Survey Report

Perception mapping of clinicians on Octreotide and its therapy indication

Version No.: 1.0

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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1 INTRODUCTION

Octreotide is primarily FDA-approved for treating acromegaly and thyrotrophinomas, demonstrating greater efficacy than bromocriptine in clinical trials. It is also effective in managing carcinoid syndrome, particularly during carcinoid crises, and is the drug of choice for treating VIPomas, especially when metastasized or unresponsive to conventional therapies [1]. Octreotide is used off-label for conditions like refractory diarrhoea associated with chemotherapy, graft-versus-host disease, and AIDS-related cryptosporidiosis [2]. It has shown potential in several other conditions, including gastroenteropancreatic neuroendocrine tumours, thymic malignancies, and Zollinger-Ellison syndrome, though further research is needed for broader therapeutic use [3].

Octreotide is a category B medication, according to the FDA, meaning no identifiable foetal risk has been documented in animal reproduction studies, but studies involving pregnant women are inadequate and ill-defined. Although data on octreotide use during breastfeeding is limited, some case reports indicate that the subcutaneous form of octreotide can be found in breast milk at levels comparable to serum concentrations, though oral absorption of the drug in infants is inefficient [4]. In paediatric patients, especially those under six, the efficacy and safety of octreotide remain uncertain due to the lack of randomized controlled trials. Reports suggest potential serious adverse events in infants under two, such as hypoxia and necrotizing enterocolitis, though a clear connection to octreotide is not established [5]. In the geriatric population, clinical studies are insufficient, but caution is advised with lower initial doses and careful titration due to the higher likelihood of decreased organ function and comorbid conditions in older patients [6].

Overall, while octreotide is a useful drug for specific conditions like acromegaly and certain tumours, its use in vulnerable populations such as pregnant women, breastfeeding mothers, children, and the elderly must be approached with care. Continuous monitoring and further studies are necessary to better understand its safety and efficacy across these groups.

2 RATIONALE OF THE STUDY

Clinicians' perception of octreotide and its therapeutic indications revolves around its established role in treating conditions such as acromegaly, neuroendocrine tumors (NETs), and gastrointestinal disorders. Octreotide, a somatostatin analog, is widely recognized as a first-line treatment in non-surgical management of acromegaly by inhibiting excess growth hormone production, with consensus guidelines supporting its efficacy in achieving biochemical control in 40-60% of cases. Additionally, clinicians view octreotide as valuable in neuroendocrine tumor management, where it suppresses excessive hormone secretion and provides symptomatic relief. Studies show that octreotide scanning is also crucial for identifying and assessing tumor progression, making it an essential tool for clinical decisions. Octreotide's use extends to the treatment of acute pancreatitis, where it aids in reducing pancreatic enzyme release and inflammation, improving outcomes for patients with severe cases. These clinical insights are shaping the therapeutic applications and perception of octreotide in varied medical settings.

This survey is designed to explore and map physicians perceptions on Octreotide and its therapy indication. The rationale for conducting the survey includes the management of conditions like acromegaly, the emergence of Octreotide as a novel therapy, the need to understand its acceptance and use in combination treatments, and the alignment of clinical guidelines with real-world practice. By assessing physician perspectives, the survey aims to identify the indications influencing the adoption of Octreotide and its combinations, as well as any barriers that may hinder its wider application in clinical practice. This will provide valuable insights into optimizing acromegaly management and improving patient outcomes.

3 STUDY OBJECTIVE

To assess the perception, practice patterns, and clinical experiences of Indian physicians regarding the therapy indication and the use of Octreotide.

4 METHODS

This study was a cross-sectional, questionnaire-based survey designed to assess the perceptions, practices, and clinical experiences of Indian physicians regarding the use of Octreotide in the management of acromegaly. The survey consisted of 15 structured questions, addressing topics such as the frequency of Octreotide use, treatment protocols, efficacy and safety perceptions, and factors influencing treatment decisions. Physicians with relevant experience in endocrinology or related fields were identified through professional networks and medical associations and invited to participate. After providing informed consent, participants completed the questionnaire electronically, with responses securely stored for analysis. The target sample size was 85 physicians, selected to ensure a diverse and representative sample from across various regions of India.

Data analysis will involve both descriptive and inferential statistics. Descriptive statistics will be used to summarize demographic information and response frequencies. Inferential statistics, such as chi-square tests or logistic regression, will be applied where appropriate to explore associations between physician characteristics and their treatment practices or perceptions. Ethical approval will be obtained from an Independent Ethics Committee, and all participants will be assured of confidentiality, with their responses anonymized. No treatment will be administered, as the study focuses solely on gathering insights into current clinical practices and perceptions regarding Octreotide use. The findings will be compiled into a comprehensive report and may be shared through scientific publications or conference presentations.

5 RESULTS

A total of 78 HCPs participated in the survey. Below is the summary of the responses.

1. What is your first line management of unresectable metastatic, symptomatic or clinically significant tumor burden or clinically significant progressive disease?

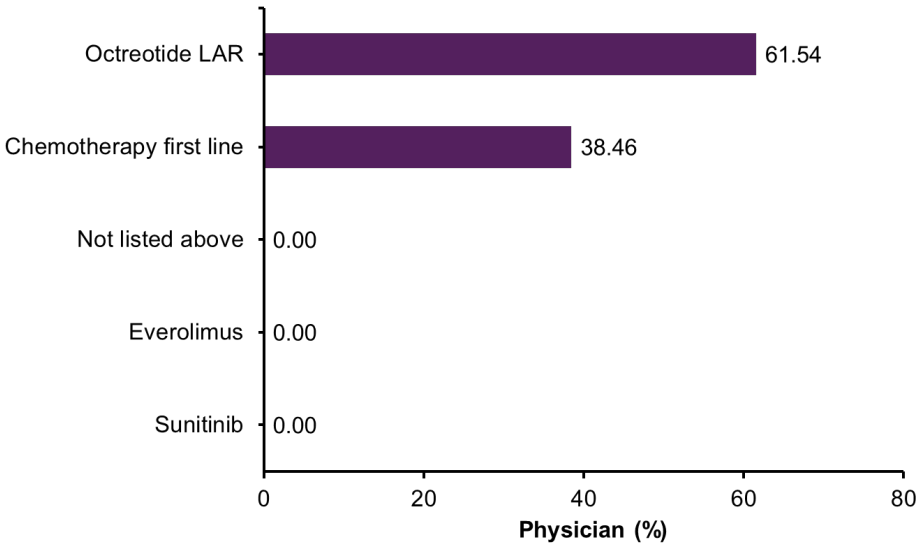
a. Chemotherapy first line

b. Octreotide LAR

c. Sunitinib

d. Everolimus

e. Not listed above



- The majority of physicians (61.54%) prefer Octreotide LAR (long-acting release) as the first-line treatment for managing symptomatic metastatic disease.
- A majority (38.46%) of physicians preferred chemotherapy as the first-line treatment for clinically significant progressive disease.
- None of the physicians prescribed any other regimen.

