Ischemic Cardiovascular Event Rates in Pioglitazone Trials

	Pioglitazone Patients	Controls	Relative Risk Reduction
All trials	4.4% (n = 8,554)	5.7% (n = 7,836)	17%
PROactive trial	11.6% (n = 2,605)	13.6% (n = 2,633)	16%
Trials other than PROactive	1.2% (n = 5,949)	1.8% (n = 5,203)	25%

Note: Results based on 19 clinical trials totaling 16,390 patients with type 2 diabetes.
Source: Dr. Perez

ELSEVIER GLOBAL MEDICAL NEWS

Pioglitazone Cut Ischemic Cardiac Event Rate by 17%

BY BRUCE JANCIN
Denver Bureau

MUNICH — Treating type 2 diabetic patients with the insulin-sensitizing drug pioglitazone conferred a highly significant 17% reduction in ischemic cardiovascular events, according to a large meta-analysis.

The relative risk reduction was comparable among patients at relatively low cardiovascular risk and those at very high risk, Dr. Alfonzo Perez reported at the annual congress of the European Society of Cardiology.

The meta-analysis included 19 randomized, double-blind clinical trials totaling 16,390 patients with type 2 diabetes. The comparator was most often metformin, a sulfonylurea drug, or placebo. The trials ranged in duration from 4 months to nearly 4 years.

The primary end point in the meta-analysis was a composite comprising all-cause mortality, acute MI, or stroke. The rate was consistently lower in the pioglitazone (Actos) group from the earliest point of follow-up, although the event curves diverged significantly starting only at about 1 year, said Dr. Perez of the Takeda Global Research and Development Center Inc., which markets the drug.

The largest contribution to the meta-analysis came from the 5,238-patient Prospective Pioglitazone Clinical Trial in Macrovascular Events (PROactive), which was also the only study designed to look at cardiovascular outcomes. In the other 18 trials, cardiovascular events were garnered from the detailed adverse event reports.

The relative risk reduction was comparable among patients at relatively low risk and those at very high risk.

DR. PEREZ

PROactive (Lancet 2005;366:1279-89) showed a significant 16% relative risk reduction in the combined end point used in the meta-analysis. But the PROactive population was at far higher cardiovascular risk than most participants in the other trials. For example, at baseline, 48% of PROactive participants had a history of MI and 19% had a prior stroke, compared with just 8% and 1%, respectively, in the other studies. Also, patients in PROactive averaged a nearly 10-year history of diabetes, 3 years longer than patients in the other trials.

For this reason, Dr. Perez and his coinvestigators analyzed the outcome data both with and without PROactive included. That way, he explained, it would be possible to determine whether the PROactive benefits extended to type 2 diabetic patients at lower cardiovascular risk. This indeed was the case (see chart).

Pioglitazone is known to increase the risks of edema and heart failure. The rate of heart failure in the meta-analysis was 2.3% in the pioglitazone group and 1.8% in controls.

However, patients in the pioglitazone group who developed heart failure did not have a higher mortality rate than did controls with heart failure. In fact, their mortality rate was 24%, compared with 32% among controls with heart failure, Dr. Perez continued. ■