Diabetes Drug Improves Lipoatrophy in HIV

BY DIANA MAHONEY

MONTREAL — A drug approved for use in diabetes may reverse HIV-associated lipoatrophy and insulin resistance, a study has shown.

In a randomized, controlled trial of 71 HIV-positive patients with documented peripheral fat wasting, patients who received 4 mg of the thiazolidinedione agent rosiglitazone (Avandia) twice daily for 48 weeks had significant gains in limb fat, and decreases in insulin resistance and insulin levels, compared with patients on placebo, Dr. Grace McComsey reported at the Conference on Retroviruses and Opportunistic Infections.

All patients had been treated for at least 12 months (but not during the 6 months prior to study enrollment) with one of the thymidine nucleoside reverse transcriptase inhibitor (tNRTI) drugs that have been linked to lipoatrophy, said Dr. McComsey of Case Western Reserve University in Cleveland.

The mean 911-g increase in limb fat with treatment was significantly greater than the 253-g increase with placebo.

DR. McCOMSEY

Lipoatrophy is cosmetically disturbing and stigmatizing for individuals with HIV, and has been linked to decreased adherence to antiretroviral therapy as well as lipid and glycemic abnormalities associated with an increased risk for myocardial infarction and atherosclerotic disease, Dr. McComsey noted.

In vitro studies have suggested that drugs in the glitazone class stimulate production of the peroxisome proliferator-activated receptor gamma (PPAR-gamma) protein, which plays a key role in adipocyte differentiation, and clinical trials have linked the drugs to increased subcutaneous fat in people with diabetes. But data from HIV studies have been mixed, Dr. McComsey said. Many of the clinical trials in HIV have included patients who have remained on the tNRTI drugs zidovudine or stavudine, which inhibit PPAR-gamma, so "it is possible that the two drugs cancel each other out with respect to the effect on lipoatrophy," she said. The current study is the first to assess the effect of a glitazone on lipoatrophy in HIV-infected patients on tNRTI-sparing regimens, she added.

More than 90% of the patients in the current study had well-controlled HIV, with a viral load less than 400 copies/mL and a mean CD4 cell count between 600 and 700 cells/mm^3. Serial dual-energy x-ray absorptiometry scans and fasting metabolic assessments were used to evaluate changes in metabolic and limb fat, Dr. McComsey said.

At baseline, the mean limb fat measures in the rosiglitazone and placebo groups were statistically similar, at 6,533 g and 6,413 g. Baseline lipid and glycemic characteristics also were similar, except for a higher mean total cholesterol level in the placebo arm, Dr. McComsey reported.

At week 48, both groups had increased limb fat consistent with the absence of tNRTIs, Dr. McComsey said. The mean 911-g increase in the treatment group was significantly greater than the mean 253-g increase in the placebo group, she said, and only the treatment arm had decreases from baseline in the mean homeostasis model assessment for insulin resistance and insulin levels.

Total cholesterol levels were significantly higher in the treatment group after 48 weeks, but triglyceride and non–HDL cholesterol levels did not change significantly within or between groups, Dr. McComsey said. Similarly, total bone mineral density, CD4 cell count, and body mass index did not change.

Because some studies in the general population have linked rosiglitazone with an increased risk of cardiovascular disease and decreases in bone density leading to fracture risk, Dr. McComsey and her colleagues are currently analyzing the drug's effect on markers for atherosclerosis, inflammation, and bone status in patients with HIV, she said.

Dr. McComsey reported no relevant financial conflicts of interest. ■