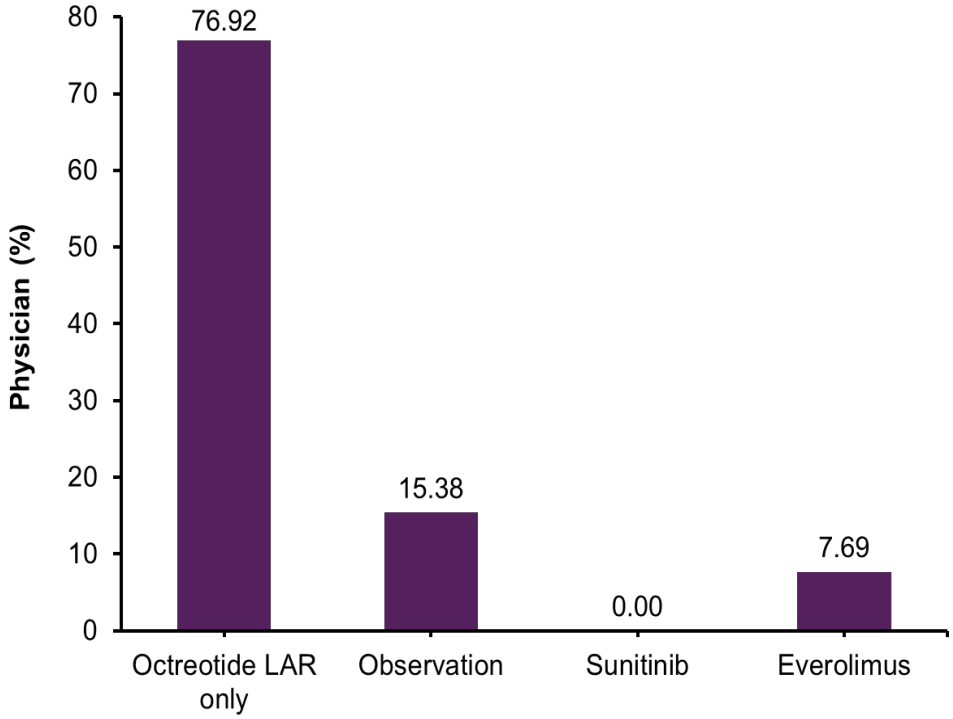
2. What is your first line management of unresectable metastatic, asymptomatic, low tumor burden, and stable disease NET.

a. Octreotide LAR only

b. Observation

c. Sunitinib

d. Everolimus



- The majority of physicians (76.92%) prefer Octreotide LAR as the first-line treatment for line management of unresectable metastatic, asymptomatic, low tumor burden, and stable disease NET.
- A smaller group of physicians (15.38%) opt for observation, suggesting a more conservative approach in some cases.
- A few physicians (7.69%) chose Everolimus, but it's much less favored than Octreotide LAR.While no physicians preferred Sunitinib.

3. Which investigation you prefer for radiological diagnosis of NET?

a. CT

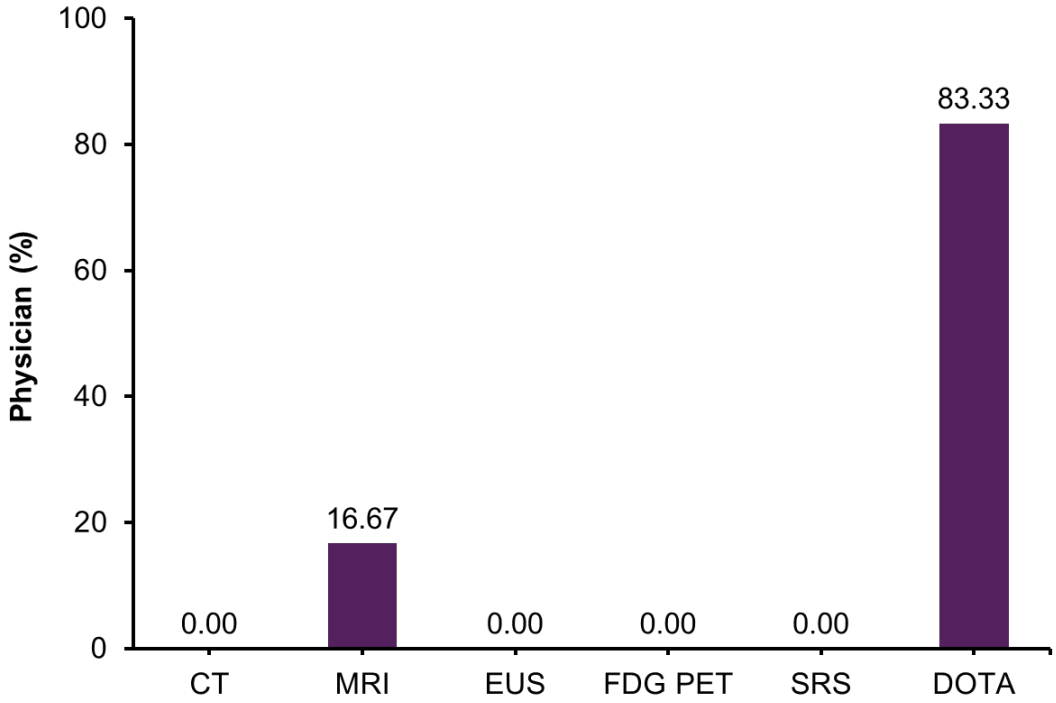
b. MRI

c. EUS

d. FDG PET

e. SRS

f. DOTA



- The majority (83.33%) of physicians prefer DOTA for radiological diagnosis of NET.
- A significant portion (16.67%) of physicians prefer MRI for radiological diagnosis of NET.
- While, none of the physicians prefer CT, EUS, FDG PET and SRS for radiological diagnosis of NET.

