A Prospective Observational Study of GLP-1 and GLP-1/GIP Receptor Agonists in Patients with Well-Differentiated Neuroendocrine Tumors

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Background

Neuroendocrine tumors (NETs) are heterogeneous neoplasms with rising incidence and diverse clinical behavior. Although well-differentiated, low- to intermediate-grade NETs typically exhibit indolent growth, their management is complex, especially when addressing metabolic comorbidities such as obesity and diabetes.

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists (e.g., tirzepatide) have demonstrated substantial benefits for weight loss, glycemic control, cardiovascular health and are increasingly utilized.

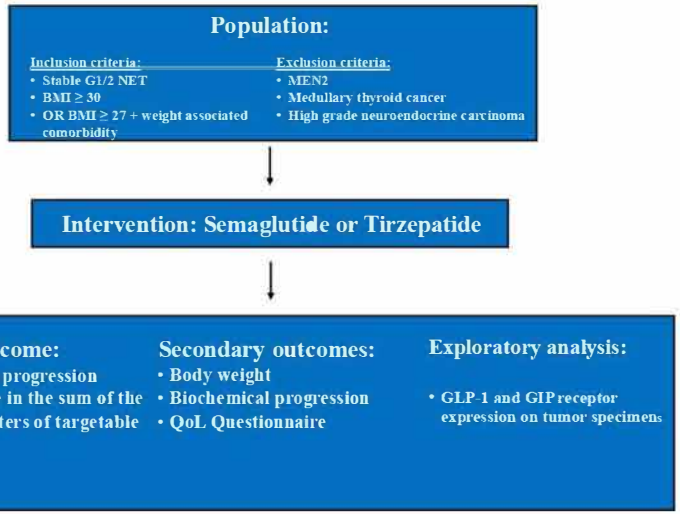
Preclinical studies have demonstrated expression of GLP-1 and GIP receptors in NETs and raised concerns for tumor proliferation with receptor activation, while some recent retrospective clinical analyses suggest possible benefits. However, prospective safety data in patients with active NETs are lacking.

References & Abstract

Results

Enrollment is ongoing with a planned accrual of 30 patients.

Interim analyses will evaluate progression and safety signals.



Conclusions

*This is the **first prospective study** to assess the **safety** of **GLP-1 and GLP-1/GIP receptor agonists** in patients with active **NETs.** Findings will guide future clinical decision-making and support evidence-based use of these agents in this population.*

Methods

This is a single-institution, prospective observational study designed to evaluate the safety and metabolic efficacy of GLP-1 and GLP-1/GIP receptor agonists in patients with grade 1 or 2 NETs.

Eligible patients must have measurable (RECIST v1.1), stable disease on imaging within 90 days prior to enrollment, and no evidence of progression in the preceding 6 months.

Key exclusions include grade 3 NETs/NEC, history of medullary thyroid carcinoma, or MEN2.

Patients will receive semaglutide or tirzepatide following standard titration schedules. Radiographic assessments will occur every 12 weeks to monitor tumor progression. Biochemical progression will be assessed in functional NETs on the same schedule via relevant biomarkers.

The primary endpoint is rate of radiographic progression.

Key secondary endpoints include biochemical progression, changes in quality-of-life scores via EORTC QLQ-GI.NET21, percent weight loss, changes in hemoglobin A1c and lipid profiles. An exploratory analysis will examine correlation of outcomes with GLP-1 and GIP receptor expression in tumor tissue.

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