Research team responds to concerns about international insulin drug trial

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Accumulating safety data from the large, international ORIGIN trial have been reviewed by its independent data monitoring committee, who have concluded that there is no cause for concern.

This six-year study, which is lead by McMaster University professors Dr. Hertzel Gerstein and Dr. Salim Yusuf of the Population Health Research Institute, is determining whether insulin glargine and/or omega 3 fatty acids can reduce cardiovascular events in 12,578 people with elevated blood sugar levels from around the world.

The data monitoring committee, headed by Professor Rory Collins of the University of Oxford, is auditing the trial for safety, but did extra reviews recently after an article in the European journal *Diabetologia* in June suggested a connection between use of insulin glargine and cancer.

The committee reviewed all data collected to date in the two treatment groups and concluded there is no cause for concern. It also found no reason to alter the design of the study for safety reasons.

"The ORIGIN investigators are reassured by the findings of the independent data committee," said Dr. Gerstein. "We look forward to continuing this trial, which will provide critical information regarding the effect of insulin glargine and omega 3 fatty acids on important clinical outcomes."

The ORIGIN (Outcome Reduction with an Initial Glargine Intervention)

trial is sponsored by Sanofi-Aventis which manufactures insulin glargine. The study involves patients from every continent and is co-ordinated by researchers at the Population Health Research Institute at McMaster University and Hamilton Health Sciences in Hamilton, Ontario, Canada. The results are expected in 2011.

Recently, the following statement about the concerns was issued to the collaborating researchers involved in the study:

Regarding Glargine Insulin and Cancer

A recently published database analysis in the journal *Diabetologia* suggested a link between the use of glargine insulin and cancer. Although the results of this report were not confirmed in other database analyses, it has generated questions about the safety of glargine insulin. Such questions can best be answered by prospective, long-term follow-up of large numbers of patients enrolled in randomized trials of glargine versus other therapies.

The ORIGIN trial (Outcome Reduction with an Initial Glargine INtervention) randomized more than 12,500 people with dysglycemia (elevated glucose levels due to impaired fasting glucose, impaired glucose tolerance or early diabetes) to one injection of insulin glargine per day versus usual care. It is determining whether targeting normal fasting glucose levels with insulin glargine reduces cardiovascular outcomes compared to standard management. Participants have been followed for an average of four years to date for a total exposure of more than 50,000 person-years. Data are collected related to all major serious health outcomes, including cancers. Accumulating data are reviewed regularly by an Independent Data Monitoring Committee charged with auditing the safety of the trial. In light of the questions raised by the recent publication, this committee of experts has recently reviewed data related to cancers in both treatment groups and has

concluded that there is no cause for concern and no reason to alter the design of the study for safety reasons.

The study is due to end in 2011, when detailed analyses will be published. In the meantime, the data will continue to be collected and audited for safety by this independent group. To maintain a high-quality and unbiased study, researchers and the manufacturer of insulin glargine do not (and will continue to not) have access to data summarizing outcomes by treatment group until the study is over.

Source: McMaster University (news : web)