NANETS/SNMMI Consensus Statement on Patient Selection and Appropriate Use of 177Lu-DOTATATE Peptide Receptor Radionuclide Therapy

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**Background**

With the growing use of $^{177}$Lu-DOTATATE peptide receptor radionuclide therapy (PRRT), there are many unanswered questions regarding patient selection. In this document, we review the literature on the use of $^{177}$Lu-DOTATATE in neuroendocrine tumors (NETs) of different primary origin, discuss issues of controversy, and review potential contraindications to treatment.

The present consensus statement was developed collaboratively by NANETS and the SNMMI. The North American Neuroendocrine Tumor Society (NANETS) is a multidisciplinary professional society of neuroendocrine specialists in North America that was founded in 2005. NANETS mission is to improve neuroendocrine tumor disease management through increased research and educational opportunities. NANETS is committed to a multidisciplinary approach and consists of doctors and scientists involved in different specialties of NETs. The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is an international scientific and professional organization founded in 1954 to promote the science, technology, and practical application of nuclear medicine. In addition to publishing journals, newsletters, and books, the SNMMI also sponsors international meetings and workshops designed to increase the competencies of nuclear medicine practitioners and to promote new advances in the science of nuclear medicine.

**Materials and methods**

**Systematic Review**

To inform the development of these guidelines, a systematic review of evidence was performed. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (1). A literature search of Pubmed and the CENTRAL database resulted in 1,195 potentially relevant articles using the following search string: (“peptide receptor radionuclide therapy” OR “radioisotope therapy” OR “radionuclide therapy” OR “radiolabeled therapy” OR Yttrium-90 OR 90Y OR Y-90 OR “(90)y” OR “(177)Lu” OR “Lu(177)” OR Lutetium-177 OR 177Lu OR Lu-177 OR PRRT) AND (neuroendocrine OR carcinoid OR paraganglioma OR pheochromocytoma OR neuroblastoma OR somatostatin). Papers that were excluded included those in non-NET patients, duplications, studies including Indium-111, non-original articles, and those without reported outcomes (Figure 1). After a review of the abstracts and titles, 153 articles were determined to meet the criteria for inclusion in this review. Given the focus of this work, reports using $^{177}$Lu-DOTATATE were prioritized. Articles were then selected and grouped according to the primary site of tumor.

**Scoring of appropriateness**

In developing these guidelines, the workgroup members used the following definition of appropriateness to guide their considerations and group discussions: “The concept of appropriateness, as applied to health care, balances risk and benefit of a treatment, test, or procedure in the context of available resources for an individual patient with specific characteristics”. The workgroup scored each scenario as “appropriate,” “may be appropriate,” or “rarely appropriate” on a scale from 1 to 9. Scores 7–9 indicate that the use of the procedure is appropriate for the specific scenario and is generally considered acceptable. Scores 4–6 indicate that the use of the procedure may be appropriate for the specific scenario. This implies that more research is needed to classify the scenario definitively. Scores 1–3 indicate that the use of the procedure is rarely appropriate for the specific scenario and generally is not considered acceptable.

**Definition of somatostatin-receptor positivity**

$^{177}$Lu-DOTATATE PRRT should only be used to treat somatostatin receptor (SSTR)-positive tumors. Typically, positivity is defined as intensity of uptake in sites of disease that exceeds the normal liver, a threshold that was originally defined for use with $^{68}$In-pentetreotide planar scintigraphy. Nevertheless, the same threshold is often applied to $^{68}$Ga-DOTATATE PET imaging despite the fact that the PET scan tends to overestimate uptake compared to scintigraphy (2). Although the FDA approval of $^{177}$Lu-DOTATATE limits its use to gastroenteropancreatic (GEP)-NETs, there are other indications where SSTR-PRRT may be beneficial. Consideration of the site of primary tumor is important in determining if a patient should be treated with PRRT. Below we discuss the evidence for the use of $^{177}$Lu-DOTATATE for the treatment of NET subtypes assuming that the disease is SSTR-positive on SSTR-PET or scintigraphy. SSTR-negative disease should not be treated using $^{177}$Lu-DOTATATE.

