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

Rosenstock J, Baron MA, Dejager S, Mills D, Schweizer A. **Comparison of vildagliptin and rosiglitazone monotherapy in patients with type 2 diabetes: a 24-week, double-blind, randomized trial.** Diabetes Care. 2007;30:217-23.

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 A_{1c} (HbA_{1c}) 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/m^2 (mean 32 kg/m^2), no drug treatment in the previous 12 weeks, and no antidiabetic agent for > 3 consecutive months in the past. Patients with a history of type 1 diabetes, acute metabolic diabetic complications, or serious heart or liver disease were excluded.

Intervention: Vildagliptin, 100 mg daily in 2 divided doses (n = 519), or rosiglitazone, 8 mg daily in a single dose (n = 267). Placebo tablets for the alternate treatment were used to maintain blinding.

Outcomes: Change from baseline in HbA_{1c}, fasting plasma glucose, and fasting plasma lipid levels and in body weight.

Patient follow-up: 86% (intention-to-treat analysis).

MAIN RESULTS

Both drugs reduced HbA_{1c} level to a similar extent, but vildagliptin did not reduce fasting plasma glucose level as much as did rosiglitazone (Table). Body weight increased in the rosiglitazone group but not in the vildagliptin group (Table). Vildagliptin reduced fasting plasma lipid levels more than did rosiglitazone: difference in mean change was –9% for triglycerides, –14% for total cholesterol, –16% for low-density lipoprotein cholesterol, –16% for non-high density lipoprotein (HDL) cholesterol, and –9% for total-to-HDL cholesterol ($P \geq 0.01$ for all). The increase in HDL cholesterol level was lower in the vildagliptin group (4% vs 9%, $P = 0.003$). Groups did not differ for overall adverse events, including hypoglycemia (1 mild event in each group).

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‡

Outcomes	Change from baseline		Difference in mean change from baseline 95% CI	
	Vildagliptin	Rosiglitazone		
Hemoglobin A_{1c} level	–1.1%	–1.3%	0.2%	–0.01 to 0.39§
				P value
Fasting plasma glucose level (mmol/L)	–1.3	–2.3	1.0	< 0.001
Body weight (kg)	–0.3	1.6	–1.9	< 0.001

‡CI defined in Glossary.

§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 HbA_{1c} 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 HbA_{1c} 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 HbA_{1c} 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 HbA_{1c} 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 HbA_{1c} 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 HbA_{1c} 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

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