**Therapeutics**

**Vildagliptin was noninferior to rosiglitazone for glycemic control in type 2 diabetes but caused less weight gain**


**Clinical impact ratings:** Endocrinology ★★★★★☆

**Question**
In patients with type 2 diabetes, what are the relative efficacy and tolerability of vildagliptin and rosiglitazone?

**Methods**

**Design:** Randomized controlled noninferiority trial.

**Allocation:** [Concealed]†.*

**Blinding:** Blinded [patients, clinicians, data collectors, outcome assessors, data analysts, and monitoring committee]†.*

**Follow-up period:** 24 weeks.

**Setting:** 202 centers in 11 countries in the Americas and Europe.

**Patients:** 786 patients 18 to 80 years of age (mean age 54 y, 58% men) with type 2 diabetes, hemoglobin A1c (HbA1c) level 7.5% to 11.0% (mean 8.7%), fasting plasma glucose level < 15 mmol/L (mean 10.3 mmol/L), body mass index 22 to 45 kg/m2 (mean 32 kg/m2), no drug treatment in the previous 12 weeks, and no antidiabetic agent targeted adverse effects (e.g., weight gain, heart failure, retinal edema, and osteoporotic fractures), and with the glitazars, agents that lower HbA1c level but seem to have an ever-increasing list of patient-important outcomes as prevention of diabetes complications and safety, must occur before the enthusiastic incorporation of these drugs into practice.

We learned this lesson with the glitazones, agents that also lower HbA1c level but caused less weight gain and a better lipid profile.

**Conclusion**
In patients with type 2 diabetes, vildagliptin was noninferior to rosiglitazone for glycemic control and resulted in less weight gain and a better lipid profile.

**Source of funding:** Novartis Pharmaceuticals.

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*See Glossary.
†Information provided by author.

**Vildagliptin vs rosiglitazone for type 2 diabetes at 24 weeks‡**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Change from baseline</th>
<th>Difference in mean change from baseline 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin A1c level</td>
<td>−1.1%</td>
<td>−1.3%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Fasting plasma glucose level (mmol/L)</td>
<td>−1.3</td>
<td>−2.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>−0.3</td>
<td>1.6</td>
<td>−1.9</td>
</tr>
</tbody>
</table>

‡Criterion for noninferiority was met because the upper limit of the CI was < 0.4%.

**Commentary**

The gliptins are new oral agents for the treatment of type 2 diabetes. The U.S. Food and Drug Administration has begun approval of these drugs with trials designed to show that their use reduces HbA1c level by about 1% as single agents, similar to glitazones, as shown in the trial by Rosenstock and colleagues, and as add-on agents with metformin or glitazones. However, measurement of HbA1c level in patients with type 2 diabetes may not capture all the benefits and downsides of new diabetes agents. Thus, large trials of sufficient duration, with such patient-important outcomes as prevention of diabetes complications and safety, must occur before the enthusiastic incorporation of these drugs into practice.

We learned this lesson with the glitazones, agents that also lower HbA1c level but seem to have an ever-increasing list of patient-important adverse effects (e.g., weight gain, heart failure, retinal edema, and osteoporotic fractures), and with the glitazars, agents that lower HbA1c level and were on the verge of approval, except for data that suggested increased risk for cardiovascular events (1).

The absence of reliable data on patient-important benefits forces patients and clinicians to choose among the available diabetes medications based on the relative importance of avoiding short-term harms and costs. Patients interested in minimizing cost and weight gain may choose metformin, which was associated with reduced risks for death and other important diabetes-related complications in the U.K. Prospective Diabetes Study (2). Metformin shares the favorable side-effect profile of the gliptins (minimal effect on weight and hypoglycemia) and would have been a helpful comparator in this monotherapy trial. If proved similar in HbA1c level reduction, metformin would, however, retain its central role in the management of type 2 diabetes because of its long track record of safety and lower cost.

As it stands, gliptins are interesting new agents that reduce HbA1c level without major effect on weight and hypoglycemia but at increased cost and with uncertainty about harms and long-term benefits.

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**References**