**Evidence for use based on primary site**

**Midgut NET**

The NETTER-1 study is the only randomized phase III clinical study offering high level evidence of efficacy with $^{177}$Lu-DOTATATE. This study was performed in midgut NETs and is discussed in more detail below. Additionally, numerous single-arm studies and clinical series provide additional data on risk and benefit, some in patients receiving only $^{177}$Lu-DOTATATE (3,4) and others with combinations of
**Pancreatic NET**
Pancreatic NET (pNET) is the second most common site of origin for metastatic GEP-NETs, and a number of retrospective studies have reported results with \(^{177}\)Lu-DOTATATE in this population. Compared to midgut NETs, pNETs appear to have a slightly higher ORR which ranges from 45-60%, although OS and PFS are consistent with or slightly shorter than seen with midgut (4-6,9,10) (Table 1). Outside of the NETTER-1 trial, there are two prospective studies in pNETs: the first is the IEO Phase 1-2 trial, which included 14 pNET patients and reported an overall response rate of 57% (8/14) (11), and the second is a study of 60 pNET patients with an overall response rate of 30% (18/60) (12). Based on registry data, the Food and Drug Administration (FDA) included pNET within the indication for \(^{177}\)Lu-DOTATATE, and PRRT should be considered for treatment of progressive pNET patients (Appropriateness Score 8).

**Bronchial NET**
Several papers have reported the use of PRRT in pulmonary neuroendocrine tumors, treated with both \(^{90}\)Y-DOTATOC and \(^{177}\)Lu-DOTATATE (Table 1). Overall response rates ranged from 13-30%, while progression free survival ranged from 19-28 months and overall survival ranged from 32-59 months. Bronchial NETs are categorized into two groups, typical and atypical carcinoid tumors, which are considered distinct from the more aggressive large-cell and small-cell neuroendocrine carcinoma. Not unexpectedly, typical bronchial carcinoids appear to be more responsive to PRRT, although the majority of papers do not distinguish response rates between the subsets. One issue concerning bronchial NETs is the relatively small percentage of tumors which express sufficient somatostatin receptors to be candidates for therapy, although in one recent manuscript, 76% of 143 bronchial NETs were positive on somatostatin receptor scintigraphy (13). Although the literature is not definitive, there appear to be significantly higher levels of SSTR expression in typical bronchial carcinoids compared to atypical carcinoids (14). In patients with SSTR-positive tumors, \(^{177}\)Lu-DOTATATE therapy can be considered as a potential therapeutic option after progression on everolimus (Appropriateness Score 7).

Treatment with \(^{177}\)Lu-DOTATATE prior to everolimus is considered less appropriate (Appropriateness Score 6).

**Tumors of Unknown Primary**
Tumors of unknown primary are becoming less common since the introduction of SSTR-PET. To date, there are no studies performed only in patients with tumors of unknown primaries, although a number of studies report results for a subset of patients with unknown primaries (Table 1). Efficacy seems to be comparable to what is reported with a known gastrointestinal or pancreatic primary. Therefore, decisions to treat with PRRT in unknown primaries should mirror those in patients with GEP-NETs and \(^{177}\)Lu-DOTATATE therapy should be considered in patients who progress despite treatment with first-line somatostatin analog therapy (Appropriateness Score 8).

**Paraganglioma / Pheochromocytoma**
Paraganglioma and pheochromocytoma (para/pheo) constitute a heterogeneous group of tumors with varying underlying genomic variations and variable SSTR expression. SDHB-associated subtype has been well evaluated and has a high expression of SSTRs (15). There are several small single-center retrospective studies evaluating PRRT in para/pheo (some in the context of larger series including other neuroendocrine tumors) that demonstrate ORR ranging from 7-29% (16,17), with the highest reported response rate from a manuscript that described a combination of
Chemotherapy and PRRT (18) (Table 1). Currently there is an ongoing prospective clinical trial evaluating the efficacy of 177Lu-DOTATATE in patients with advanced para/pheo (NCT03206060). It should be noted that 131I-iohexogene (MIBG) was approved by the Food and Drug Administration for the treatment of MIBG-positive para/pheo (19). While 177Lu-DOTATATE may be promising in this disease, treatment at this time should be limited to patients whose tumors are MIBG-negative (Appropriateness Score 7). Treatment of MIBG-positive patients with 177Lu-DOTATATE in place of therapeutic 131I-iohexogene is considered less appropriate (Appropriateness Score 6).

