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Vildagliptin

A Viewpoint by Marc Evans

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Type 2 diabetes mellitus accounts for up to 95% of patients with diabetes and results from defective insulin secretion on the background of insulin resistance. The incretin hormones are important factors in maintaining insulin secretion. Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide (GLP)-1 are intestinal hormones that stimulate insulin secretion following glucose ingestion, thus exerting hypoglycaemic effects. GLP-1 also decreases glucagon secretion and increases both β-cell mass and function. Both GIP and GLP-1 are decreased in type 2 diabetes, and endogenous GLP-1 has a short half-life of 1–2 minutes because of its inactivation by the catabolic enzyme dipeptidyl peptidase-4 (DPP-4).

GLP-1 analogues, GLP-1 peptide agonists and GLP-1 fusion proteins are potential therapeutic options to increase the bioavailability of GLP-1, but these agents are poorly absorbed orally and must be administered intravenously or subcutaneously. An alternative approach to increasing the proportion of active GLP-1 is to inactivate DPP-4.

Vildagliptin (Galvus®)[1] is a low-molecular-weight orally active DPP-4 inhibitor which may be administered once or twice daily with a dose range of 50–100 mg/day. It has a plasma half-life of <2 hours. In clinical studies, vildagliptin reduced glycosylated haemoglobin by up to 1% when used as monotherapy in active comparator trials, demonstrating noninferiority to rosiglitazone but not to metformin, or as combination therapy with insulin, pioglitazone or metformin. Vildagliptin was well tolerated with no significant weight gain, hypoglycaemic episodes or gastrointestinal adverse events, and with less weight gain compared with thiazolidinedione therapy and fewer gastrointestinal adverse events compared with metformin.

Vildagliptin is currently undergoing pre-approval evaluation in the US as an oral therapy for type 2 diabetes. By increasing bioavailable GLP-1 along with direct potential effects of DPP-4 inhibition on increasing β-cell mass, vildagliptin has the potential to influence glucose metabolism in people with type 2 diabetes. Together with a favourable tolerability profile, these features suggest that vildagliptin may be a valuable addition to current antidiabetic therapies. ▲

1 The use of trade names is for product identification purposes only and does not imply endorsement.