

# 8th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV

San Francisco, California - September 24 - 26, 2006

INTERNATIONAL  
MEDICAL  
PRESS

## CELL DEATH IS PREDOMINANTLY SEEN IN PREADIPOCYTES OF HIV INFECTED SUBJECTS WITH OR WITHOUT LIPOATROPHY

*Antiviral Therapy* 2006; 11:L28 (abstract no. 41)

GA McComsey<sup>1</sup>, M O'Riordan<sup>1</sup>, J Ganz<sup>2</sup>, DE Libutti<sup>3</sup>, LE Gerschenson<sup>4</sup>, CA Kruse<sup>4</sup>, N Storer<sup>1</sup>, J JewettTennant<sup>1</sup>, S Goldman<sup>2</sup> and M Gerschenson<sup>3</sup>

<sup>1</sup>Rainbow Babies and Childrens' Hospital and Case Western Reserve University, Cleveland, OH, USA; <sup>2</sup>University Hospitals of Cleveland, Cleveland, OH, USA; <sup>3</sup>University of Hawaii, Honolulu, HI, USA; <sup>4</sup>Carlaz Biotechnology Inc., San Diego, CA, USA

---

**BACKGROUND:** The pathogenesis of lipodystrophy remains unclear. Prior studies were conflicting regarding the presence and extent of fat apoptosis in fat of HIV+ subjects with lipodystrophy. Importantly, the relationship of fat apoptosis to lipodystrophy remains speculative.

**METHODS:** Forty-four HIV (+) subjects from a cross-sectional cohort were assessed for metabolic parameters. Evaluations included excisional adipose tissue biopsies from the lower abdomen to measure mtDNA copies/cell by real-time PCR, fat apoptosis by TUNEL, and histology by H&E; whole body DEXA scanning; PBMC mtDNA levels. The relationship between continuous variables was reported using Spearman correlation.

**RESULTS:** Forty-four patients enrolled (77% males, 55% white, median age 45 years); 35 with established lipodystrophy (median limb fat 4.4 kg) and 9 were naïve to all antiretrovirals (median limb fat 7.66 kg). All subjects in the lipodystrophy group had HIV-1 RNA <50 copies/ml, 39% were on PI containing regimen, and all were receiving thymidine analogue-containing regimen (10 d4T; 25 ZDV) for a median duration of 72 months. Median (range) % adipocyte and preadipocyte death observed by H&E were 2.7% (0–13.1%) and 11.2 (0–29.5%) in the lipodystrophy group and 1.3% (0–21.4%) and 14.7% (5.4–33.3) in the ARV naïve group, respectively ( $P=0.22$  and  $P=0.30$  for between group comparison for % adipocytes and preadipocytes). A positive correlation was found between % cell death in adipocytes and in preadipocytes ( $r=0.46$ ;  $P=0.005$ ). Fat mtDNA levels tended to be lower in the lipodystrophy group (790 versus 1372 in ARV naïve;  $P=0.12$ ), and negatively correlated with % preadipocyte death ( $r=0.49$ ;  $P=0.003$ ) and weakly with % adipocyte death ( $r=0.33$ ;  $P=0.05$ ). There was

weak correlation between fat mtDNA levels and PBMC mtDNA levels ( $r = -0.34$ ;  $P = 0.05$ ). No correlation was found between limb fat and either % preadipocyte death, % adipocyte death, or fat mtDNA levels. In addition, no consistencies were found between cell death by H&E and TUNEL generated apoptosis scores.

**CONCLUSION:** A similar high amount of cell death was seen in the fat of lipoatrophy subjects and ARV naïve subjects. Although the level of cell death negatively correlated with adipose tissue mtDNA levels, no correlation was found with limb fat. Cell death was mostly seen in the preadipocytes. Lastly, the lack of consistencies found between cell death by H&E and TUNEL generated apoptosis scores suggest the presence of other types of cell death besides apoptosis. Longitudinal follow up of these subjects with serial biopsies is ongoing.

2006-09-24

41

Copyright © 2006 - [International Medical Press Ltd.](#) Reproduction of this abstract (other than one copy for personal reference) must be cleared through the International Medical Press Ltd. 2-4 Idol Lane, London EC3R 5DD UK.