4. Which biochemical parameter you consider for definitive diagnosis of NET.

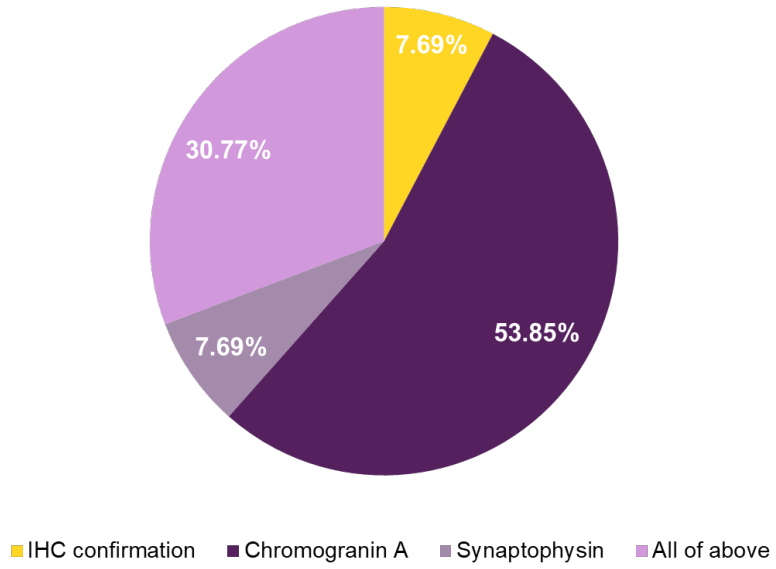
a. IHC confirmation.

b. Chromogranin A

c. Synaptophysin

d. All of above

e. Not listed in above options



- The majority of physicians (53.85%) consider Chromogranin A as a key parameter for diagnosing NET.
- A smaller portion of physician (7.69%) consider IHC confirmation and synaptophysin, as the most important parameter for diagnosing NET.
- A significant portion (30.77%) of physicians choose all of the above i.e (HC confirmation, Chromogranin A, and Synaptophysin, as the most important parameter for diagnosing NET.

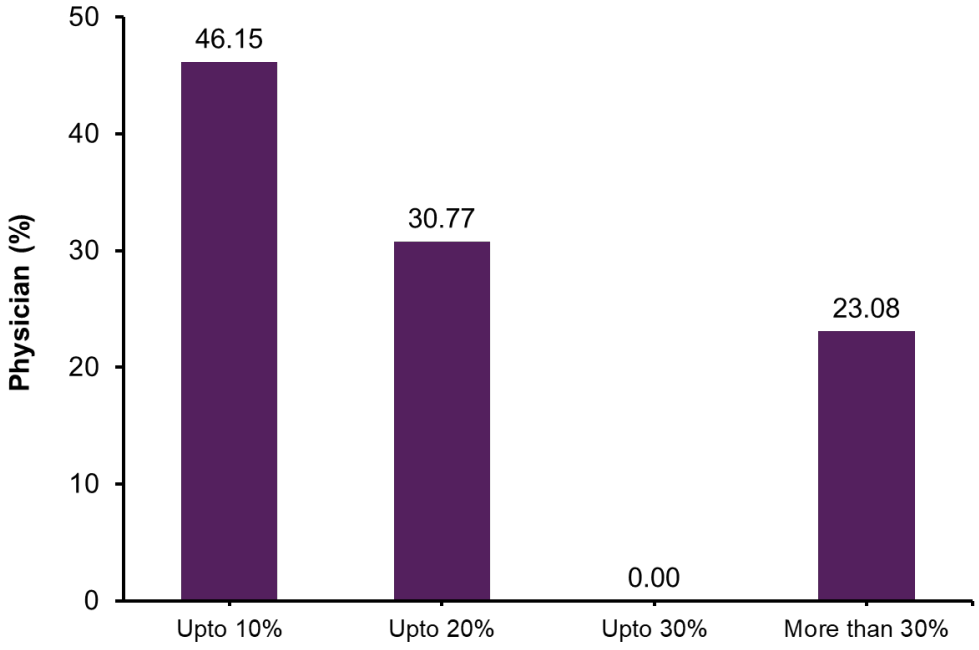
5. What % of your patients take TKI as first line for NET

a. Upto 10%

b. Upto 20%

c. Upto 30%

d. More than 30%



- Nearly half of the physicians (46.15%) reported that up to 10% of patients receive TKI as the first-line treatment.
- A smaller group of physicians (30.77%) indicated that up to 20% of patients receive TKI as first-line therapy.
- A smaller percentage of physicians (23.08%) reported using TKI in more than 30% of their patients.
- No physicians reported using TKI for up to 30% of their patients.

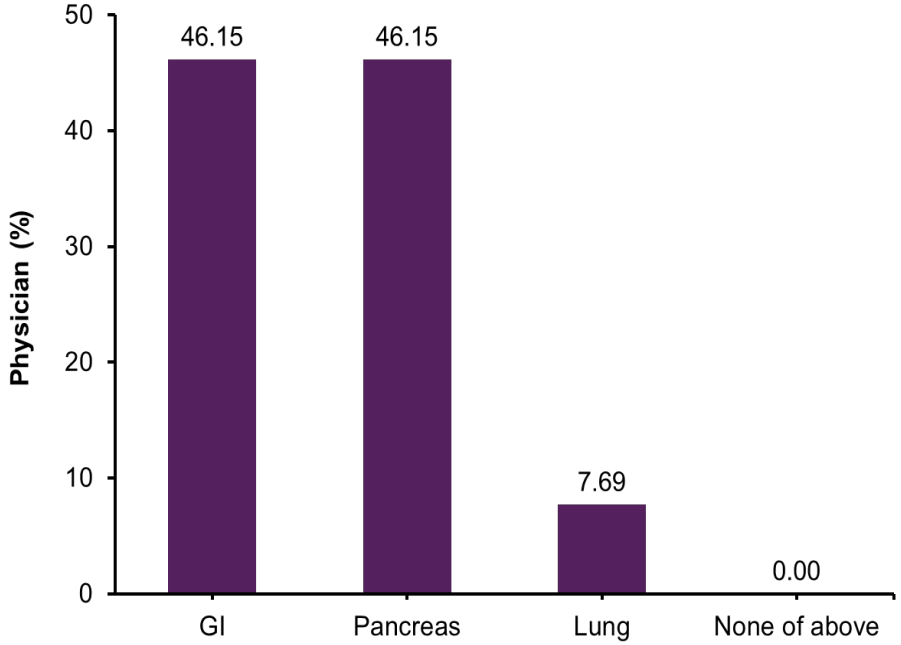
6. What is the most common location of Neuroendocrine tumor in your clinical practice?

