Survey Report

Octreotride and its therapy indication

Version No.: 1.1

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.

Table of content

1 INTRODUCTION

Octreotide is an FDA-approved therapy used in the management and treatment across various medical conditions [1]. Octreotide is a medication that belongs to the class of drugs known as somatostatin analogs, a hormone that inhibits the release of numerous hormones including growth hormone, insulin, glucagon, and others [1,2].

Octreotide has proven superior to bromocriptine in managing acromegaly and thyrotrophinomas, and shows exceptional efficacy in controlling carcinoid syndrome crises and managing VIPoma and refractory metastatic cases. Additionally, octreotide serves as a first-line therapy for reducing high-output diarrhea in conditions like AIDS-related cryptosporidiosis. While initial studies demonstrate promising results in conditions such as hyperinsulinemia, diabetes, pancreatitis, dumping syndrome, and postprandial hypotension, further research is essential to fully integrate octreotide into definitive treatment guidelines for these diseases. Additionally, it is widely used in the management of neuroendocrine tumors (NETs) due to its ability to suppress hormone hypersecretion and slow tumor growth [1,3].

Octreotide inhibits hormone secretion (e.g., GH, TSH, insulin, glucagon) by binding somatostatin receptors; it induces vascular smooth muscle contraction via L-type calcium channels, activating myosin light-chain kinase through calcium release from the sarcoplasmic reticulum via ryanodine receptors and IP3 formation [1]. It administered intravenously or subcutaneously due to poor oral absorption, is well tolerated with comparable bioavailability via both routes. Serum levels rise proportionally with dosage. Its disposition exhibits a biphasic pattern: an initial half-life of 9 to 13 minutes followed by a terminal phase lasting 90 minutes considerably longer than that of somatostatin. It primarily metabolized by the liver, exhibits prolonged plasma half-life in cirrhotic patients [4].

Moreover, octreotide is pivotal in treating NETs, which arise from endocrine and nervous system cells, sharing structural and immunohistochemical similarities with secretory granules. Over 25 years, it's become crucial for managing gastroenteropancreatic NETs, showing potent anti-secretory effects and diverse mechanisms [5]. Octreotide formulations is generally well tolerated with

established safety in clinical use, often improving quality of life. Common adverse effects include injection site pain mild hyperglycemia, and gastrointestinal issues like loose stools, cramping, nausea, and flatulence. Long-term adverse effects beyond short-term studies remain less certain and potentially underestimated [5].

Thus, this study aimed to comprehensively examine the therapeutic indications, pharmacological mechanisms, safety profile, and clinical outcomes associated with octreotide therapy across various medical conditions.

2 RATIONALE OF THE STUDY

The rationale for this study was to investigate octreotide's therapeutic effectiveness across diverse medical conditions, focusing on its ability to suppress hormones, manage symptoms, and potentially influence disease progression and quality of life. This research aimed to enhance clinical outcomes and inform evidence-based treatment guidelines.

3 STUDY OBJECTIVE

The primary objective of this study was to assess octreotide's efficacy in hormone secretion control, symptom management, safety profile, and its impact on disease progression and quality of life across diverse patient populations.

4 METHODS

This study proposed a retrospective analysis of patient records to evaluate the clinical outcomes of octreotide therapy across various healthcare centers. The research involved administering a 15-question survey covering aspects such as patient demographics, diagnostic methods, treatment durations, clinical results, and preferences regarding scientific engagement. Physicians were identified and invited to participate through professional networks and medical associations, ensuring they received detailed information prior to their involvement.

The survey responses were collected electronically and stored securely to safeguard patient confidentiality. Subsequently, a rigorous statistical analysis was conducted to summarize the findings and identify significant trends in octreotide therapy outcomes. The target sample size for this study was set at 100 Indian physicians to ensure a diverse and representative dataset that could support meaningful statistical analysis.

