

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.

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.



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

DR. MCCOMSEY

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/mm³. 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 de-

creases 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. ■



IMPORTANT TREATMENT CONSIDERATIONS

PRISTIQ 50-mg Extended-Release Tablets are indicated for the treatment of major depressive disorder in adults.

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of PRISTIQ or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. PRISTIQ is not approved for use in pediatric patients.

Contraindications

- PRISTIQ is contraindicated in patients with a known hypersensitivity to PRISTIQ or venlafaxine.
- PRISTIQ must not be used concomitantly with an MAOI or within 14 days of stopping an MAOI. Allow 7 days after stopping PRISTIQ before starting an MAOI.

Warnings and Precautions

- All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose. Consider changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Families and caregivers of patients being treated with antidepressants should be alerted about the need to monitor patients.
- Development of a potentially life-threatening serotonin syndrome may occur with SNRIs and SSRIs, including PRISTIQ, particularly with concomitant use of serotonergic drugs, including triptans, and with drugs that impair the metabolism of serotonin (including MAOIs). If concomitant use is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Concomitant use of PRISTIQ with serotonin precursors is not recommended.
- Patients receiving PRISTIQ should have regular monitoring of blood pressure since sustained increases in blood pressure were observed in clinical studies. Pre-existing hypertension should be controlled before starting PRISTIQ. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported. For patients who experience a sustained increase in blood pressure, either dose reduction or discontinuation should be considered.