

**Pioglitazone Delays the Need for Permanent Insulin Use: Results From PROactive**

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Type 2 diabetes (T2D) is a progressive disease requiring multiple therapies; many patients eventually need insulin. We evaluated the time to permanent insulin use in patients not treated with insulin at baseline in PROactive.

PROactive randomized 5238 patients with T2D and macrovascular disease to PIO (up to 45 mg) or placebo (PBO). Two-thirds of the total study population (PIO=1741; PBO=1737) were not on insulin at baseline. Within this cohort, baseline mean A1C was 7.9% in both groups. We defined permanent insulin therapy as daily use for ≥90 days, or ongoing use at death/final visit.

Twice as many PBO (n=362) as PIO patients (n=183) progressed to permanent insulin use. At mean follow-up, the Kaplan-Meier rates for time to permanent insulin use were 11% for PIO and 21% for PBO (HR=0.47; 95%CI:0.39,0.56; P<0.0001). PIO patients not on insulin at baseline showed improved A1C compared with PBO patients at final visit (6.97% vs 7.49%, P<0.0001). The 2-fold increase in insulin use in the PBO group was irrespective of the baseline oral regimen. Half as many in the PIO (58 [3.6%]) as in the PBO group (117 [7.2%]) were on insulin without MET or SU at study end.

Proportion receiving glucose-lowering regimens without insulin at baseline and with insulin at final visit				
	PIO N=1741		PBO N=1737	
	Baseline oral treatment, n (%)	Receiving Insulin at Final Visit n/N* (%)	Baseline oral treatment, n (%)	Receiving Insulin at Final Visit n/N* (%)
MET alone	253 (14.5)	8/238 (3.4)	261 (15.0)	16/247 (6.5)
SU alone	508 (29.2)	30/476 (6.3)	493 (28.4)	67/453 (14.8)
MET+SU	654 (37.6)	95/613 (15.5)	660 (38.0)	190/610 (31.1)
Other <sup>^</sup>	326 (18.7)	24/305 (7.9)	323 (18.6)	55/304 (18.1)

**\*N with final visit data available <sup>^</sup>No medication, or acarbose or repaglinide (+/- MET +/- SU)**

More patients in the PIO group had edema (26% vs 15%; P<0.0001) and hypoglycemia (21% vs 16%; P<0.0001).

Progression to permanent insulin use was reduced by 50% at 3 years with PIO vs PBO and better glycemic control was seen with PIO. The decreased need for insulin in the PIO group was irrespective of baseline treatment.