

40TH ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

The 40th Annual Meeting of the EASD was held from September 5 to 9 in Munich.

Over Half of Patients Reach Goal with Rosiglitazone Plus Metformin

The combination of rosiglitazone maleate (Avandia, GlaxoSmithKline) and metformin helped >60% of patients to achieve the glucose target of <7% HbA1c and nearly 40% of patients to reach <6.5%. Results of this 6-month, real-life study of 11,014 patients showed that rosiglitazone plus metformin reduced patients' blood pressure.

"These new data are exciting as they demonstrate that by using the combination of [rosiglitazone] plus metformin physicians in daily practice can now effectively control their type 2 diabetes patients' blood sugar levels to international treatment goals," said lead investigator, Christoph Rosak, MD, from the department of metabolic disease, Krankenhaus Sachsenhausen, Frankfurt, Germany.

"Controlling glucose levels to targets of <6.5% to 7% HbA1c has previously been challenging, particularly as conventional monotherapy fails to control blood glucose over the long term. Our new data also show that in the population studied [rosiglitazone] plus metformin had the extra benefit of lowering patients' blood pressure."

Currently, only about 30% of patients with type 2 diabetes have glucose levels below recommended targets.

This data came from a pooled analysis of two large observational studies of real-life daily practice in Germany.

Reduced Symptoms of DPN for Patients Taking Ruboxistaurin

Patients with diabetic peripheral neuropathy (DPN) who took the investigational drug ruboxistaurin (Eli Lilly and Company) experienced relief of a broad range of symptoms of DPN independent of the simultaneous use of pain-palliative oral medications. These analyses were from a previously reported study. Patients were administered the Neuropathy Total Symptom Score-6 test (NTSS-6), a questionnaire that measures the frequency and intensity of six positive sensory symptoms of DPN: numbness, prickling, aching pain, burning pain, lancinating pain and allodynia.

In two additional analyses, the validity of a self-admin-

istered version of the NTSS-6 was demonstrated, and another showed a strong correlation between the presence of positive sensory symptoms characteristic of DPN and a lower quality of life.

"We are very encouraged by this early evidence of ruboxistaurin's ability to reduce a broad range of symptoms, but it is also important to improve the recognition and diagnosis of diabetic nerve damage," said Vladimir Skljarevski, MD, neurologist, senior clinical research physician and investigator for Lilly's ruboxistaurin effort.

"These data suggest physicians can encourage patients to take this simple test (NTSS-6-SA) with reliability to help detect [DPN] earlier. To succeed against this potentially devastating condition and improve quality of life, we need to attack [DPN] on all fronts."

EUROPEAN SOCIETY OF CARDIOLOGY CONGRESS 2004

The ESC Congress 2004 was held from August 28 to September 1 in Munich.

Rimonabant Beneficial in Weight Loss and Metabolic Risk Factor Improvement

The first-year results of the 2-year, phase III trial Rimonabant in Obesity-Europe (RIO-Europe) trial showed that overweight or obese patients taking the selective cannabinoid type 1 (CB1) blocker had a significant reduction in weight, waist circumference and improvements in lipid and glycemic profiles.

The 1,507 patients in the international, multicenter trial were assigned to treatment with this first-in-class agent at 20 mg/day, 5 mg/day or placebo. Luc Van Gall, MD, professor of diabetology, metabolism and clinical nutrition, University Hospital Antwerp, Belgium, reported that lipid improvement was partially independent of weight loss, indicating that the drug has a direct effect on metabolic parameters. The drug, Acomplia, is from Sanofi-Aventis.

At baseline patients had a body mass index ≥ 30 kg/m² or >27 with a comorbidity. After 1 year, patients assigned 20 mg/day rimonabant lost an average of 8.6 kg versus 4.8 kg for the 5-mg group and 3.6 kg for placebo. Close to 70% of patients assigned 20 mg lost 5% of their body weight versus 44.2% of those assigned 5 mg and 30.5% for placebo.