Special circumstances
Renal insufficiency
To inform the development of these guidelines, a Clinical experience and trial evidence accumulated over the past two decades have demonstrated that PRRT with 177Lu-DOTATATE is generally well-tolerated. Chronic and permanent toxicity affecting the kidneys is rare if necessary precautions and attention to specific risk factors are undertaken. Renal irradiation, and consequently the risk of toxicity, is significantly decreased when positively charged amino acids, such as lysine and arginine, are co-infused with the treatment, due to the competitive inhibition of reabsorption at the proximal tubule. Examining the outcomes of more than 2,500 patients (20-27), it is apparent that PRRT with 99mTc-peptides is associated with a significant risk for reduction of renal function. In subjects treated with 177Lu-DOTATATE, the incidence of severe, end-stage renal damage is very rare, with only sporadic cases reported in the literature (23,26), mainly in patients with compromised renal function at baseline. Indeed, the NETTER-1 study demonstrated no evidence of clinically significant worsening of renal dysfunction among 11 patients with baseline mild renal dysfunction (GFR 50-59) and 13 patients with moderate renal dysfunction (GFR<50) treated on the 177Lu-DOTATATE arm of the study (28).

Severe renal dysfunction has generally been considered a contraindication to treatment with 177Lu-DOTATATE. Many institutional series have required a minimum glomerular-filtration rate (GFR) of 50 cc/hour. Based on available data, we do not consider a GFR <50 to be a contraindication to 177Lu-DOTATATE use. For patients with severe baseline renal dysfunction defined as GFR <30, 177Lu-DOTATATE should be used only in exceptional circumstances. Of note, hydronephrosis represents a particular concern as it impairs renal excretion and increases exposure to radiation. As much as possible, hydronephrosis should be corrected prior to initiation of 177Lu-DOTATATE treatment. Patients on dialysis may be treated with 177Lu-DOTATATE but, as with other radiopharmaceutical therapies, this should be done very carefully, with consideration for dose reduction and dosimetry.

Prior chemotherapy
It is still unclear whether prior cytotoxic chemotherapy increases risk of myelodysplastic syndrome (MDS) or acute leukemia (AL) associated with 177Lu-DOTATATE. In one small series of 20 patients treated with an alkylating agent (primarily streptozocin) and subsequently treated with 177Lu-DOTATATE, 4 cases of MDS/AL were observed (29). Compared to typical patients treated with PRRT in the same institution (4), these 20 patients had more cycles of chemotherapy, more cycles of alkylating agents, had experienced more frequent early high-grade hematotoxicity, and tended to more frequently have bone metastases. Conversely, the largest series of patients treated with 90Y- and/or 177Lu-peptides, identified an incidence of 2.3% for MDS and 1.8% for leukemia (of which 75% evolved from MDS), with a median latency from exposure of 4.4 years (26). In these patients, only 29% of MDS and 22% of leukemia could be correlated to prior chemotherapy. Therefore, it remains uncertain whether prior chemotherapy, and temozolomide-based treatment in particular, is associated with increased risk of MDS/AL after 177Lu-DOTATATE therapy or not.

Mesenteric and peritoneal disease
In certain clinical circumstances, we recommend caution prior to consideration of 177Lu-DOTATATE. Mesenteric tumors are often characterized by substantial surrounding desmoplasmia. There are theoretical concerns that radiation may exacerbate the desmoplasmic process, thus leading to increase in symptoms. Similar theoretical concerns pertain to patients with extensive peritoneal carcinomatosis in whom radiation may lead to bowel obstruction. Certain centers prescribe short courses of prophylactic steroids (e.g. 1-2 weeks) starting immediately after each dose of 177Lu-DOTATATE.

High-grade disease
177Lu-DOTATATE has been studied almost exclusively in patients with low or intermediate-grade neuroendocrine neoplasms (NENs). Consequently, there is limited evidence to support the use of 177Lu-DOTATATE in grade 3 disease (30-32). Several studies demonstrate that very high proliferative indexes (ie Ki-67 > 35-55%) are associated with inferior outcomes. Zhang, et al
reported the largest retrospective study to date of 69 patients with SSTR-expressing G3 NENs with a Ki-67 > 20% who received PRRT (33). The median PFS was 9.6 months and median OS was 19.9 months. Notably, patients with Ki-67 > 55% had the shortest survival (PFS 4 months, OS 7 months). Due to the potential heterogeneity of disease in this patient population, confirmation of SSTR expression across all metastases is essential. Additional imaging with 18F-FDG PET may also be of use to fully characterize all sites of disease.

