

Pioglitazone in Triple Oral Therapy: Long-Term Glycemic Results From PROactive

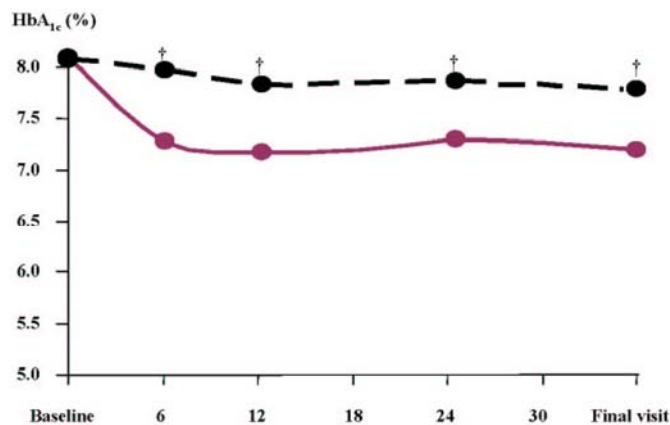
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Type 2 diabetes (T2D) is a progressive disease that eventually requires multiple agent therapy, including insulin. We looked at the long-term glycemic effects of pioglitazone (PIO) add-on therapy in a cohort of patients with T2D and macrovascular disease who entered PROactive on metformin plus sulfonylurea (MET+SU).

PROactive randomized patients to either PIO or PBO, in addition to other blood-glucose and cardiovascular medications, which were adjusted as necessary to treat to IDF target. PIO doses were force-titrated to 45 mg. Mean follow-up was 34.5 months. Within the MET+SU cohort (n=1314), mean baseline A1C and lipid values were similar between groups.

Significantly greater reductions in A1C were noted with PIO compared with PBO ($p<0.0001$).

Changes in glycemic control (as measured by HbA_{1c}) over time with PIO (solid lines) or PBO (dashed lines) in patients receiving MET plus SU



† $p<0.0001$ versus placebo

The significant improvement in A1C with PIO vs PBO was shown with the following changes in associated glucose-lowering medication: more PIO patients had either MET or SU dropped from their regimen (16%) and fewer had insulin added to their regimen (16%) than PBO patients (8% and 31%, respectively). The MET dose increased by 19 mg with PIO vs 228 mg with PBO ($p<0.0001$). SU doses decreased or were unchanged in the PIO group (glibenclamide = -1.4 mg vs -0.2 mg for PBO, $p=0.013$; gliclazide = -33 mg vs -23 mg for PBO,

p=0.270; glimepiride = 0 mg vs +0.6 mg for PBO, p=0.009).

Edema occurred in 29% of patients in the PIO group vs 17% in the PBO group (p<0.0001) and hypoglycemia occurred in 27% in the PIO group vs 20% in the PBO group (p=0.0013). There was a weight increase of 4.1 kg in the PIO group and a decrease of 0.7 kg in the PBO group (p<0.0001).

Intensifying a dual oral therapy regimen to a triple oral regimen by adding PIO resulted in a sustained improvement in glycemic control and a reduced need for insulin, with a good overall safety profile.