SANDIEGO — Ruboxistaurin, a specific Diabetic Nephropathy Patients

New Drug Shows Promise for Metabolic Disorders

BY DOUG BRUNK
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SAN DIEGO — Ruboxistaurin, a specific protein kinase C beta inhibitor, had favorable effects on albuminuria and renal function in patients with diabetic nephropathy, according to results from the first human trial of the drug.

"Ruboxistaurin is a promising novel therapy that may improve upon established therapies for diabetic nephropathy," Katherine R. Tuttle, M.D., said at the annual scientific sessions of the American Diabetes Association.

A lot of data show 'that diabetic nephropathy, even in advanced stages, is potentially reversible. Perhaps this builds the bit of evidence. Large-scale trials should be performed to confirm its effectiveness and safety.'

Developed by Eli Lilly & Co., ruboxistaurin is the first of the specific protein kinase C inhibitors being investigated for the treatment of diabetic peripheral neuropathy, diabetic retinopathy, and diabetic nephropathy.

In a year-long multicenter, randomized, double-blind trial funded by Lilly, Dr. Tuttle and her associates randomized 123 subjects to receive ruboxistaurin 32 mg/day or placebo. Study participants who were taking ACE inhibitors, angiotensin receptor blockers, or both remained on the drugs for the entire trial.

Over the course of 12 months, investigators at 17 sites in the United States obtained periodic measurements of the participants’ urinary albumin/creatinine ratio (ACR), blood pressure, estimated glomerular filtration rate (GFR), and hemoglobin A1c levels.

By month 12, the mean ACR had decreased by 24% among subjects in the ruboxistaurin group but had not changed in the placebo group, reported Dr. Tuttle of Providence Medical Research Center and The Heart Institute of Spokane, Washington.

The change in urinary ACR in the ruboxistaurin group appeared as early as 1 month into the study and was maintained over the 12-month trial. The mean estimated GFR declined by a mean of 4.8 mL/min per year in the placebo group but did not change significantly in the ruboxistaurin group.

Blood pressure and hemoglobin A1c levels did not differ significantly between the two groups over the study period. The most frequently reported adverse event was hypertension, which required intervention in 8% of subjects in the placebo group, compared with none in the ruboxistaurin group.

Dr. Tuttle, who is a paid consultant to Lilly, noted that it will “take at least several hundred if not more” subjects per treatment arm to confirm the findings in a future trial.

Ruboxistaurin nephropathy patients in about 40% of people with type 2 diabetes and is responsible for 40%-50% of incident end-stage renal disease in the United States.

Becaplermin Improves Healing of Diabetic Neuropathic Foot Ulcers

BY HEIDI SPLUTE
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CHICAGO — Diabetic neuropathic foot ulcers treated with becaplermin were 30% more likely to heal during a 20-week study than ulcers not treated with the drug, David J. Margolis, M.D., said at the annual meeting of the Wound Healing Society.

The need for effective treatment is great, Dr. Margolis noted. Approximately 12% of diabetic patients develop foot ulcers; 80,000 amputations per year are attributed to diabetes.

In a retrospective cohort study of 206 patients, 10% were treated with becaplermin (Regranex), a topical recombinant human platelet-derived growth factor (rhPDGF).

The relative risk that the becaplermin-treated ulcers would heal after 2.5 weeks was 1.33 compared with standard care, and the relative risk of amputation was 0.65, similar to results from previous clinical trials, said Dr. Margolis, of the University of Pennsylvania. He and his colleagues estimated treatment effect was greatest for elderly patients, rather than by using propensity scores to control for selection bias.

Propensity studies involve additional probability and attempt to pin down which demographic factors contribute to results in a real-world setting. "We are trying to model why people received therapy," Dr. Margolis said. The cases were drawn from a database of patients treated between 1998 and 2004 at a wound care center affiliated with Curative Health Services. "Some people had only 2 weeks of treatment, and others had 20 weeks," Dr. Margolis noted. The mean length of treatment was 14 weeks.

Overall, 13% of the patients were treated with rhPDGF, and in general, these patients were more likely to be younger and male, and to have older wounds, than patients who were not treated with rhPDGF, he noted.

When asked how the Food and Drug Administration regards propensity studies, Dr. Margolis admitted that data of this type are not likely to prompt a change in drug labeling, for example. However, the FDA recognizes that the large sample size used in propensity score studies can provide useful information, he added.

The study was supported in part by funding from Ethicon Inc., which produces becaplermin (Regranex).