a. GI

b. Lung

c. Pancreas

d. None of above



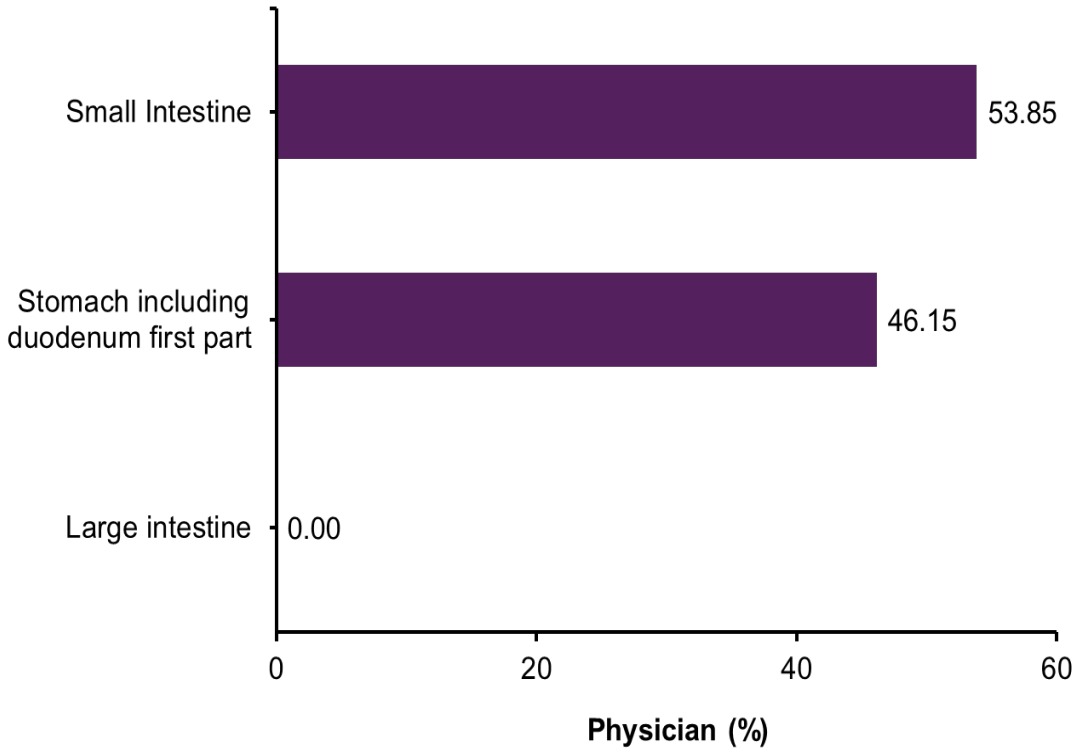
- The majority (46.15%) of physicians reported GI, as the most common location of neuroendocrine tumor in their clinical practice.
- An equal percentage of physicians (46.15%) also reported that pancreatic NETs was the most common in their practice.
- A smaller proportion (7.69%) of physicians reported lung as the most common location of neuroendocrine tumor in their clinical practice.
- No physicians selected option “none of the above," confirming that GI and pancreatic locations are the primary sites for NETs in their practice.

7. Within GI location which is most common location of Neuroendocrine tumor in your clinical practice?

a. Small Intestine

b. large intestine

c. Stomach including duodenum first part



- The majority of physicians (53.85%) identified the small intestine as the most common site for GI NETs during their clinical practice.
- A significant portion (46.15%) of physicians reported stomach including the first part of the duodenum as the most common site for GI NETs.
- While, 9 No respondents selected the large intestine as the most common site for GI NETs.

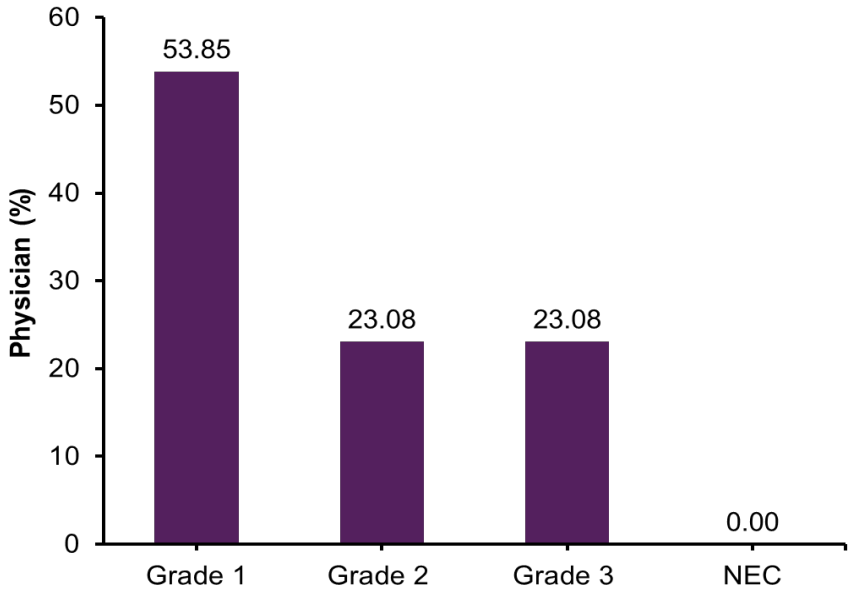
8. What is the most common Grade of neuroendocrine tumor you commonly see in your clinical practice at overall all sites?

a. Grade 1 NET

b. Grade 2 NET

c. Grade 3 NET

d. NEC (neuroendocrine carcinomas)

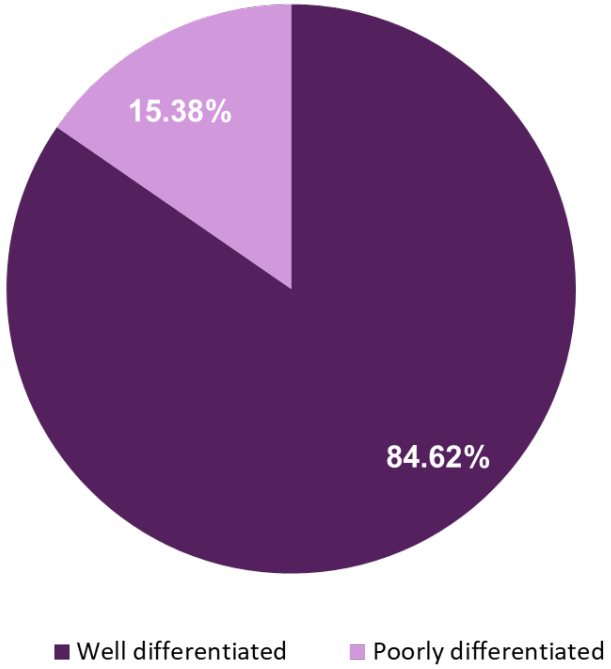


- The majority of physicians (53.85%) reported that Grade 1 NETs are the most commonly seen during their practice.
- A smaller proportion of physicians (23.08%) selected Grade 2 NETs, as the most common seen during their practice.
- While, another 23.08% physicians selected Grade 3 NETs, as the most common seen during their practice
- No physicians selected NEC (Neuroendocrine Carcinomas) as the most common seen during their practice.

