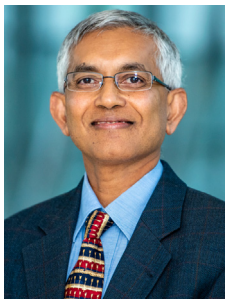
Preface

Neuroendocrine Neoplasms: Molecular Imaging and Therapy



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Editor

There have been transformative changes in molecular imaging diagnosis and radiopharmaceutical therapy for neuroendocrine neoplasms. This issue of *PET Clinic* "Neuroendocrine Neoplasms: Molecular Imaging and Therapy" updates critical basic and clinical practice aspects of PET imaging and therapy.

^{68}Ga-DOTATATE and ^{18}F-FDG-PET/CT are now used as the standard of care in the molecular imaging phenotyping of patients. As DOTATATE PET/CT is more sensitive for well-differentiated, and FDG-PET/CT is more sensitive for poorly differentiated, neuroendocrine neoplasms or neuroendocrine carcinomas, these two imaging tests provide complementary information that allows the most accurate phenotyping, illustrating the intralesion and interlesion heterogeneity of these tumors. Moderate to intense DOTATATE uptake (above liver uptake) indicates sufficient expression of somatostatin type-2 receptors, making patients eligible for ^{177}Lu DOTATATE therapy. However, FDG-PET/CT provides prognostic information, as patients with no FDG uptake have better survival outcomes, even among patients with well-differentiated neuroendocrine tumors (NETs). Therefore, patients who demonstrate intense FDG uptake and no DOTATATE uptake are deemed ineligible for ^{177}Lu DOTATATE therapy due to poor response and survival outcomes. This strategy of selecting patients based on the molecular expression of targets and patients who would benefit most from ^{177}Lu DOTATATE therapy prevents unnecessary comorbidities from ineffective treatment and would minimize inappropriate health system expenses. In addition, total body dynamic PET/CT could provide kinetic parameters and time activity curves, which may provide further biologic information for tumor heterogeneity and the potential for predicting therapy selection and response.

Increasingly, ^{177}Lu DOTATATE therapy is used as the standard of care to treat well-differentiated, locally advanced, inoperable NETs progressing on somatostatin analogues. Long-term follow-up data have confirmed the significant progression-free survival advantage and excellent tolerability. Ongoing further clinical trials are investigating the utility of ^{177}Lu DOTATATE against Everolimus (COMPETE; NCT03049189), ^{177}Lu DOTATATE versus standard of care for patients with aggressive grade 2 and 3 GEP NETs (COMPOSE; NCT04919226), and ^{177}Lu DOTATATE with long-acting octreotide versus high-dose (60 mg) long-acting octreotide as first-line therapy (NETTER-2; NCT03972488), which will further expand the indications in the future. In addition, other studies are investigating the use of ^{177}Lu DOTATATE for other somatostatin receptor–expressing tumors, such as small cell lung cancer (NCT05142696) and meningiomas (NCT03971461). Furthermore, real-world data are evolving from India for treating NET patients (PRRT naive and those refractory to ^{177}Lu DOTATATE) with ^{225}Ac DOTATATE.

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At the time of analysis, median progression-free survival was not achieved for the population in this study and was about 30 months for those who received ^{177}Lu DOTATATE. Ongoing clinical trials (NCT05153772, NCT05477576) in this space will shed more information on the success of alpha therapy in the future.

The therapy response assessment in neuroendocrine neoplasms is challenging due to tumor heterogeneity, their slow-growing nature, and longer time for response to manifest. Therefore, a combination of biologic, anatomic, and functional response parameters is necessary to estimate the accurate therapy response.

The scientific and clinical opportunities in diagnosing and treating neuroendocrine neoplasms are unlimited, and the future of the field is promising. This issue of *PET Clinic* outlines the current clinical practice and explores the scientific and clinical opportunities in the future.

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