Pediatric patients

Neuroendocrine tumors (NETs) are rare in pediatric patients (34). In addition to NETs, PRRT may be useful in neuroblastoma and paraganglioma/pheochromocytoma, particularly if 131I-MIBG therapy is not an option or if patients have progressed after MIBG therapy. However, there are limited data on PRRT in children. The largest study to date evaluated 90Y-DOTATOC in 17 patients with various NETs and demonstrated minimal or partial response in 41% of patients. (35). Two smaller studies which included a total of 10 patients demonstrated efficacy, but also demonstrated marrow toxicity in those patients previously treated with MIBG (36,37). In patients with neuroblastoma, it is not clear whether 177Lu-DOTATATE should be used given the extensive experience with MIBG. Overall, PRRT appears promising in pediatric patients with NETs and neuroblastoma, although at this time 177Lu-DOTATATE use should be limited to tumors that are negative on MIBG imaging.

Timing of treatment

In nearly all cases described in the literature, patients treated with 177Lu-DOTATATE had already progressed on a first-line SSA. While progression is typically defined radiographically, select patients may be treated based on symptomatic progression. Due to the long-term safety and efficacy of SSAs, first-line treatment with 177Lu-DOTATATE is generally not appropriate. Certain exceptions to this rule include patients with very high tumor burden where any further growth would entail significant risk. The decision to treat with 177Lu-DOTATATE, in the second-line or beyond, needs to be considered in the context of the larger systemic treatment landscape.

For patients with typical, hormone-secreting midgut NETs, systemic treatment options beyond first-line SSA are limited. In this population, the RADIANT-2 study compared everolimus combined with octreotide to placebo plus octreotide, and did not demonstrate a significant improvement in PFS (38). Therefore, 177Lu-DOTATATE should be considered the 2nd-line systemic treatment of choice for most patients with functional somatostatin-receptor positive midgut NETs.

In advanced non-functioning GI and bronchial NETs, everolimus was shown to significantly improve PFS compared to placebo (39). Decisions regarding sequencing of 177Lu-DOTATATE versus everolimus must be individualized, with SSTR expression levels factored into the decision, although in bronchial NETs everolimus should be considered prior to 177Lu-DOTATATE.

For patients with pancreatic NETs, multiple systemic treatment options exist including everolimus, sunitinib, and capecitabine/temozolomide chemotherapy. The latter is likely most appropriate for patients with relatively aggressive or symptomatic tumors, irrespective of SSTR expression. Further research is needed to develop evidence-based recommendations on sequencing of 177Lu-DOTATATE with respect to these alternative treatment options.

Liver targeted therapy

Hepatic arterial embolization is a common approach to patients with unresectable, liver-dominant midgut NETs. Meta-analyses suggest a radiographic response rate of approximately 50%, with a higher rate of symptomatic response. There are no completed clinical trials comparing various embolization modalities, and thus significant controversy exists regarding the optimal embolic approach: bland embolization versus chemoembolization or 90Y-radioembolization. However, despite the lack of prospective evidence, liver embolization remains an appropriate, guidelines-endorsed alternative to 177Lu-DOTATATE in patients with liver-dominant metastases, and offers the potential for rapid symptom palliation among patients with carcinoid syndrome or other secretory symptoms (40,41). There exist some concerns regarding interaction between 177Lu-DOTATATE and prior liver-directed therapies. In one small series, increased hepatotoxicity with PRRT was observed in patients who had undergone prior liver-directed therapy (42). Of particular concern is the risk of cumulative hepatic radiation toxicity in patients who have undergone prior radioembolization, a procedure itself associated with risk of long-term radiation-induced hepatic injury. Patients with extensive hepatic disease are potentially at risk of developing radiation hepatitis, although there is little evidence of chronic hepatic toxicity with 177Lu-DOTATATE, even among patients with high liver tumor burden (43).
**Surgery**
Surgical resection of the primary tumor and subtotal resection of metastatic disease plays an important role in NET patients. Limited retrospective data suggests that debulking prior to PRRT can result in improved response to PRRT and PFS (44).

