

Update On Gut Hormone-based Diabetes Treatment

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Abstract

Gut hormones are peptide hormones produced by the digestive tract that regulate digestion, nutrient absorption and metabolism eg. GLP-1, GIP, Glucagon, Amylin. The earliest gut hormone-based therapy for diabetes is the DPP-4 inhibitors eg. Vildagliptin, Sitagliptin, Linagliptin, which inhibit the DPP-4 enzyme that breaks down the incretin hormones (GLP-1 and GIP). The increase in circulating GLP-1 and GIP result in improve glycemia. The next class is the GLP-1 receptor agonist (GLP-1RA) which is based either on the exendin molecule (eg. Exenatide, Lixisenatide) or the human GLP-1 molecule (eg. Liraglutide, Dulaglutide, Semaglutide). The advantage of these GLP-1RA is the benefit of weight reduction in addition to glucose lowering and Liraglutide and Semaglutide have also been approved as obesity management medication in people with obesity without diabetes. GLP-1RAs (Liraglutide, Dulaglutide, Semaglutide) have also been shown to reduce the risk of major CV events in people with diabetes and more recently, Semaglutide have also been shown to reduce the risk of major CV events in people with obesity without diabetes. The newest class of gut hormone-based therapy is the dual incretin (GLP-1 and GIP) receptor agonist, Tirzepatide, which can result in more glucose lowering and weight reduction. This agent has also been approved as obesity management medication in people with obesity without diabetes.

There are now a number of agents being developed for the treatment of diabetes and obesity. Glucagon receptor (GCGR) agonism has been shown to increase energy expenditure. Hence the development of GLP-1RA and GCGR agonist is expected to provide superior body weight reduction versus GLP-1RA alone. Mazdutide and Survodutide are 2 such agents being developed. Triple receptor agonist (GLP-1/GIP/GCGR agonist), Retatrutide, has been developed and shown to result in more glucose and body weight reduction. Other agents being studied are GLP-1 and Amylin receptor agonist (CagriSema, Amycretin) and GLP-1RA and GIP-R inhibitor (MariTide). In the oral formulation, small molecule GLP-1RA, Orforglipron and oral Amycretin are in the development.

In summary, gut hormone-based therapy has shown remarkable success not only for diabetes but also for obesity management. It also has the potential to reduce long term diabetes and obesity complications such as CV and CKD events. [*J Assoc Clin Endocrinol Diabetol Bangladesh, 2025;4(Suppl 1): S6*]

Keywords: Gut hormones, Obesity, GLP-1 receptor agonist (GLP-1RA), Dual incretin (GLP-1 and GIP) receptor agonist, Triple receptor agonist (GLP-1/GIP/GCGR agonist)

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