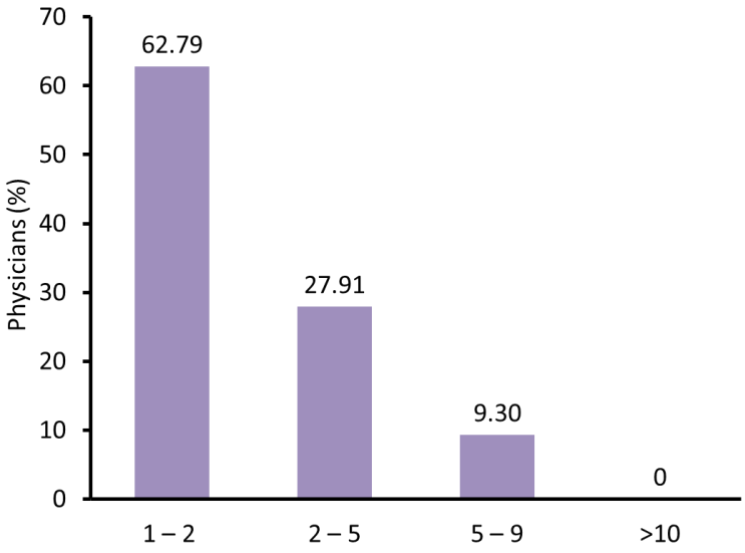
Ethical considerations were paramount throughout the study, encompassing the acquisition of informed consent from patients, adherence to strict confidentiality measures for medical records, and compliance with ethical guidelines governing retrospective data analysis. Once the data were analyzed, the results were compiled into a comprehensive report. Depending on the relevance and suitability, findings were disseminated through scientific publications and presentations at conferences to contribute valuable insights to the medical community. This dissemination aimed to foster scientific dialogue and potentially influence clinical practices for optimizing patient care in the realm of octreotide therapy.

5 RESULTS

A total of 137 physicians participated in the survey. Below is the summary of the responses.

Question 1: How many patients of functional NET per month?

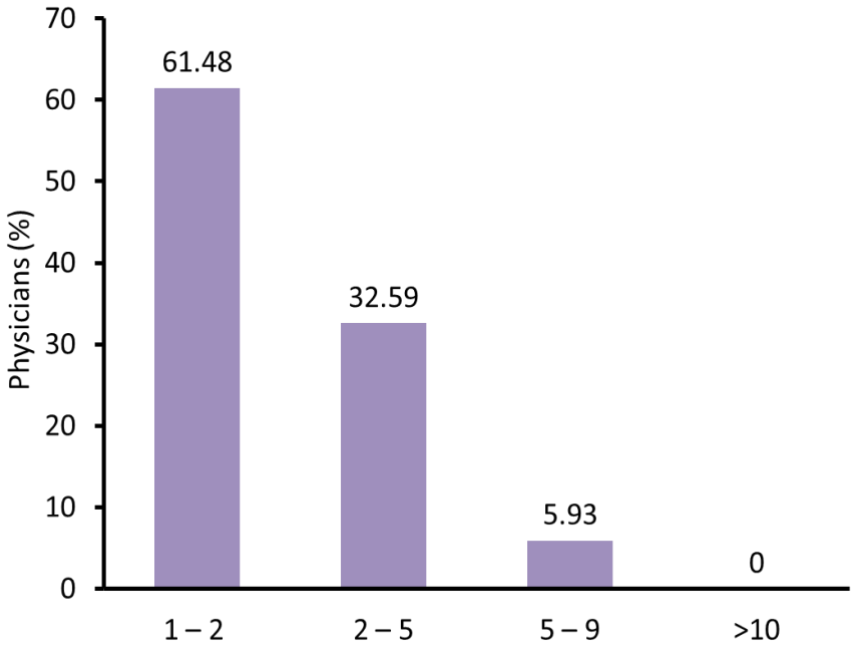
Options	Number of physicians (N=129)
1 – 2	81 (62.79)
2 – 5	36 (27.91)
5 – 9	12 (9.30)
>10	0
Data presented as n (%).	