**Overall considerations**
Due to lack of trials comparing the numerous treatment options, selection and sequencing of treatments are not evidence based, and must be made based on cross-trial comparisons, and assessments of risk versus benefit in individual patients.

**Future Directions**
With the clinical approval of $^{177}$Lu-DOTATATE, there are many possibilities for future research and optimizing clinical care with PRRT. These include optimizing the number of therapy cycles and administered activity, consideration of repeat therapy, delivering the therapy intra-arterially, the use of different radionuclides, and using novel peptides to bind SSTRs. Although the NETTER-1 trial used four treatments at a fixed activity, optimizing the number of treatments or the administered activity of each administration may allow for decreased toxicity and improved efficacy. By measuring treatment effect during therapy or measuring lesional/organ dose, it may be possible to adjust the treatment schedule to increase efficacy. Currently, it is unclear how and whether one should use patient specific dosimetry to adjust the administered activity, and many feel that giving a fixed activity works well for the majority of patients. This idea of repeat-PRRT has been evaluated in retrospective studies (45-47). If a patient responds well to one complete course of $^{177}$Lu-DOTATATE, then it is reasonable to conclude that they may respond well to another course of $^{177}$Lu-DOTATATE when they subsequently progress. These studies showed that repeat-PRRT is safe and effective, although the PFS is not as long compared to the initial PRRT course. Many patients have liver dominant disease, and in these patients intra-arterial $^{177}$Lu-DOTATATE administered via the hepatic artery has been proposed (48,49). In theory, this provides higher delivery to the tumor, while reducing the systemic circulation and associated side effects.

Both $^{90}$Y and $^{177}$Lu have been used for PRRT, and each may provide different benefits given their different physical properties (50). The electron emitted from $^{90}$Y has a higher energy and would be beneficial for bulkier tumors. Conversely, the longer path length of $^{90}$Y will also have a greater bystander effect on normal tissues such as the bone marrow and kidneys resulting in higher toxicity. The relative benefits of $^{90}$Y vs $^{177}$Lu have not been studied. Similarly, the use of alpha-emitters is another area of active research.

DOTATATE is a SSTR analog, which becomes internalized after activating the receptor. SSTR antagonists have been developed that have a higher binding specificity to the SSTR such that even though they do not activate the receptor nor get internalized into the cell, they potentially deliver a high dose of radiation (51,52). Famotidine). When increasing the amino acid rate to the target of 320 mL/hour, additional doses of 5-HT3 antagonist may be required with the addition of a D2 receptor antagonist (e.g. prochlorperazine). Benzodiazepines may also be required for anticipatory nausea and vomiting (8). Steroids, such as dexamethasone can also be administered after infusion of $^{177}$Lu-DOTATATE.

Additionally, cooling and pressure aids may also be beneficial to help with the possible side effects of the amino acid solution infusion. Patient education is highly important at the beginning of the procedure to ensure the patient understands the importance of where and how to contain emesis under these circumstances.

**Conclusion**
The decision to initiate $^{177}$Lu-DOTATATE therapy in a patient with progressive neuroendocrine tumor is complex and should be made within the setting of a multidisciplinary discussion. $^{177}$Lu-DOTATATE should be considered when treating GEP-NETs, and tumors of unknown origin, generally after progression on somatostatin analog. In patients with bronchial carcinoids, $^{177}$Lu-DOTATATE should be considered after everolimus, and in patients with para/pheo, therapy should be limited primarily to patients with MIBG-negative disease.


