Supportive Measures and Finer Practice Points in \textsuperscript{177}Lu-DOTATATE PRRT for NET: Aiming for Optimal Disease Management

\textbf{TO THE EDITOR:} Peptide receptor radionuclide therapy (PRRT) has gained substantial popularity and is now among the frequently considered options for the management of advanced neuroendocrine tumors (NETs) \cite{1}. Although the work-up and treatment protocol are now quite standard in most practicing centers, the attending nuclear medicine specialist should be well versed in some of the finer aspects associated with this form of therapy for bettering overall management. Herein, we address and share our own experiences and thoughts on certain relevant points pertaining to PRRT practice.

\textbf{Antiemetic Protocol.} Nausea and vomiting related to PRRT are primarily due to metabolic acidosis related to coinfusion of a positively charged amino acid (administered to competitively block the megalin-cubilin pathway–based proximal renal tubular reabsorption of the radiopeptide). In our experience, a combination of ondansetron and corticosteroid is most effective and should be administered intravenously on a routine basis before the therapy. It is superior in reducing the incidence of emetic tendency as compared with a single agent. This protocol is already in place for metastatic palliation as well. Increased albumin reduces fluid overload and prevents cardiac dysfunction, especially in patients with carcinoid heart syndrome.

\textbf{Management and Preparation of a Symptomatic Patient.} Although there exists some practice diversity regarding withdrawal of long-acting somatostatin analogs before PRRT, most centers follow a withdrawal period of at least 4 wk; highly symptomatic patients, especially those in their initial few cycles of PRRT, would need short-acting formulations of octreotide administered through subcutaneous injection (100 \textmu g 2–3 times a day) until 1 d before the therapy. After a cycle of PRRT, symptomatic patients could be given long-acting preparations monthly until 1 mo before the next scheduled PRRT cycle.

\textbf{Preventing Acute Syndrome Related to Hormone Release.} PRRT, in general, is well tolerated and has minimal acute side effects; however, there remains a theoretic risk of acute precipitation of syndrome due to sudden hormone release that would need urgent management: this risk is more likely in patients with large functioning hepatic metastases. Priming this group of patients with cyproheptadine from 1 to 2 d before PRRT may help: we have adopted this practice on a regular basis, and in our experience with close to 500 therapeutic procedures we have not encountered acute syndrome in any of them.

\textbf{Patients with Poor Nutrition Status.} Nutrition status is particularly relevant in developing countries in which the baseline nutrition status of patients is poor. Tryptophan loss, gastrointestinal loss of protein, and liver metastases leading to hepatic dysfunction are other causes of severe hypoalbuminemia, leading to anasarca, abdominal distension, breathlessness, and general deterioration of the patient. In our experience, aggressive oral and intravenous albumin supplementation in this group of patients, along with octreotide therapy before and (if required) after PRRT, increases the number of patients who can undergo PRRT. Increasing intravascular albumin levels improves renal blood flow and reduces the chances of holding back PRRT or its complications. Increased albumin reduces fluid overload and prevents cardiac dysfunction, especially in patients with carcinoid heart syndrome.

\textbf{Individualized Management.} Developing an individualized model is the need of the hour in the management algorithm of NETs, which are a widely heterogeneous group of malignancies with a broad range of tumor differentiation \cite{2}. A high Mib1 index and avid \textsuperscript{18}F-FDG uptake are biomarkers of aggressive behavior in NETs, and treatment with chemotherapy or targeted therapy in addition to PRRT may improve the outcome. This, of course, needs examination in a prospective setting.

\textbf{Dose Fractionation in Neoadjuvant Setting Versus Metastatic Palliation.} The usual administered activity of \textsuperscript{177}Lu-DOTATATE ranges from 5,550 to 7,400 MBq (150–200 mCi) administered at a 10- to 12-wk interval for 4–6 cycles. With some promise of this agent in the neoadjuvant scenario being reported \cite{3,4}, it needs to be determined whether the same dose fractionation schedule holds well for metastatic palliation as well. It is imperative that in the former setting a more aggressive approach and fewer cycles be used, whereas in a purely palliative setting a fractionated regime incorporating more cycles with smaller doses over a longer period could be useful.

\textbf{Choice of Medications for Symptomatic Support.} A substantial fraction of patients harbors a constellation of symptoms, especially during their initial courses of PRRT. In addition to the short-acting octreotide formulation, they
would need symptomatic support for pain relief (tramadol, reasonably safe in mild to moderate renal and hepatic dysfunction, is a good agent for pain management) and for debilitating abdominal spasm (a not infrequent accompaniment in these patients; drotaverine or dicyclomine are useful agents).

**Conclusion.** The successful delivery of PRRT in patients with NET requires that multiple appropriate supportive measures be considered for symptomatic management. The value of joint dialogue between nuclear medicine physicians and gastrointestinal oncologists for developing an optimal protocol cannot be overemphasized.

**REFERENCES**


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