9. Of all your patients with neuroendocrine tumors, majority are?

a. Well differentiated

b. Poorly differentiated

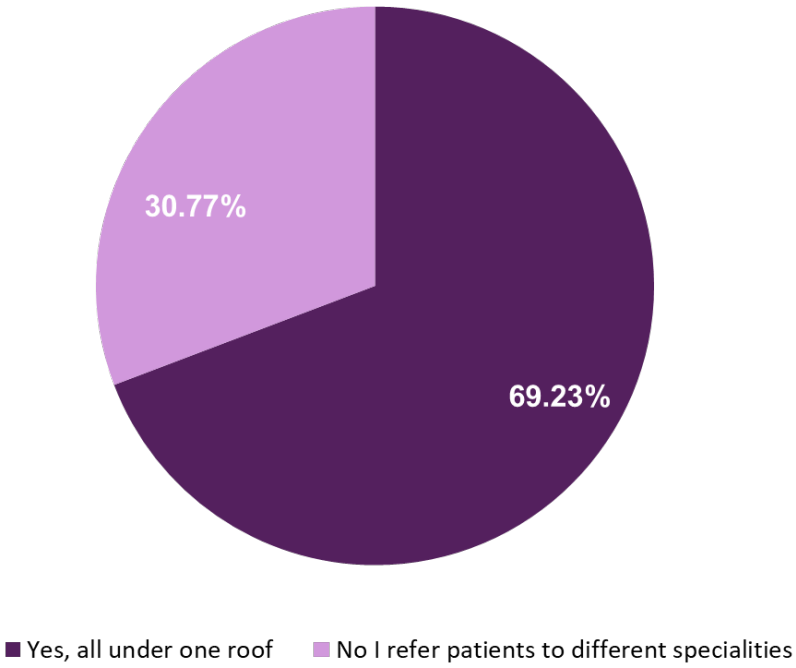


- The majority of physicians (84.62%) reported that the majority of their patients have well-differentiated NETs.
- A smaller proportion of respondents (15.38%) indicated that the majority of their patients have poorly differentiated NETs.

10. Do you have team of multispecialty to manage neuroendocrine tumors in your hospital (including interventional radiology, pathologist, nuclear medicine, surgery etc)?

a. Yes, all under one roof

b. No I refer patients to different specialties



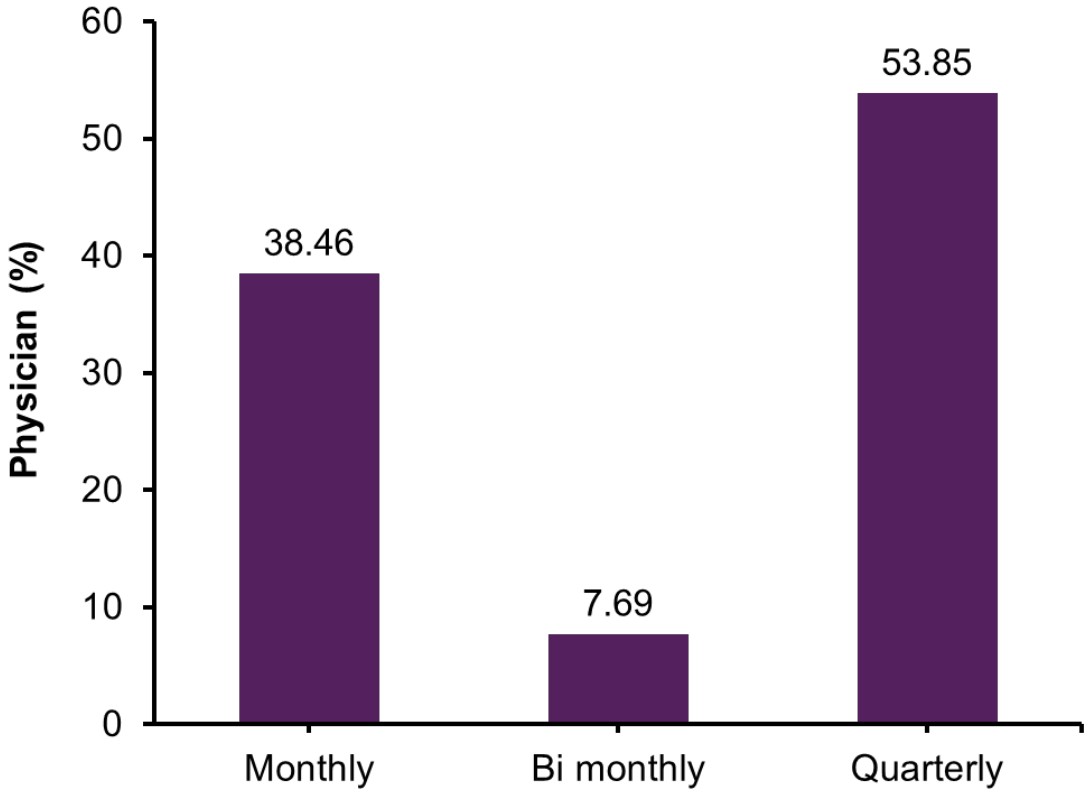
- A majority of physician (69.23%) indicated that their hospital has a multispecialty team available for the management of NETs, with all relevant specialties (e.g., interventional radiology, pathology, nuclear medicine, surgery) working together in the same facility.
- While, a smaller number of physician (30.77%) reported that they refer patients to different specialties for management of NETs.

11. At what intervals patients with metastatic NET follow up

a. Monthly

b. Bi monthly

c. Quarterly



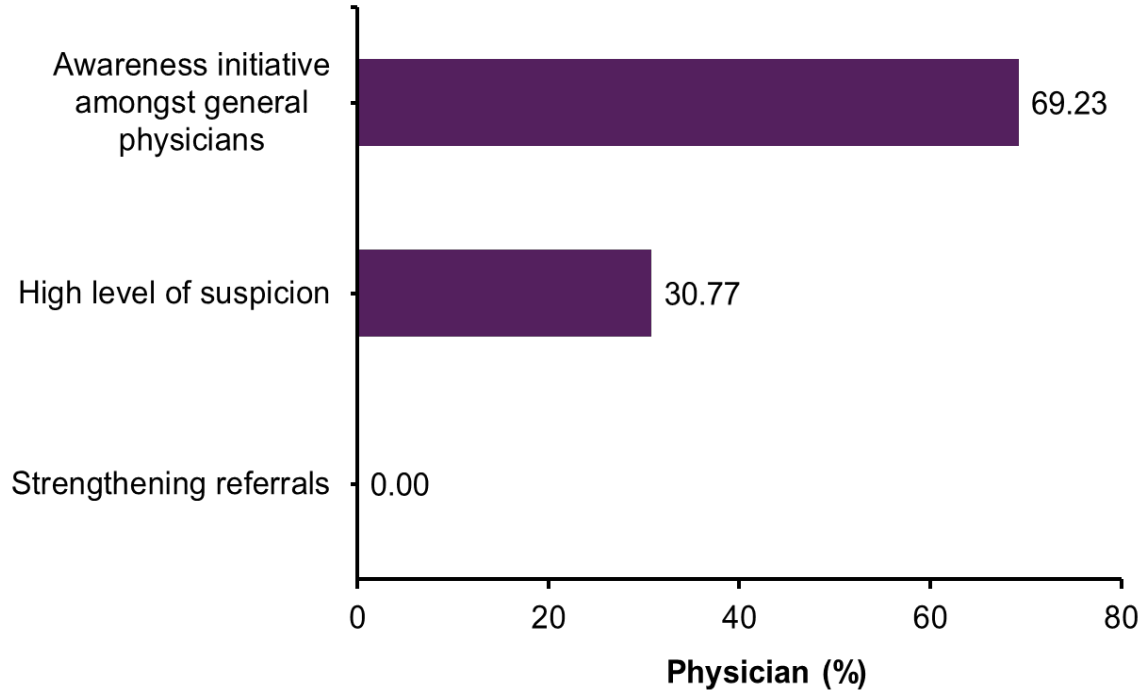
- The majority (53.85%) of physicians follow up with metastatic NET patients on a quarterly basis.
- While, a significant portion (38.46%) of respondents follow up with their metastatic NET patients on a monthly basis.
- A smaller group (7.69%) reported a bi-monthly follow-up interval.