- The majority of physicians (62.79%) saw 1 to 2 patients with functional NETs per month.
- A significant number of physicians (27.91%) reported seeing between 2 to 5 patients per month, suggesting a moderate caseload of patients with this condition.
- A smaller percentage of physicians (9.30%) reported seeing between 5 to 9 patients per month, indicating a higher volume of patients compared to the previous categories.

Question 2: How many patients of non-functional NET per month?

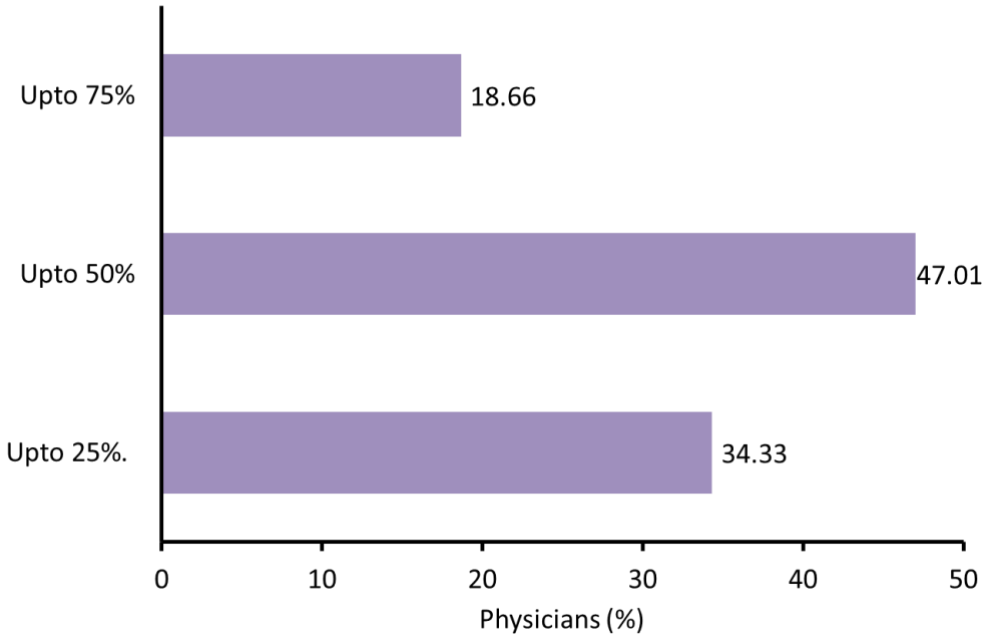
Options	Number of physicians (N=135)
1 – 2	83 (61.48)
2 – 5	44 (32.59)
5 – 9	8 (5.93)
>10	0
Data presented as n (%).	



- The majority of physicians (61.48%) reported seeing between 1 to 2 patients with non-functional NETs per month.
- A significant number of physicians (32.59%) reported seeing between 2 to 5 patients per month, indicating a moderate caseload of patients with this condition.
- A smaller percentage of physicians (5.93%) reported seeing between 5 to 9 patients per month, suggesting a higher volume of patients compared to the previous categories.

Question 3: In your clinical practice what % patients who have non-functional NET are well differentiated?

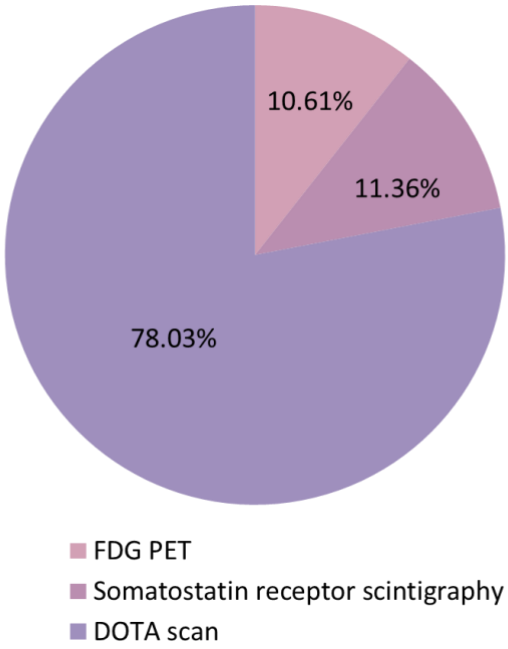
Options	Number of physicians (N=134)
Upto 25%	46 (34.33)
Upto 50%	63 (47.01)
Upto 75%	25 (18.66)
Data presented as n (%).	