Table 1: Experience with PRRT by site of primary tumor.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Patients*</th>
<th>Treatment</th>
<th>ORR</th>
<th>PFS</th>
<th>OS</th>
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<tr>
<td><strong>Midgut Neuroendocrine Tumors (Grade 9)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Strosberg (7)</td>
<td>2017</td>
<td>116</td>
<td>$^{177}$Lu-DOTATATE</td>
<td>18%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Sabet (3)</td>
<td>2015</td>
<td>61</td>
<td>$^{177}$Lu-DOTATATE</td>
<td>13%</td>
<td>33</td>
<td>61</td>
</tr>
<tr>
<td>Horsch (5)</td>
<td>2016</td>
<td>138</td>
<td>$^{177}$Lu-DOTATATE, $^{90}$Y-DOTATOC</td>
<td>NR</td>
<td>51</td>
<td>NR</td>
</tr>
<tr>
<td>Brabander (4)</td>
<td>2017</td>
<td>181</td>
<td>$^{177}$Lu-DOTATATE</td>
<td></td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>Baum (6)</td>
<td>2018</td>
<td>315</td>
<td>$^{177}$Lu-DOTATATE</td>
<td></td>
<td>22</td>
<td>69</td>
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<tr>
<td><strong>Pancreatic Neuroendocrine Tumors (Grade 8)</strong></td>
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<tr>
<td>Baum (6)</td>
<td>2018</td>
<td>315</td>
<td>$^{177}$Lu-DOTATATE, $^{90}$Y-DOTATOC</td>
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<td>20</td>
<td>44</td>
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<tr>
<td>Horsch (5)</td>
<td>2016</td>
<td>172</td>
<td>$^{177}$Lu-DOTATATE, $^{90}$Y-DOTATOC</td>
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<td>39</td>
<td>53</td>
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<td>Brabander (4)</td>
<td>2017</td>
<td>133</td>
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<td>71</td>
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<tr>
<td>Ezziddin (10)</td>
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<td>68</td>
<td>$^{177}$Lu-DOTATATE, 41/68</td>
<td>60%</td>
<td>34</td>
<td>53</td>
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<tr>
<td>Sansovini (53)</td>
<td>2017</td>
<td>60</td>
<td>$^{177}$Lu-DOTATATE, 18/60</td>
<td>30%</td>
<td>29</td>
<td>NR</td>
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<tr>
<td>Garske-Román (9)</td>
<td>2018</td>
<td>48</td>
<td>$^{177}$Lu-DOTATATE, 22/49</td>
<td>45%</td>
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<tr>
<td><strong>Bronchial Carcinoid (before everolimus Grade 6; after everolimus Grade 7)</strong></td>
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<td>Mariniello (54)</td>
<td>2016</td>
<td>114</td>
<td>$^{177}$Lu-DOTATATE, $^{90}$Y-DOTATOC</td>
<td>13%</td>
<td>28</td>
<td>59</td>
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<td>Baum (6)</td>
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<td>75</td>
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<td>20</td>
<td>52</td>
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<td>Parghane (56)</td>
<td>2017</td>
<td>22</td>
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<td>11%</td>
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<td>Sabet (57)</td>
<td>2017</td>
<td>22</td>
<td>$^{177}$Lu-DOTATATE</td>
<td>27%</td>
<td>27</td>
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Table 1, continued

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<th>Unknown Primary Tumor (Grade 8)</th>
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<tr>
<td>Baum (6)</td>
<td>2018</td>
<td>151</td>
<td>177Lu-DOTATATE 90Y-DOTATOC</td>
<td>NR</td>
<td>13</td>
<td>S3</td>
<td></td>
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<tr>
<td>Brabander (4)</td>
<td>2017</td>
<td>82</td>
<td>177Lu-DOTATATE</td>
<td>35%</td>
<td>29/82</td>
<td>29</td>
<td>S3</td>
</tr>
<tr>
<td>Delpassand (58)</td>
<td>2014</td>
<td>7</td>
<td>177Lu-DOTATATE</td>
<td>NR</td>
<td>11</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Bodei (11)</td>
<td>2011</td>
<td>3</td>
<td>177Lu-DOTATATE</td>
<td>0%</td>
<td>0/3</td>
<td>NR</td>
<td>NR</td>
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<th>Paraganglioma / Pheochromocytoma (MIBG positive Grade 5; MIBG negative Grade 7)</th>
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<tbody>
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<td>Forrer (17)</td>
<td>2008</td>
<td>28</td>
<td>177Lu-DOTATATE 90Y-DOTATOC</td>
<td>7%</td>
<td>2/28</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Kong (18)</td>
<td>2017</td>
<td>20</td>
<td>177Lu-DOTATATE</td>
<td>29%</td>
<td>5/17</td>
<td>39</td>
<td>NR</td>
</tr>
<tr>
<td>van Essen (16)</td>
<td>2006</td>
<td>12</td>
<td>177Lu-DOTATATE</td>
<td>17%</td>
<td>2/12</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

* only within NET subtype (n), ORR = overall response rate, PFS = progression free survival (in months), OS = overall survival (in months), NR = not reported/reached