12. What is most important for early diagnosis / awareness for early diagnosis of NET?

a. Awareness initiative amongst general physicians

b. High level of suspicion

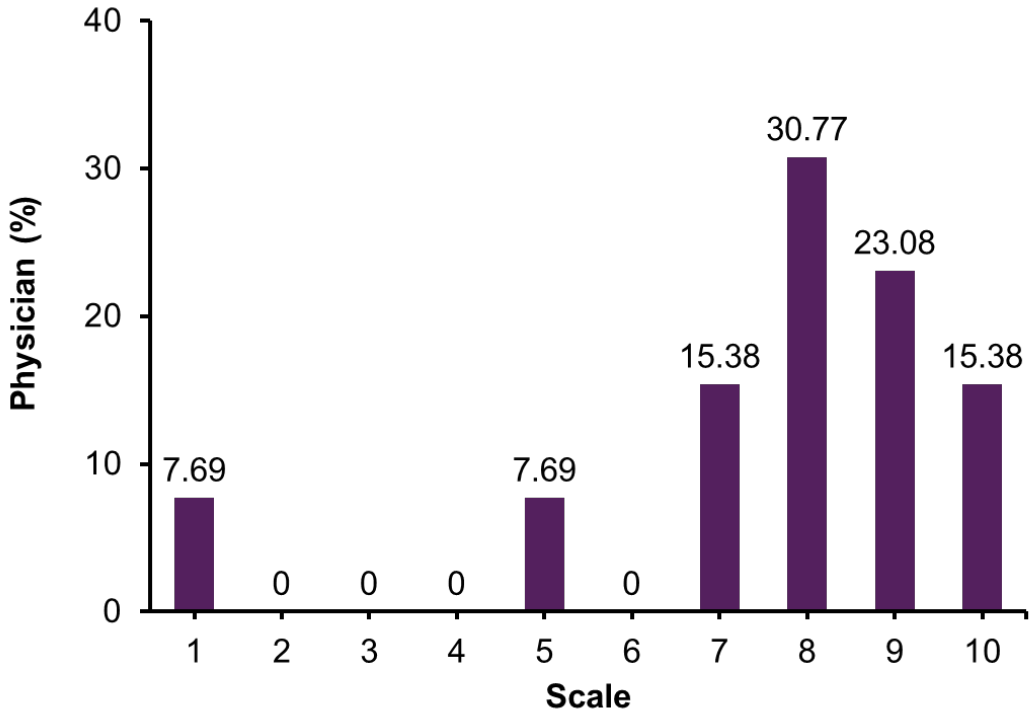
c. Strengthening referrals



- The majority of physicians (69.23%) believe that awareness initiatives among general physicians are the most important factor for the early diagnosis of NETs.
- A significant portion (30.77%) emphasized the importance of maintaining a high level of suspicion for NETs.
- None of the physician preferred strengthening referrals as the most important factor early diagnosis / awareness for early diagnosis of NET.

13. How would you rate efficacy with octreotide long acting in your patients on below scale? (1 worse – 10 best)

Scale: 1 2 3 4 5 6 7 8 9 10



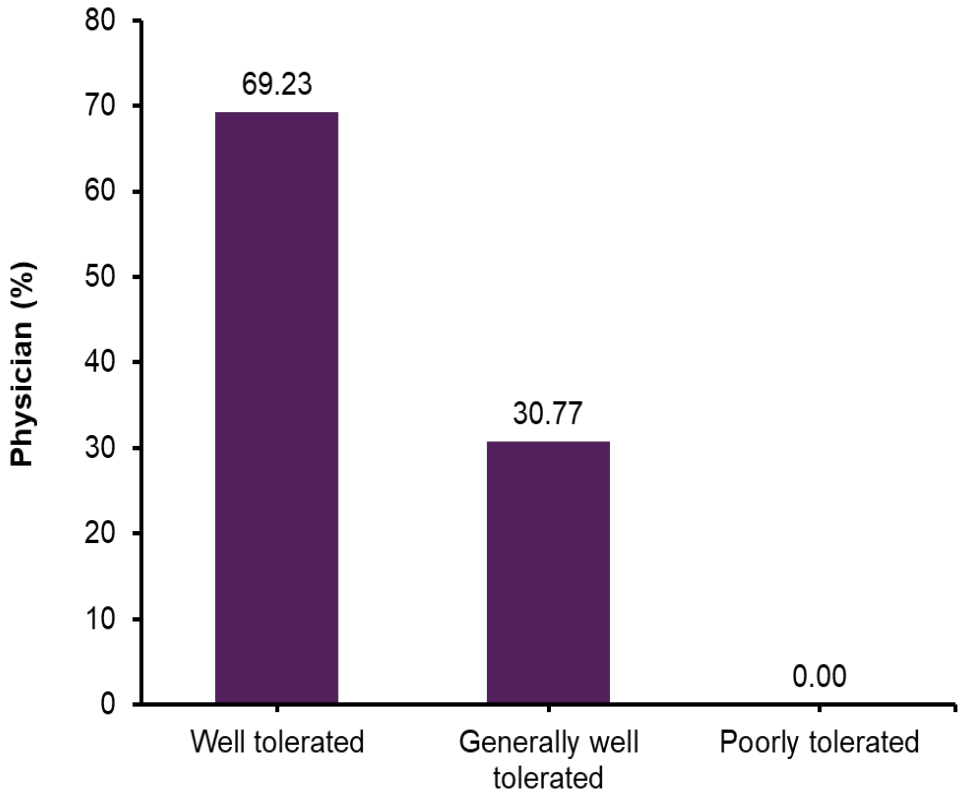
- The majority of physicians (30.77%) rate 8 for the efficacy with octreotide long acting in the patients.
- A significant portion (23.08%) %) rate 9 for the efficacy with octreotide long acting in the patients.
- A smaller group (15.38%) rate 7 and 10 each, for the efficacy with octreotide long acting in the patients.
- While, 7.69% of physicians rate 1 and 5 each, for the efficacy with octreotide long acting in the patients.
- None of the physician's rate 2, 3, 4 and 6.

14. How would you rate compliance with octreotide long acting in your patients?

a. Well tolerated

b. Generally well tolerated

c. Poorly tolerated



- The majority (69.23%) of physicians reported a response well tolerated rate of compliance with octreotide long acting in the patients.
- A significant portion (30.77%) of physicians reported a generally well tolerated rate of compliance with octreotide long acting in the patients.
- None of the physician rate poorly tolerated rate.