- The majority of physicians (47.01%) reported that up to 50% of their patients with non-functional NETs are well differentiated.
- A considerable number of physicians (34.33%) indicated that up to 25% of their non-functional NET patients are well differentiated, highlighting variability in the extent of differentiation among cases seen in clinical practice.
- A smaller group of physicians (18.66%) reported that up to 75% of their non-functional NET patients are well differentiated, indicating that for some clinicians, a higher proportion of their patients fall into this category.

Question 4: What is most common investigation you do for NET diagnosis and confirmation?

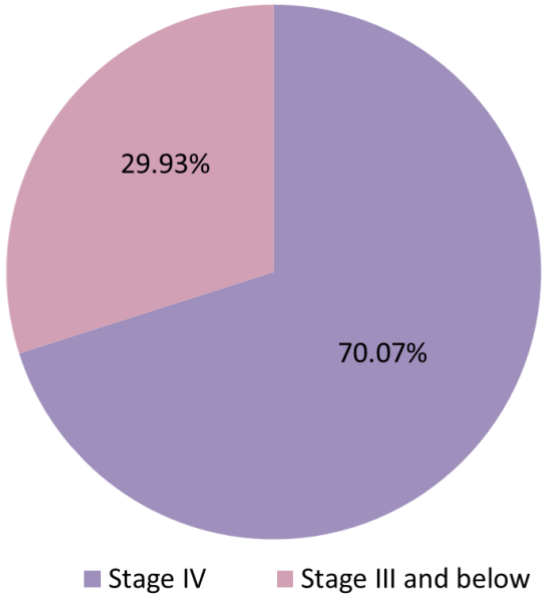
Options	Number of physicians (N=132)
DOTA scan	103 (78.03)
Somatostatin receptor scintigraphy	15 (11.36)
FDG PET	14 (10.61)
Data presented as n (%). DOTA, defense of accidents; FDG PET, fluorodeoxyglucose-positron emission tomography.	



- This indicates that the majority of physicians (78.03%) rely on DOTA scan as the primary investigation for diagnosing and confirming NETs.
- A smaller number of physicians (11.36%) used somatostatin receptor scintigraphy, which is another imaging technique that targets somatostatin receptors on NET cells.
- FDG PET (10.61%) was used by a minority of physicians. It detects areas of increased glucose metabolism, which may be useful in certain types of NETs that are more metabolically active.

Question 5: At what stage does NET patients generally present in your clinical practice?

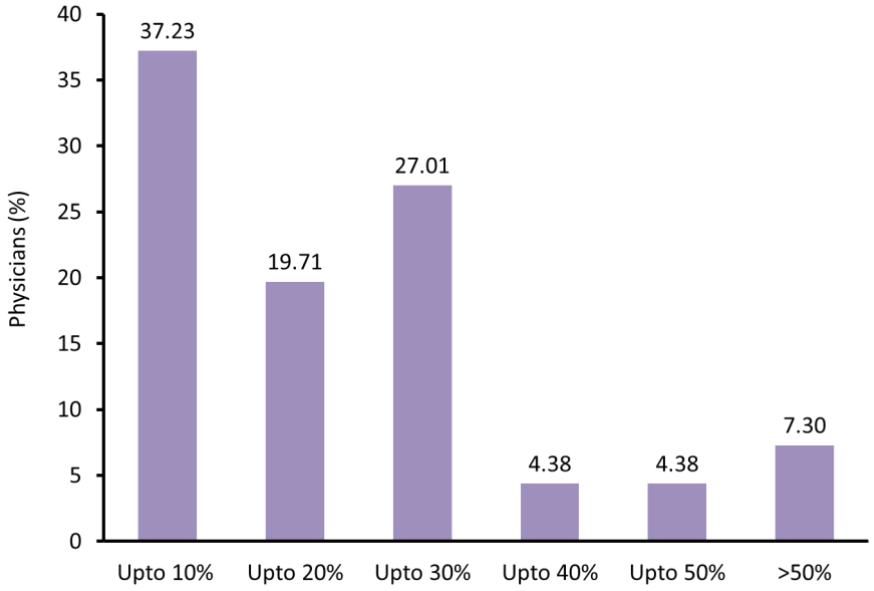
Options	Number of physicians (N=137)
Stage IV	96 (70.07)
Stage III and below	41 (29.93)
Data presented as n (%).	



