Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy.

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BACKGROUND: The efficacy of thiazolidinediones, as compared with other oral glucose-lowering medications, in maintaining long-term glycemic control in type 2 diabetes is not known. **METHODS:** We evaluated rosiglitazone, metformin, and glyburide as initial treatment for recently diagnosed type 2 diabetes in a double-blind, randomized, controlled clinical trial involving 4360 patients. The patients were treated for a median of 4.0 years. The primary outcome was the time to monotherapy failure, which was defined as a confirmed level of fasting plasma glucose of more than 180 mg per deciliter (10.0 mmol per liter), for rosiglitazone, as compared with metformin or glyburide. Prespecified secondary outcomes were levels of fasting plasma glucose and glycated hemoglobin, insulin sensitivity, and beta-cell function. **RESULTS:** Kaplan-Meier analysis showed a cumulative incidence of monotherapy failure at 5 years of 15% with rosiglitazone, 21% with metformin, and 34% with glyburide. This represents a risk reduction of 32% for rosiglitazone, as compared with metformin, and 63%, as compared with glyburide ($P<0.001$ for both comparisons). The difference in the durability of the treatment effect was greater between rosiglitazone and glyburide than between rosiglitazone and metformin. Glyburide was associated with a lower risk of cardiovascular events (including congestive heart failure) than was rosiglitazone ($P<0.05$), and the risk associated with metformin was similar to that with rosiglitazone. Rosiglitazone was associated with more weight gain and edema than either metformin or glyburide but with fewer gastrointestinal events than metformin and with less hypoglycemia than glyburide ($P<0.001$ for all comparisons). **CONCLUSIONS:** The potential risks and benefits, the profile of adverse events, and the costs of these three drugs should all be considered to help inform the choice of pharmacotherapy for patients with type 2 diabetes. (ClinicalTrials.gov number, NCT00279045 [ClinicalTrials.gov].).