Index	24.5 (22.2, 27.5)	24.2 (22.3, 25.8)	0.2 (-0.3, 0.9)	-0.1 (-0.6, 0.6)	0.12
Glycaemic					
2-hour glucose	5.7 (4.8, 7.0)	6.4 (5.2, 8.3)	0.3 (-0.9, 1.0)	1.4 (-0.7, 2.4)	0.18
HOMA score	2.1 (1.6, 3.9)	2.4 (1.6, 3.6)	-0.1 (-1.1, 0.5)	-0.1 (-1.2, 1.3)	0.71
Safety					
CD4 count (cells/mm ³)	417 (352, 577)	466 (384, 779)	-9 (-64, 68)	0 (-93, 98)	0.95
Viral Load	1.7 (1.7, 1.7)	1.7 (1.7, 3.1)	0 (0, 0)	0 (0, 0)	0.62

* Values are n (%) or median (interquartile range).

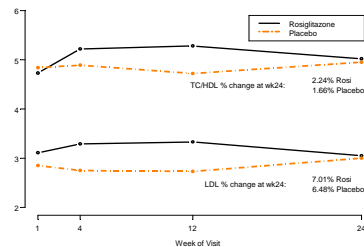
RESULTS

- 78 of the 96 enrolled patients were evaluable with 24 weeks of follow-up data available.
- The median percentage change in arm fat, leg fat, trunk fat and total body fat at 24 wks was not significantly different between rosiglitazone and placebo groups.
- Median percentage changes at 24 wks in cholesterol, triglycerides (TG), HDL, and OGTT responses, as well as 24-week changes in HOMA, QUICKI and McAuley indices were not significantly different between groups.
- 3 (4%) subjects changed anti-retroviral therapy during the study. 8 subjects were started on lipid lowering therapy during the study (6 randomized to Rosiglitazone and 2 to placebo). 4 patients had grade ≥ 3 adverse events (2 with elevation in AST and 2 with elevations in TG).

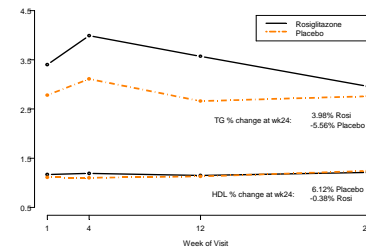
Percentage Change from Baseline to 24 Weeks of Follow-up
DEXA Scan Measurements of Arm, Leg and Trunk Fat



Median TC/HDL Ratio and Median LDL



Median HDL and Median TG



CONCLUSIONS

- This randomized placebo controlled trial failed to show a benefit of rosiglitazone 4mg od on fat redistribution in subjects affected by HIV LD over 24 weeks follow up.
- No significant differences in lipid profiles were found between treatment and control groups over time.
- Adverse effects were uncommon.

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