- The data highlights that a significant majority (70.07%) of NET patients in clinical practice present at stage IV, indicating widespread metastatic disease at the time of diagnosis.
- A smaller but notable proportion (29.93%) of patients present at stage III or below, suggesting varying degrees of disease progression and presentation.
- The predominance of stage IV presentations underscores the challenges in early detection.
- It highlights the critical need for improved screening strategies and awareness to potentially identify NETs at earlier stages when treatment outcomes may be more favorable.

Question 6: What % of your patients go for PRRT treatment?

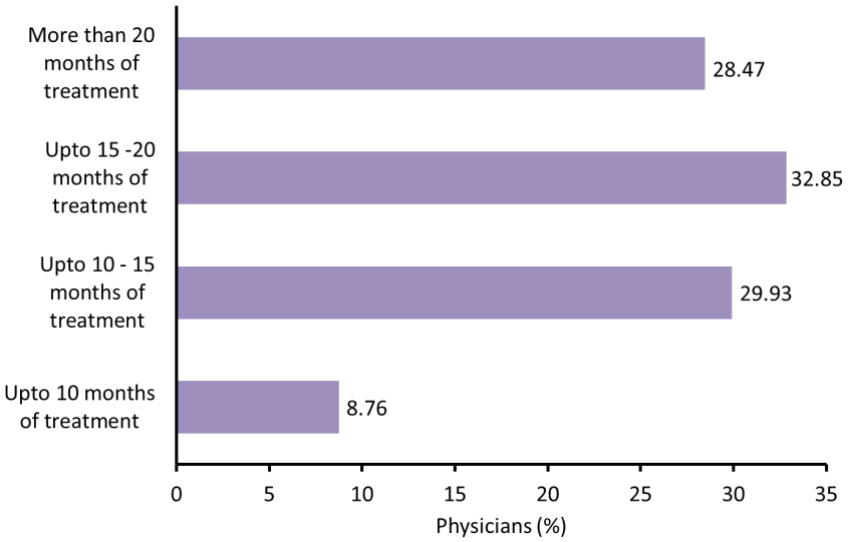
Options	Number of physicians (N=137)
Upto 10%	51 (37.23)
Upto 20%	27 (19.71)
Upto 30%	37 (27.01)
Upto 40%	6 (4.38)
Upto 50%	6 (4.38)
More than 50%	10 (7.30)
Data presented as n (%). PRRT, peptide receptor radionuclide therapy.	



- The largest group of physicians (37.23%) reported that up to 10% of their patients receive PRRT.
- A significant proportion (19.71%) reported that up to 20% of their patients undergo PRRT, suggesting a broader but still targeted use of this treatment modality.
- Similarly, 27.01% of physicians reported that up to 30% of their patients receive PRRT, indicating its increasing but measured application in the treatment of NETs.

Question 7: What is the average duration or how long your patients with non-functional metastatic NET continue to take octreotide?