The number of patients with metabolic syndrome at baseline (44.2%) was halved after treatment with 20 mg

rimonabant versus placebo. And HDL cholesterol increased by 27% in the patients assigned the 20-mg dose ($P < .001$ vs placebo).

Rimonabant is the first selective CB1 blocker to be developed for the management of cardiovascular risk factors including obesity, metabolic syndrome, dyslipidemia, type 2 diabetes and tobacco dependence.

Two-thirds of Cardiovascular Patients Have Abnormal Glucose Levels

Much of the cardiovascular disease (CVD) population also has diabetes and glucose intolerance, yet the conditions often go undiagnosed in these patients, according to results of a screening study of more than 40,000 patients.

The Nateglinide and Valsartan Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) screening results of 43,509 patients found that those with risk factors for heart disease had nearly the same percentage of diabetes, impaired glucose tolerance (IGT) and impaired fasting glucose as those diagnosed with heart disease, according to John McMurray, MD, of the University of Glasgow, Scotland.

"The failure to diagnose [IGT] is a missed opportunity to prevent the development of diabetes through lifestyle interventions," McMurray said at a news conference.

NAVIGATOR has enrolled 9,524 patients to study the effect of valsartan versus nateglinide on the progression of type 2 diabetes and/or heart disease. Of the 9,125 enrolled who have documented CVD, only 34% have normal glucose levels, McMurray said.

INTERNATIONAL SOCIETY OF HYPERTENSION IN BLACKS 2004, DISPARITIES IN CARDIOVASCULAR HEALTH: BRIDGING THE GREAT DIVIDE

ISHIB 2004 was held from June 13 to 16 in Detroit.

Aggressive Treatment Helps Blacks with Diabetes, Hypertension Meet Blood Pressure Goals

Black patients with type 2 diabetes and hypertension were better able to reach rigorous blood pressure goals with aggressive treatment using combination therapy. Researchers found that a combination of amlodipine and benazepril was more effective than enalapril in getting patients to a goal of $<130/80$ mm Hg.

The Lotrel and Enalapril in African Americans with Diabetes study (LEADD), was carried out in 269 patients. Sixty percent of patients assigned amlodipine

plus benazepril reached target versus 44% of enalapril patients.

"These data show that patients can reach aggressive blood pressure goals quickly using combination therapy," said John Flack, MD, lead investigator of the study and president of ISHIB. He is associate chairman and chief quality officer at the department of medicine at Wayne State University School of Medicine in Detroit. "As a clinician, however, my most important objective is to get patients to their blood pressure target and this study demonstrates that aggressive use of combination therapy can help significantly more patients get to goal than single therapy alone.

ISHIB guidelines released last year recommend black patients be treated to a goal of $<130/80$ mg.

TZDs May Protect Against Progression of Renal Disease in Type 2 Diabetic Patients

A study of 40 cases and 98 controls showed that thiazolidinediones (TZDs) may protect against the progression of renal disease in patients with type 2 diabetes. TZDs, in the treatment of diabetes, appear to have beneficial effects on markers of renal risk independent of glycemic control.

In this primarily black population, researchers from Wayne State University School of Medicine found that patients not taking TZDs were more likely (17.3%) to reach end stage renal disease (ESRD) than those taking the drug (5%). Diabetic nephropathy is the number one cause of ESRD in the United States.

Glycemic Control Predicts Extrarenal Microvascular Complications, Not Renal Survival

While blood pressure, not glycemic control is a predictor of renal survival in diabetic patients, glycemic control does predict extrarenal microvascular complications. Researchers concluded that good metabolic control is important for black diabetic patients with renal disease.

Investigators from Wayne State University reviewed charts of all diabetic patients (a predominately black population) for renal function and microvascular and macrovascular disease; 154 had significant HbA1c measurements. After adjusting for age, duration of diabetes and renal function, there was no significant association of glycemic control with renal survival. Blood pressure was significantly associated with renal survival, but not with extrarenal microvascular complications after adjustment for glycemic control.

