Review: Rosiglitazone or pioglitazone as add-on therapy is effective for glycemic control in type 2 diabetes


**Question**
In patients with type 2 diabetes mellitus, is rosiglitazone or pioglitazone more effective than other antidiabetic agents when used either as monotherapy or add-on therapy?

**Data Sources**
Studies were identified by searching 7 databases and Web sites of regulatory and health technology-assessment agencies, reviewing bibliographies of selected articles, and contacting manufacturers.

**Study Selection**
Studies were selected if they were randomized controlled trials (RCTs) comparing rosiglitazone or pioglitazone, as monotherapy or as add-on therapy, with other antidiabetic agents in patients $> 18$ years of age with type 2 diabetes.

**Data Extraction**
Data were extracted independently by 2 reviewers on study quality using the Jadad 5-point scale, study length, comparator drug, dosage, and results. The main outcomes were mean differences from baseline to endpoint in glycosylated hemoglobin (HbA1c) and fasting plasma glucose (FPG) levels.

**Main Results**
11 RCTs of rosiglitazone and 8 RCTs of pioglitazone met the selection criteria.

2 RCTs of rosiglitazone monotherapy could be pooled: Rosiglitazone decreased FPG but not HbA1c levels more than glyburide or repaglinide (Table). Pooling among add-on therapy studies showed rosiglitazone decreased HbA1c (8 RCTs) and FPG (7 RCTs) levels more than continuing monotherapy with a nonthiazolidinedione agent (Table). 2 trials of monotherapy with pioglitazone that could be pooled showed less decrease in HbA1c levels with pioglitazone than with glyburide or repaglinide (Table). 1 trial showed a nonsignificantly smaller decrease in FPG level with pioglitazone monotherapy than with repaglinide (Table). Add-on therapy with pioglitazone decreased HbA1c (6 RCTs) and FPG (5 RCTs) levels more than nonthiazolidinedione monotherapy (Table).

**Conclusions**
In patients with type 2 diabetes, little evidence exists to support rosiglitazone or pioglitazone being more effective monotherapy than existing antidiabetic agents. When added to a nonthiazolidinedione agent, both drugs reduce glycosylated hemoglobin and fasting plasma glucose levels more than monotherapy with a nonthiazolidinedione agent.

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For correspondence: Mr. M. Boucher, CCOHTA, Ottawa, Ontario, Canada. E-mail michellb@ccohta.ca.

### Rosiglitazone (Ros) or pioglitazone (Pio) vs other antidiabetic drugs for type 2 diabetes mellitus*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Interventions</th>
<th>Number of trials</th>
<th>Study duration (wk)</th>
<th>Weighted mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>Ros monotherapy</td>
<td>2</td>
<td>24 to 52</td>
<td>$-0.08$ ($-0.65$ to $0.49$)†</td>
</tr>
<tr>
<td></td>
<td>Pio monotherapy</td>
<td>2</td>
<td>24 to 26</td>
<td>$0.46$ ($0.03$ to $0.90$)</td>
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<tr>
<td></td>
<td>Ros add-on</td>
<td>8</td>
<td>24 to 26</td>
<td>$-1.29$ ($-1.37$ to $-1.22$)</td>
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<tr>
<td></td>
<td>Pio add-on</td>
<td>6</td>
<td>12 to 24</td>
<td>$-1.29$ ($-1.60$ to $-0.99$)</td>
</tr>
<tr>
<td>FPG (mmol/L)</td>
<td>Ros monotherapy</td>
<td>2</td>
<td>24 to 52</td>
<td>$-0.62$ ($-1.07$ to $-0.17$)</td>
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<tr>
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<td>Pio monotherapy</td>
<td>1</td>
<td>24</td>
<td>$0.89$ ($-0.26$ to $2.04$)†</td>
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<tr>
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<td>Ros add-on</td>
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<td>24 to 26</td>
<td>$-2.82$ ($-3.15$ to $-2.48$)</td>
</tr>
<tr>
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<td>Pio add-on</td>
<td>5</td>
<td>12 to 24</td>
<td>$-2.87$ ($-3.59$ to $-2.15$)</td>
</tr>
</tbody>
</table>

*HbA1c = glycosylated hemoglobin; FPG = fasting plasma glucose. CI defined in Glossary. A random-effects model was used.

†Not significant.

Boucher and colleagues showed that the introduction of thiazolidinediones can have an important effect on the budget of publicly funded drug programs in Canada. A full economic analysis to help better understand the true costs of rosiglitazone and pioglitazone is not available.

Putting the review in the context of current clinical need and practice, PPAR-γ agonists could be considered appropriate add-on therapy in patients already taking oral glucose-lowering therapy, or as monotherapy where oral glucose-lowering drugs are not tolerated. The precise role of PPAR-γ agonists in combination with insulin injections has yet to be established.

Philip Home, DM, DPhil, FRCP
University of Newcastle upon Tyne
Newcastle upon Tyne, England, UK

**References**