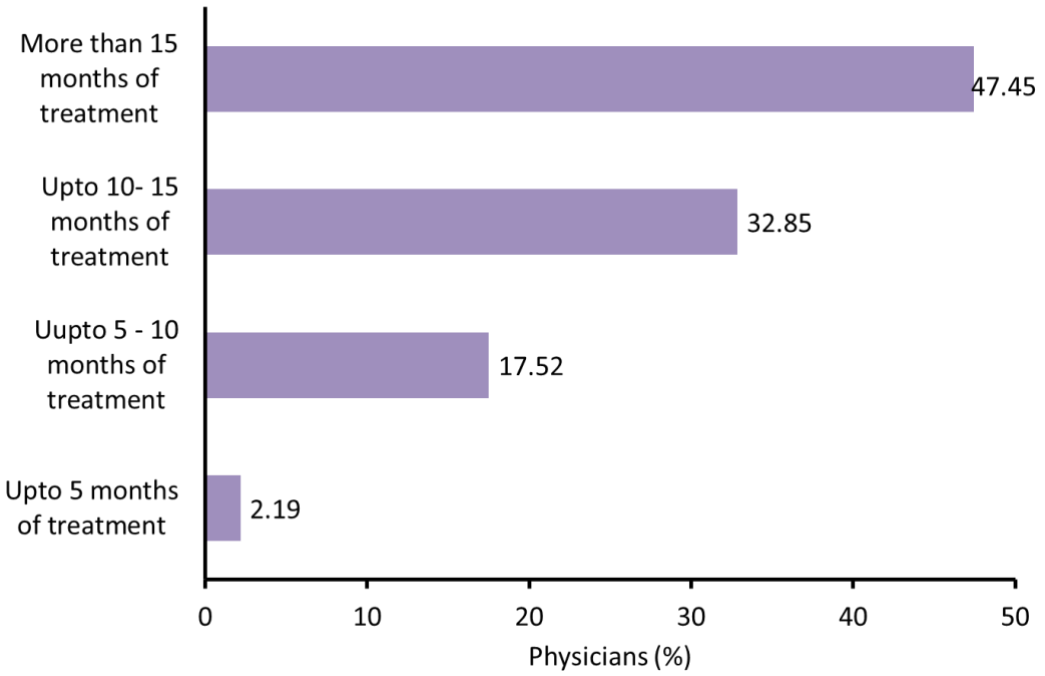
Options	Number of physicians (N=137)
On an average patient take upto 10 months of treatment	12 (8.76)
On an average patient take upto 10 - 15 months of treatment	41 (29.93)
On an average patient take up to 15 -20 months of treatment	45 (32.85)
On an average patient more than 20 months of treatment	39 (28.47)
Data presented as n (%).	



- Minority of physicians (8.76%) reported that, on average, their patients with NETs take treatment for up to 10 months.
- Nearly one-third of physicians (29.93%) indicated that patients typically continue treatment for 10 to 15 months.
- The largest proportion of physicians (32.85%) reported an average treatment duration of 15 to 20 months.
- A significant number of physicians (28.47%) reported that patients continue treatment for more than 20 months on average.

Question 8: What is the average duration or how long your patients with functional metastatic NET continue to take octreotide?

Options	Number of physicians (N=137)
On an average patient take upto 5 months of treatment	3 (2.19)
On an average patient take upto 5 - 10 months of treatment	24 (17.52)
On an average patient take upto 10-15 months of treatment	45 (32.85)
On an average patient more than 15 months of treatment	65 (47.45)
Data presented as n (%).	