15. What % of your patients go for PRRT treatment?

a. Upto 10%

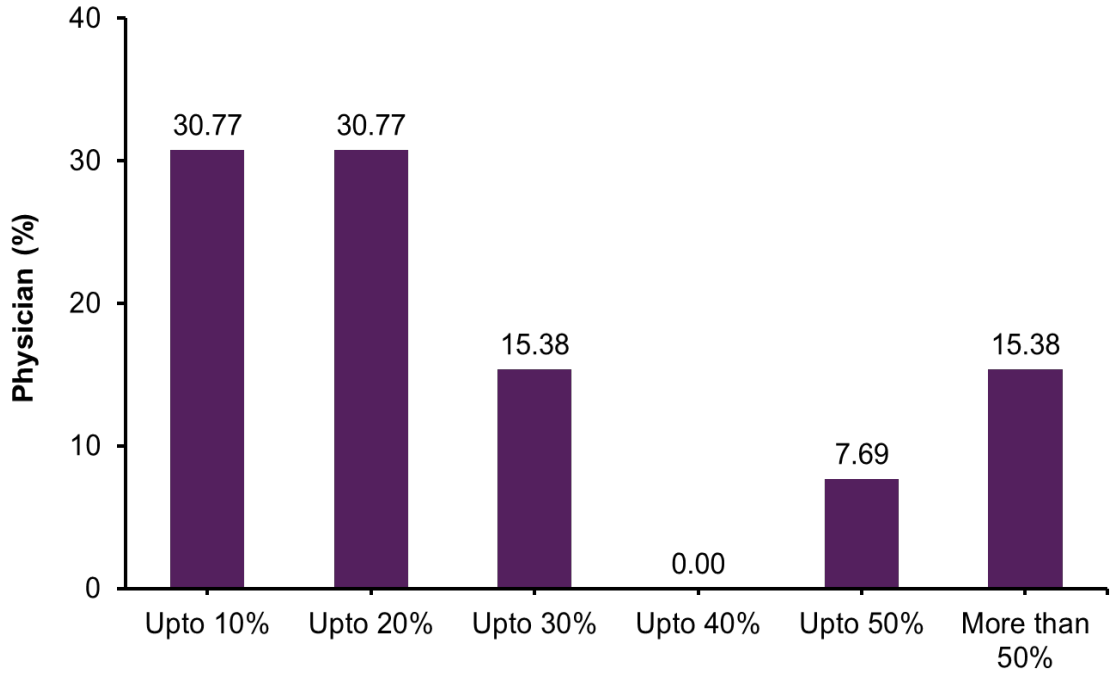
b. Upto 20%

c. Upto 30%

d. Upto 40%

e. Upto 50%

f. More than 50%



- The majority (30.77%) of physicians reported that up to 10% of their patients go for PRRT treatment.
- Another 31% of physicians reported that up to 20% of their patients go for PRRT treatment.
- Around 15% of physicians reported that up to 30% of their patients go for PRRT treatment.
- A small percentage (7.69%) of physicians reported PRRT in up to 50% of their treatment cases.
- About 15.38% of physicians reported PRRT in more than 50% of their treatment cases.
- No physicians reported receiving PRRT treatment in up to 40% of cases.

6 SUMMARY

A recent survey of physicians highlighted key trends in the management of neuroendocrine tumors (NETs). A significant proportion of physicians (61.54%) preferred Octreotide LAR as the first-line treatment for symptomatic metastatic disease, while chemotherapy was favored by 38.46% for clinically significant progressive cases. For unresectable, metastatic, asymptomatic, and stable disease, Octreotide LAR was also the most commonly recommended first-line treatment (76.92%), although a smaller group (15.38%) adopted a more conservative approach with observation.

For radiological diagnosis of NETs, DOTA was overwhelmingly preferred (83.33%), followed by MRI (16.67%). Chromogranin A was considered a key diagnostic parameter by 53.85% of physicians, with a smaller number emphasizing the importance of IHC confirmation and synaptophysin. Moreover, the majority of physicians (69.23%) believed that awareness initiatives among general practitioners were critical for the early diagnosis of NETs.Regarding treatment practices, Octreotide LAR was generally well tolerated, with most physicians (69.23%) reporting good compliance among patients. A significant portion of physicians also used peptide receptor radionuclide therapy (PRRT), with about 31% of patients undergoing treatment in up to 20% of cases.

In terms of NET tumor locations, the gastrointestinal (GI) and pancreatic regions were the most common sites observed in practice, with the small intestine and stomach being the most frequent GI sites. Grade 1 NETs were most commonly seen (53.85%), and a majority of physicians (84.62%) reported treating well-differentiated NETs. Follow-up intervals varied, with 53.85% of physicians conducting quarterly checkups for metastatic NET patients, while others preferred more frequent (monthly) or less frequent (bi-monthly) follow-ups. A multidisciplinary approach for managing NETs was common, with 69.23% of physicians reporting that their hospitals offered comprehensive care within a single facility.

7 DISCUSSION

This survey provides valuable insights into current physician practices for managing NETs, shedding light on the treatment strategies, diagnostic preferences, and challenges faced by healthcare professionals. The data suggests a strong preference for Octreotide LAR as the first-line treatment for symptomatic metastatic NETs (61.54%), reflecting its established efficacy and widespread use. Additionally, Octreotide LAR is similarly favored for managing unresectable, asymptomatic, low tumour burden, and stable NETs (76.92%). However, a smaller group of physicians prefer a more conservative approach, opting for observation (15.38%) in select cases. These findings indicate that while Octreotide LAR remains the cornerstone of treatment for most NET patients, there is still room for individualized care based on disease characteristics and patient response.

In terms of diagnostic approaches, the preference for DOTA (83.33%) as a radiological diagnostic tool highlights its pivotal role in accurately identifying NETs, while MRI is also considered valuable by a minority (16.67%). Chromogranin A is largely regarded as a key diagnostic parameter, underscoring its importance in assessing tumour presence and progression. Moreover, the survey reveals a high level of compliance with Octreotide LAR among patients, with 69.23% of physicians reporting good tolerance. This reflects not only the effectiveness of the drug but also the manageable side effect profile, which contributes to its widespread use. The data also suggests that a multidisciplinary approach to NET management is common, with 69.23% of physicians indicating that their institutions offer integrated care across specialties. This multidisciplinary care model is crucial for optimizing patient outcomes, as the complexity of NET management often requires expertise from various fields such as nuclear medicine, surgery, and pathology.

These findings highlight the ongoing evolution in the treatment and management of NETs, with a clear preference for established therapies like Octreotide LAR, but also a recognition of the need for personalized treatment strategies and further advancements in diagnostic and therapeutic tools. The survey underscores the importance of continued research to enhance patient outcomes, particularly for those with advanced or relapsed disease, and stresses the significance of raising awareness among general practitioners for early detection and intervention.

