

Incretin Mimetic Outperforms Sulfonylurea in Early Type 2 Diabetes

Liraglutide led to better glucose control and more weight loss at 1 year than did glimepiride.

Incretin mimetics stimulate glucose-related insulin secretion, inhibit glucagon secretion, and quell appetite in patients with type 2 diabetes. Exenatide (Byetta), the only incretin-mimetic drug that is available currently in the U.S., requires twice-daily injections, although a weekly formulation is in development ([JW Oct 16 2008](#)). Liraglutide is an investigational incretin-mimetic drug that can be injected once daily.

With funding from the manufacturer of liraglutide, investigators randomized 746 patients with early type 2 diabetes to daily liraglutide (1.2 mg or 1.8 mg) or the sulfonylurea glimepiride (8 mg). Mean baseline glycosylated hemoglobin (HbA_{1c}) and fasting plasma glucose levels were 8.2% and 171 mg/dL, respectively. After 1 year, patients who received high- or low-dose liraglutide had significantly greater declines in mean HbA_{1c} values than did patients who received glimepiride (declines of 1.14% and 0.84% vs. 0.51%, respectively); mean fasting plasma glucose levels also declined more with liraglutide (26 mg/dL, 15 mg/dL, and 5 mg/dL, respectively). On average, patients who received liraglutide lost 2 kg of body weight, whereas those who received glimepiride gained 1 kg — a significant difference. Liraglutide recipients experienced significantly fewer mean episodes of hypoglycemia and more nausea episodes than did glimepiride recipients.

Comment: This study, the longest randomized trial of an incretin mimetic, suggests that liraglutide is superior to a sulfonylurea as monotherapy for patients with early type 2 diabetes. Its efficacy compared with that of metformin (the currently recommended first-line drug; [JW Feb 3 2009](#)), its long-term effects on clinical endpoints, and its role in treatment of more-advanced disease remain to be established.

— [Bruce Soloway, MD](#)

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Garber A et al. Liraglutide versus glimepiride monotherapy for type 2 diabetes (LEAD-3 Mono): A randomised, 52-week, phase III, double-blind, parallel-treatment trial. *Lancet* 2009 Feb 7; 373:473.