Notably, HbA1c percentage reductions at Week-54 for each active treatment group did not differ significantly from percentage reductions achieved at Week-24, suggesting that the treatment effect of each therapy held for a year and that the superior efficacy of combination sitagliptin/metformin was not diminished over a longer period of use.

Adverse events were generally comparable among the treatment groups. Rates of hypoglycemia were low across all groups, and rates of gastrointestinal adverse events were similar across all groups. There was a slight mean loss of body weight (less than 2 kg) in all groups except sitagliptin 100 mg (gain of less than 1 kg).

"In summary," said Dr. Williams-Herman, "in patients with type 2 diabetes inadequately controlled by diet and exercise, initial combination therapy with sitagliptin and metformin over one year showed consistent and substantial glycemic improvement, a small reduction in body weight, and a favorable safety profile."

Fenofibrate Treatment and Renal Function in Type 2 Diabetes: FIELD Helsinki Substudy

Results from a substudy of FIELD (Fenofibrate Intervention and Event Lowering in Diabetes), the largest study of fibrates to date, showed no evidence for direct nephroprotection from fenofibrate use [The Field Study Investigators. *Lancet* 2005]. There was, however, an increase in plasma creatinine, according to Anne Hiukka, MD, Helsinki University Central Hospital and Biomedicum, Finland.

FIELD included nearly 10,000 type 2 diabetes patients randomly assigned to fenofibrate 200 mg or placebo for 5 years. It showed no reduction in coronary heart disease events for fenofibrate, but did show some promise in spot samples of urinary albumin/creatinine ratio and self-reported retinal laser therapy, both markers for microvascular outcomes. Increases in plasma creatinine, through an as-yet unexplained mechanism, seem to be a class effect of the fibrates. While FIELD did show some significantly reduced progression of albuminuria for fenofibrate versus placebo, approximately three-fourths of patients in both groups had no change.

The current FIELD substudy, with evaluable results for 170 patients, investigated the effect of fenofibrate treatment on prespecified renal function parameters at baseline and at 2 and 5 years. Dr. Hiukka reported that in both groups after 5 years blood pressure dropped significantly and HbA1c remained unchanged. Fasting serum glucose dropped in both groups, but significantly only in the fenofibrate group (7.9 mmol/L baseline, 7.2 mmol/L 5-years; p=0.010). Although HDL-C remained unchanged in both groups, significant decreases in total cholesterol (~18%; p=0.001), LDL-C (~20%; p=0.001), and total triglycerides (~26%; p=0.001) were reported for fenofibrate treatment versus placebo.

In addition, plasma creatinine increased significantly with fenofibrate (p<0.001) versus placebo while urinary creatinine remained the same. Creatinine clearance decreased in both groups (Δ -2.0 mL/min/1.73m^2 placebo, Δ -8.5 mL/min/1.73m^2 fenofibrate; p=0.009 vs placebo). A similar pattern was observed for eGFR [estimated glomerular filtration rate]. While there were no differences in albuminuria and proteinuria rates between groups, nocturnal urinary albumin excretion rates decreased in both groups.

The suggestions of benefit in the overall FIELD study were not borne out in this substudy. Dr. Hiukka concluded, "The data provide no evidence for direct nephroprotection by fenofibrate. However, in clinical practice, increases in plasma creatinine with fenofibrate should be recognized and followed up." She noted that the clinical relevance of increased plasma creatinine with fenofibrate administration should be established through direct measures of renal function. "We can't speculate on the potential harm from this finding."

PREDICTIVE 303: Patient Self-Adjusted Dosing a Safe and Effective Alternative

In PREDICTIVE 303 (Predictable Results and Experience in Diabetes through Intensification and Control to Target: an International Variability Evaluation), patient-directed insulin dose adjustments of once-daily insulin detemir appeared to be a safe and effective alternative to physician-directed dose adjustments in a primary care setting.

The primary objective of PREDICTIVE 303, stated lead investigator Luigi F Meneghini, MD, Diabetes Research Institute, University of Miami Miller School of Medicine, Florida, United States, was to show that patient self-