

Effects of Long-Term Pioglitazone Therapy on Serum Lipid Profiles in High-Risk Type 2 Diabetes Patients: Results From the PROactive Study

Robert Spanheimer, Meng Tan, John Yates, on behalf of the PROactive Investigators.

Diabetic dyslipidemia is characterized by high triglyceride (TGs) and low HDL-C levels. These lipid abnormalities contribute to the increased risk of atherosclerosis in patients with type 2 diabetes (T2D). We evaluated the effects of pioglitazone (PIO) therapy on lipid profiles over 2 ½ years in patients with T2D in the PROactive Study.

The PROactive Study was a double-blind, placebo-controlled study in which 5,238 patients with T2D and macrovascular disease were randomized to PIO or matching placebo (PBO) in addition to their existing glucose-lowering and CV medication, including anti-hypertensive, antiplatelet, and lipid-modifying drugs. Patients started with 15 mg doses of PIO (or PBO), and were titrated to a maximum tolerated dose of 45 mg, which was continued at the highest tolerated dose for the study duration. Mean follow up was 34.5 months, and mean exposure to study drug was 30 months. Laboratory assessments for fasting lipid levels were performed every 6 months. At baseline, 1311 (50.3%) PIO patients and 1382 (52.5%) PBO patients were on either fibrate or statin therapy. During the study, investigators were instructed to aim for the IDF [EU] treatment targets for lipids.

At study entry, mean TGs (197.5 and 199.3 mg/dL), HDL-C (44.9 and 44.9 mg/dL), and LDL-C (114.5 and 114.8 mg/dL) levels were similar in the PIO and PBO groups.

Lipid	PIO ^a n=2605	PBO ^a n=2633	P-Value Between Rx
TGs	-1.7	+12.5	<0.0001
HDL-C	+21.2	+11.3	<0.0001
LDL-C	+12.1	+8.4	0.0034
LDL-C/HDL-C	-4.39	-0.04	<0.0001

^a Mean Percent Change From Baseline at Study End

Treatment with PIO significantly improved abnormalities in TG and HDL-C associated with diabetic dyslipidemia. The LDL-C/HDL-C ratio was also significantly improved compared to PBO, despite a greater increase in LDL-C. These between-group differences were seen as early as 6 months after initiating treatment and remained significant throughout the study. At study end, 1485 (61.5%) PIO patients and 1515 (62.5%) PBO patients were on statin or fibrate

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therapy. Thus, improvements in lipid values with PIO compared to PBO were seen, despite known benefits of the lipid-altering medication being taken in a similar proportion of patients in the two treatment groups.