CO94

Advancing Diabetes Care: Novel Drug Interventions in the Management and Control of Type 2 Diabetes Mellitus

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Introduction

- Diabetes mellitus is a chronic metabolic condition characterized by elevated blood glucose levels, leading to damage in various organs such as the heart, blood vessels, eyes, kidneys, and nerves.
- In 2019, approximately 463 million people were affected by T2DM globally, and it is projected that the number will increase to 578 million by 2030 and reach 700 million by 2045—a 51% rise.
- The evaluation of a new diabetes drug can include its impact on weight loss or prevention of weight gain. Also, drugs that can effectively lower HbA1c levels are effective treatments for T2DM.

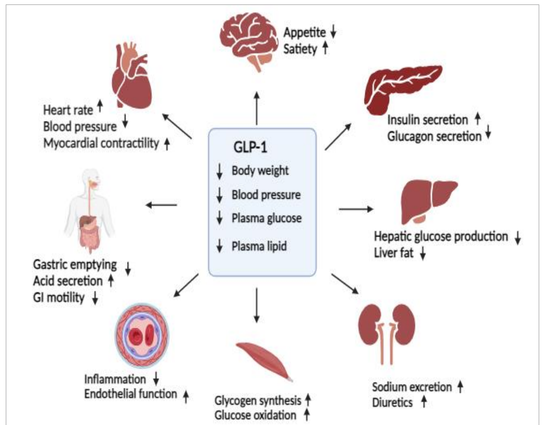

Fig 1. Mechanism of action of GLP-1

Aim & Methods

- This systematic review evaluates the efficacy and safety of five novel anti-glycemic drugs: Cotadutide, Enavogliflozin, Retatrutide, ORMD-0801, and Imeglimin. (Table 1)
- Inclusion criteria: Clinical trials evaluating the efficacy and safety of the five drugs in T2DM patients, reported data for at least one outcome of interest.
- Search strategy: PubMed, Google Scholar, CENTRAL, conference abstracts, and ClinicalTrials.gov (until March 15, 2023).
- The primary outcome for efficacy was change from baseline in HbA1c level. Secondary outcomes included change in fasting serum glucose, body weight, and adverse events.

Intervention	Manufacturing company	Mechanism of Action (Fig. 1, Fig. 7)	Stage	Route of Administration	Approval status
Cotadutide	AstraZeneca	Glucagon receptor agonists; GLP-1	Phase II	Subcutaneous	Not yet
ORMD-0801	Oramed	Ornithine decarboxylase stimulants; Phosphokinase stimulants; Protein tyrosine kinase stimulants	Phase III	Oral	Not yet
Enavogliflozin	Daewoong Pharmaceutical	SGLT2 inhibitors	Phase III	Oral	Not yet
Retatrutide	Eli Lilly and Company	Gastric inhibitory polypeptide receptor agonists; GLP-1 ; Glucagon receptor agonists	Phase II	Subcutaneous	Not yet
Imeglimin	Sumitomo Dainippon Pharma	GSIS and preservation of β-cell mass; and (b) enhanced insulin action	Phase III	Oral	Not yet (Approved for use in Japan)

