T-12

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

Aaron Pruitt[1], Heidi Weiss[2], Hardik Dand[1], Val Adams[3], Lowell Anthony[1].

[1]Department of Internal Medicine, Division of Medical Oncology, University of Kentucky; [2]Department of Internal Medicine, Division of Cancer Biostatistics, University of Kentucky; [3]Department of Pharmacy Practice and Science, University of Kentucky.

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.

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 who are receiving these agents for weight or metabolic indications.

Eligible patients must have histologically confirmed well-differentiated NETs, 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, neuroendocrine carcinomas, history of medullary thyroid carcinoma, or MEN2.

Patients will receive semaglutide (up to 2.4 mg weekly) or tirzepatide (up to 15 mg weekly) 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 (e.g., chromogranin A, 5-HIAA).

The primary endpoints are rate of radiographic progression and biochemical (defined as a change of ≥ 50% from baseline) progression. Key secondary endpoints include 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.

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.

ABSTRACT ID 33472