8 CLINICAL RECOMMENDATIONS

- Octreotide LAR should continue to be the preferred first-line treatment for symptomatic metastatic NETs. Physicians should consider standardizing treatment protocols to ensure consistent use of Octreotide LAR in eligible patients and assess its effectiveness regularly to adjust dosing or explore alternative treatments if necessary.
- Clinicians should consider individual patient factors, such as tumour progression and overall health, before opting for observation in select cases. A more conservative approach may be suitable for some patients, particularly those with stable disease, and should be revisited periodically to assess the need for active treatment.
- Given its preference among physicians (83.33%), DOTA should remain the primary diagnostic tool for NETs. Healthcare institutions should ensure that clinicians are well-equipped with the necessary technology for DOTA-based imaging to facilitate accurate diagnosis and disease monitoring. MRI may also be considered in select cases where additional imaging is required for better assessment of disease spread.
- Chromogranin A is identified as an important marker for diagnosing and monitoring NETs, with 53.85% of physicians highlighting its value. Clinicians should consider using Chromogranin A alongside other diagnostic tools such as DOTA imaging for comprehensive patient assessment. Regular monitoring of Chromogranin A levels can also help in tracking disease progression and treatment response.
- A significant majority of physicians (69.23%) work in institutions that provide multidisciplinary care for NET patients, involving specialists in nuclear medicine, pathology, surgery, and interventional radiology. Strengthening this collaborative approach is recommended, especially for complex cases requiring advanced treatments like PRRT or surgery.
- As the majority of physicians (69.23%) believe awareness initiatives are crucial for early diagnosis, healthcare systems should prioritize education for general practitioners about the signs and symptoms of NETs. Early referral to specialists can improve patient outcomes by enabling earlier diagnosis, timely treatment initiation, and better management of progressive disease.

9 CONSULTANT OPINION

The findings from this survey on the management of NETs reflect current best practices and highlight the key treatment preferences and diagnostic tools used by physicians. The preference for Octreotide LAR as the first-line treatment for symptomatic metastatic NETs is well-established, and the data reinforces its widespread use as an effective therapy. This aligns with the majority of physicians recognizing Octreotide LAR's central role in treating metastatic NETs, particularly for those with symptomatic disease, demonstrating its continued efficacy and role in clinical practice.

The survey also indicates a more nuanced approach in the treatment of asymptomatic, low tumour burden NETs, where Octreotide LAR is again preferred for initial therapy. However, a smaller group of physician’s favor observation, suggesting that for certain patients, particularly those with stable disease, a more conservative approach may be appropriate. This individualized treatment strategy emphasizes the importance of tailoring therapy based on disease characteristics and patient stability.

Diagnostic practices, especially the use of DOTA imaging, are also well-aligned with the current standard of care for NETs. DOTA is overwhelmingly preferred, reflecting its accuracy and reliability in diagnosing NETs. Chromogranin A is similarly regarded as a key marker in disease monitoring, reinforcing the importance of integrating both imaging and biomarker testing for comprehensive assessment and monitoring of disease progression.

The findings also point to the critical role of a multidisciplinary approach in managing NETs, particularly for complex cases. The majority of physicians work within institutions offering integrated care across specialties, such as surgery, nuclear medicine, and interventional radiology. This collaborative model is essential for optimizing patient outcomes and ensuring that treatment decisions are well-informed and tailored to each patient's unique clinical situation. Continued research, education, and collaboration among specialists will be crucial in advancing treatment strategies and improving outcomes for NET patients.

10 MARKET OPPORTUNITIES

The survey findings on the management of NETs present several significant market opportunities for pharmaceutical companies and healthcare providers. The continued preference for Octreotide LAR as a first-line treatment for symptomatic metastatic NETs highlights a stable demand for this therapy, which remains a cornerstone in the management of NETs. Given the high level of physician satisfaction with Octreotide LAR's effectiveness and tolerability, there is an opportunity for manufacturers to promote its use further and explore new formulations or combination therapies that could enhance patient outcomes.

Additionally, the strong preference for DOTA imaging (83.33%) suggests a continued market demand for diagnostic tools that support accurate NET diagnosis and disease monitoring. Companies specializing in radiology and nuclear medicine could capitalize on this by advancing DOTA-based imaging technologies or offering complementary imaging solutions.

Moreover, the survey's emphasis on individualized care for NET patients presents a unique opportunity for companies to introduce personalized treatment options tailored to different patient profiles. While Octreotide LAR remains dominant, there is room for the development of alternative or adjunctive therapies, especially for patients with asymptomatic, low tumor burden NETs or those with stable disease who may benefit from observation or more conservative treatment approaches. The integration of biomarkers like Chromogranin A in monitoring disease progression further underscores the potential for diagnostic and therapeutic innovations that combine imaging with biomarker testing.

This trend toward precision medicine presents an opportunity for pharmaceutical and diagnostic companies to create integrated care solutions that enhance the overall management of NETs, driving both patient outcomes and market growth in this field.

11 MARKET POSITIONING

- A majority of physicians (61.54%) continue to prefer Octreotide LAR as the first-line treatment for symptomatic metastatic NETs, establishing it as the market leader. Companies can position their Octreotide LAR formulations as the go-to therapy for symptomatic NET patients, emphasizing its proven efficacy and established role in clinical practice.
- With 76.92% of physicians favouring Octreotide LAR for managing unresectable, asymptomatic, or low tumour burden NETs, there is a clear opportunity for companies to further strengthen their position in these treatment areas. Highlighting the benefits of Octreotide LAR for stabilizing disease and improving quality of life in these patients can help reinforce its value in early-stage or stable disease management.
- The widespread use of multidisciplinary care (69.23%) in NET management offers a market opportunity for products and services that facilitate integrated care across specialties like nuclear medicine, surgery, and pathology. Companies can position their therapies as part of a comprehensive care model, optimizing patient outcomes through collaboration among specialists.
- With 83.33% of physicians selecting DOTA as their primary diagnostic tool for NETs, there is a strong market opportunity for companies that offer DOTA-based diagnostic solutions. Providing advanced DOTA imaging technologies or complementary diagnostic tools can help enhance accuracy in diagnosing and monitoring NETs, positioning companies as leaders in NET diagnostics.
- The trend toward individualized care in NET management, including observation for certain patients, creates a market for targeted therapies and personalized treatment options. Pharmaceutical companies can position their products as adaptable therapies that cater to different disease stages and patient profiles, especially for those with stable or slow-progressing disease.
- The importance of Chromogranin A in diagnosing and monitoring NETs (reported by 53.85% of physicians) presents an opportunity for companies to develop or promote companion diagnostic tools. Products that combine biomarker testing with therapeutic solutions can offer a more comprehensive approach to NET management, positioning brands as essential in the ongoing monitoring and personalization of NET care.

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