Table 1. Summary on novel drugs for T2DM

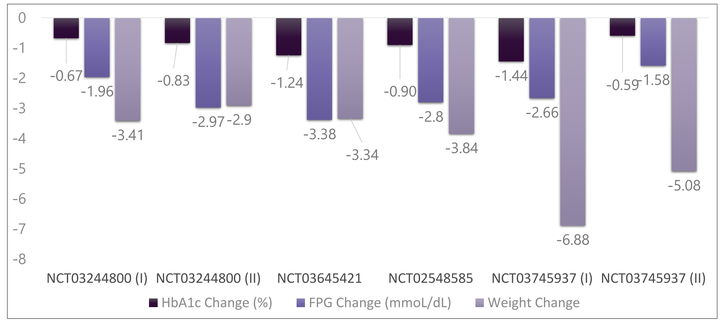

Fig 2. Change in HbA1c, FPG and body weight with Cotadutide from baseline

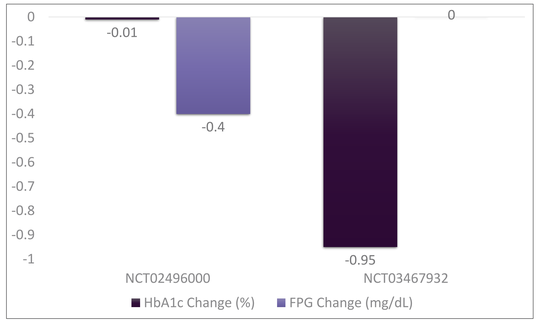

Fig 3. Change in HbA1c and FPG with ORMD-0801 from baseline

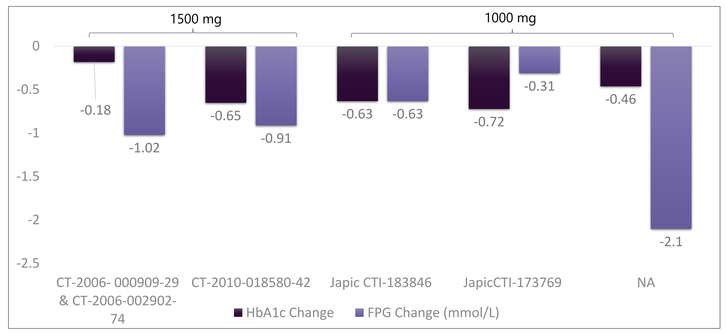

Fig 4. Change in HbA1c and FPG with Imeglimin from baseline

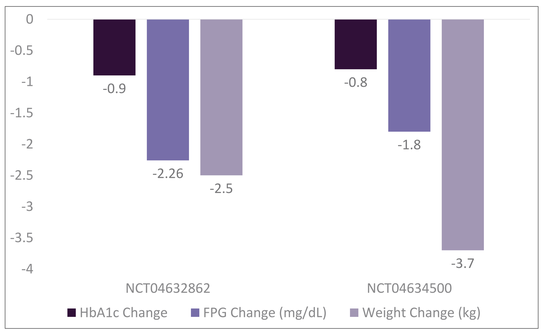

Fig 5. Change in HbA1c, FPG and body weight with Enavogliflozin from baseline

Conclusion

Limited direct head-to-head studies comparing these agents. Based on the available evidence, both GIP and GLP-1 receptor agonists and SGLT2 inhibitors have shown significant efficacy in improving glycemic control and inducing weight loss.

Consideration of risks and benefits is crucial when choosing a diabetes regimen for individual patients. Further research is needed to establish robust evidence for improving glycemic control and reducing complications.

Results

Cotadutide: Clinical trials have reported minimal to no occurrences of severe hypoglycemia. Can cause mild nausea, vomiting, diarrhea, and stomach pain. (Fig 2)

ORMD-0801: No clinically relevant changes in weight was observed. Incidence of mild hypoglycemia was similar across all ORMD-0801 groups (5% vs 6.45% in placebo). (Fig 3)

Imeglimin: No clinically relevant changes in weight. TEAEs were generally mild and less frequent with higher Imeglimin doses compared to metformin. (Fig 4)

Retatrutide: No clinically relevant changes in weight was observed. Most TEAEs were mild, with gastrointestinal disorders (nausea, vomiting, abdominal distention) being the most common. (Fig 5)

Enavogliflozin: Favorable changes in blood pressure, low-density lipoprotein cholesterol and insulin resistance. No reported cases of hypoglycemia. (Fig 6)

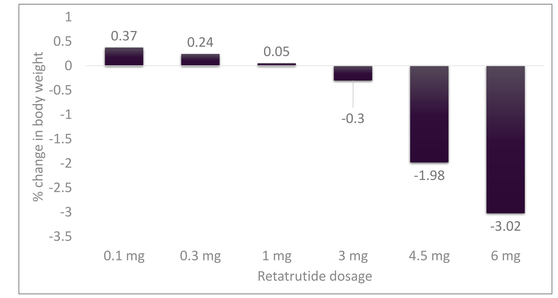

Fig 6. Body weight change from baseline to day 43 (kg) with Retatrutide

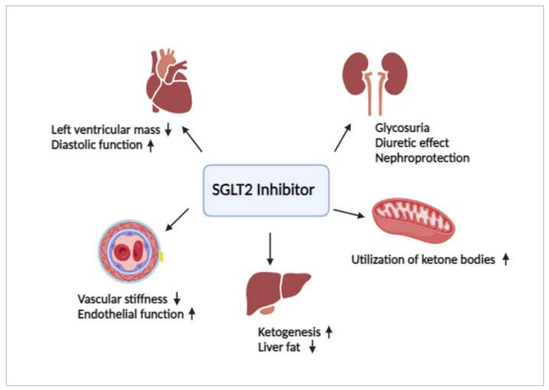

Fig 7. Mechanism of action of SGLT2

Abbreviations: GLP-1- Glucagon-like peptide 1 receptor, **SGPT2**- Sodium-glucose transporter 2 inhibitors, **GSIS**- Glucose-stimulated insulin secretion

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