

## Elevated HbA1c Associated with Cardiovascular Events in Non-Diabetics

Several large studies have shown that in diabetic patients, HbA1c is a strong predictor of cardiovascular disease, while in non-diabetics, this association is less clear. Results of the first study to examine the association of HbA1c with non-fatal cardiovascular disease in non-diabetics were reported by Esther van 't Riet, VU University Medical Center, Amsterdam, the Netherlands. The results showed that, even in non-diabetics, HbA1c elevation significantly increases the risk for non-fatal cardiovascular events.

The Hoorn Study is a population based cohort study of a general population in the Netherlands. The current analysis of cardiovascular events was based on data from 1,674 non-diabetic subjects from the Hoorn Study for whom data on HbA1c level, glucose level, and morbidity were available. Over the course of approximately 10 years, 385 non-fatal and 113 fatal cardiovascular events had occurred.

Esther van 't Riet reported that whether adjusting only for age and gender or for age and gender plus other traditional cardiovascular risk factors (eg, hypertension, smoking, LDL-cholesterol, triglycerides, and waist-to-hip ratio), subjects with HbA1c >5.6% had a significantly increased risk of a non-fatal cardiovascular event ( $p < 0.05$ ).

This association with fatal cardiovascular events was significant in the model that included only age and gender, but not when adjusted for the other traditional cardiovascular risk factors.

"The clinical meaning of this is that, even in subjects without diabetes, it is very important to maintain optimal glycemic control," she said. She added, however, that control of blood pressure and cholesterol are still more important than addressing HbA1c.

The study also examined the relationship between fasting plasma glucose and 2-hour-plasma glucose, finding no significant associations with cardiovascular disease, after correction for age, gender and other cardiovascular risk factors. Miss. van 't Riet speculated that the reason there was no association with 2-hour-plasma glucose (a relationship that has been reported in prior epidemiological studies) was that diabetic patients were excluded in the current analysis, whereas they were included in the previous studies. In addition, previous research not always adjusted for traditional cardiovascular disease risk factors.

## One-Year Data Show Combination Sitagliptin and Metformin Improves and Sustains Glucose Control in Type 2 Diabetes Compared to Metformin Alone

Debora Williams-Herman, MD, Senior Investigator at Merck Research Laboratories, Rahway, New Jersey, United States, presented results from a recent clinical trial that found that patients treated with a combination of sitagliptin and metformin achieved significant and sustained improvement in blood sugar control over a one-year period compared to metformin monotherapy, and that the combination therapy was generally well tolerated.

Following the initial 24-week placebo-controlled phase (n=1091) of the study, 748 subjects with a mean baseline HbA1c of 8.7% entered the open-label phase, continuing for another 30-weeks on their initial treatment regimens.

The groups were: sitagliptin 50 mg/metformin 1000 mg BID (n=157); sitagliptin 50 mg/metformin 500 mg BID (n=148); metformin 1000 mg BID (n=137); metformin 500 mg BID (n=122); and sitagliptin 100 mg once daily (n=106).

At 54 weeks, the investigators found a mean HbA1c reduction from baseline of 1.8% for subjects treated with combination sitagliptin 50 mg/metformin 1000 mg BID for up to 54 weeks (n=153). They also found mean HbA1c reductions from baseline of 1.4% for subjects treated with sitagliptin 50 mg/metformin 500 mg BID (n=147), 1.3% for subjects treated with metformin 1000 mg BID (n=134), 1.0% for subjects treated with metformin 500 mg BID (n=117), and 0.8% for subjects treated with sitagliptin 100 mg once daily (n=106).

In terms of achieving the target HbA1c of < 7%, 67% of the sitagliptin 50 mg/metformin 1000 mg BID subjects achieved the target A1c, compared to 44% on metformin 1000 mg BID monotherapy.

Dr. Williams-Herman reported that 48% of the subjects treated with sitagliptin 50 mg/metformin 500 mg BID, 25% of those treated with metformin 500 mg BID, and 23% of those treated with sitagliptin 100 mg once daily reached the target HbA1c goal.