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A new controlled randomized trial for pioglitazone

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Morbidity and mortality due to macro vascular complications constitute the biggest risk for patients with diabetes, and type 2 diabetes is associated with a high risk of fatal or non-fatal myocardial infarction and stroke. Pioglitazone (agonists of peroxisome proliferator-activated receptor gamma – PPAR gamma) is known to improve glycemic control and also to posses anti-inflammatory and vascular properties, that may have an impact on clinical vascular outcome. ❑

PROactive Trial was designed to investigate whether the addition of pioglitazone to patients' usual medications for glycemic, lipidemic and hypertensive management will reduce total mortality and macrovascular morbidity in high-risk patients. This was a randomized, double-blind outcome study in 5238 patients with type 2 diabetes, with a 4 years follow-up period. The patients had history of macrovascular disease and were managed with diet and/or blood glucose-lowering drugs. The subgroups were randomized to receive oral pioglitazone titrated from 15 mg to 45 mg (n = 2605) or matching placebo (n = 2633) in addition to existing therapy.

Compared to placebo, pioglitazone was associated with a significant decrease in the composite of all-cause mortality, non-fatal myocardial infarction and stroke (RR = 0.84, 0.72-0.98, $p<0.05$) in patients with type 2 diabetes who have a high risk of macro vascular events. Overall safety and tolerability were good and mortality rates from heart failure did not differ between groups.

The results of PROactive study provide important information about the pioglitazone ability to reduce macro vascular mortality and morbidity in high-risk population and could provide the first data on the modification of macro vascular disease in type 2 diabetes by a glucose-lowering agent. ❑

Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial

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