THE AMERICAN DIABETES ASSOCIATION'S 64TH SCIENTIFIC SESSIONS

The ADA's 64th Scientific Sessions were held from June 4 to 8 in Orlando, Fla.

Exenatide Improved Glucose Control, Restored Insulin Response

Exenatide, the first potential therapy in a new class of investigational drugs called incretin mimetics, significantly lowered glucose levels in a phase III study. The 30-week study followed 377 diabetic patients unable to achieve glycemic control using a maximum dose of sulfonylureas. Exenatide is being developed by Amylin and Eli Lilly and Company.

Patients were assigned 10 µg exenatide, 5 µg exenatide or placebo. Average HbA1c levels were 8.6% at the beginning of treatment; following treatment, patients assigned the 10-µg dose had an average reduction of 1% HbA1c. Patients also had an average weight loss of 2.2 lbs. Patients who chose to continue in a 52-week open-label study had sustained weight loss and HbA1c reductions.

"These data suggest that exenatide may address a fundamental defect of type 2 diabetes by enhancing the body's ability to produce and release its own insulin in a manner that mimics that of people without diabetes," said John Buse, MD, professor of medicine and director, Diabetes Care Center, University of North Carolina School of Medicine.

In a separate crossover study, exenatide restored first-phase insulin response. The new drug is derived by chemically copying the venom of gila monsters.

Less Nerve Damage Later with Intensive Diabetes Control Now

Tight control of type 1 diabetes results in reduced rates of nerve damage later, even when control has become less intense.

The Diabetes Control and Complications Trial (DCCT) was initiated 20 years ago and included 1,441 patients in a comparison of intensive versus conventional control. Most of those patients were enrolled the Epidemiology of Diabetes Interventions and Complications (EDIC) observation study, which provided the basis of these results.

"People who were treated with intensive therapy to try to keep their blood glucose levels as close to normal as possible for an average of 6 years continue to demonstrate a lower risk for developing neuropathy compared to those who were never treated with such intensive

therapy, even 8 years after the period of intensive therapy ended," reported Catherine L. Martin, MS, study coordinator for DCCT/EDIC at the University of Michigan in an ADA news release.

The initial DCCT results found that a 39% to 76% reduction in microvascular complications such as neuropathy, retinopathy and nephropathy was associated with intensive glucose control.

Heart Disease, Stroke Reduced Among Diabetic Patients Taking Atorvastatin

Atorvastatin reduced the risk of a first major cardiovascular event by more than one-third among patients with type 2 diabetes. Results of the Collaborative Atorvastatin Diabetes Study (CARDS) showed that 10 mg daily of atorvastatin (Lipitor, Pfizer) reduced the incidence of a major cardiovascular event by 37% and stroke by 48%.

The randomized, placebo-controlled trial involved 2,838 patients from 132 centers in the United Kingdom. The study was stopped early when the interim results showed a significant reduction in the risk for myocardial infarction, stroke or cardiovascular surgery. John Betteridge, MD, professor of endocrinology and metabolism at University College London, is the co-principal investigator.

CARDS is the first clinical trial to evaluate the use of a statin in people with type 2 diabetes and no previous history of heart disease or stroke.

VDT Might Improve Diabetic Peripheral Neuropathy Diagnosis

Vibration detection threshold (VDT) correlated with individual electrophysiological attributes and composite scores of lower limb nerve function in patients with DPN.

Vladimir Skljarevski, MD, and colleagues from Indianapolis evaluated 205 patients who were participating in a phase II multicenter clinical trial of roboxistaurin for the treatment of DPN. The values obtained from VDT were compared with composite scores of nerve function using a standardized neurological exam and electrophysiological measures. A significant correlation was found.

While neurological examination with nerve conduction studies are currently considered the gold standard, investigators said that alternative diagnostic methods are needed. VDT is more comfortable for the patient and does not require a highly skilled operator, therefore its use may lead to more frequent screenings and early diagnosis in the primary care setting. ■