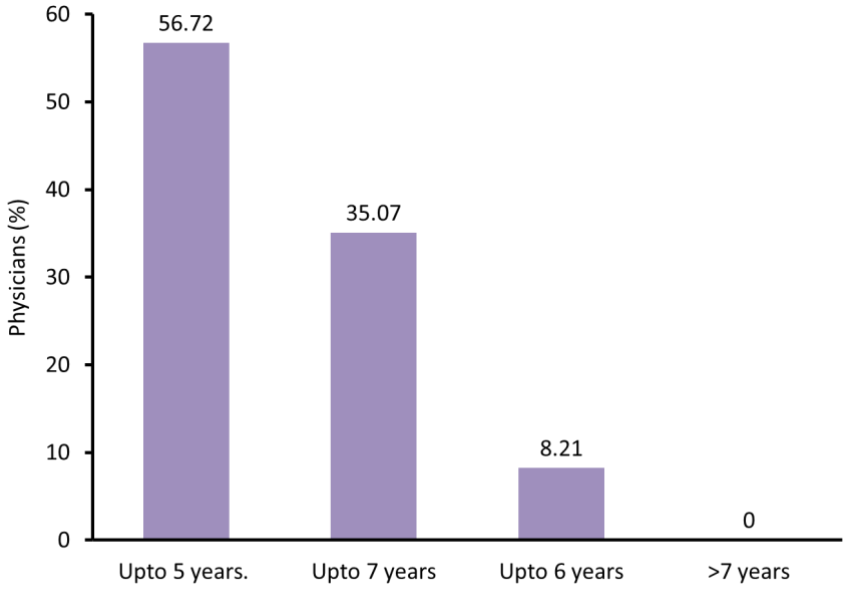


- A significant majority of physicians (47.45%) reported that, on average, their patients with functional metastatic NETs continue to take octreotide for more than 15 months.

- Additionally, 32.85% of physicians indicated that patients typically continue octreotide treatment for 10 to 15 months, indicating a substantial duration of therapy aimed at managing symptoms and disease stability.
- For 17.52% of physicians, patients are reported to take octreotide for 5 to 10 months on average, reflecting a shorter to moderate-term treatment approach depending on individual patient responses and disease progression.
- A smaller proportion of physicians (2.19%) reported an average treatment duration of up to 5 months, likely for patients who have shorter-term needs or specific responses to treatment.

Question 9: What is the average OS in your patients with metastatic NET?

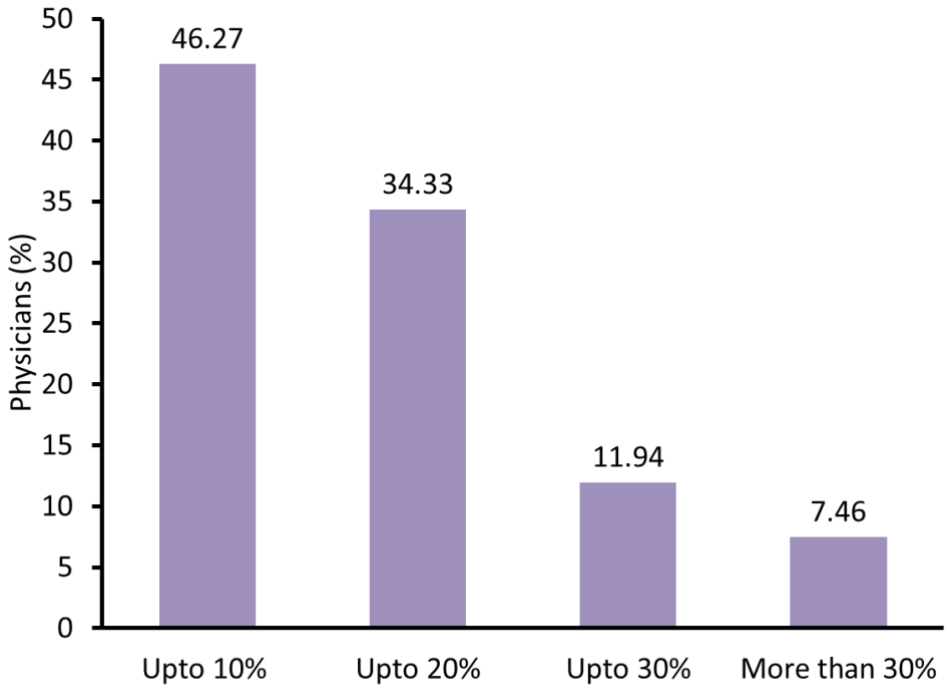
Options	Number of physicians (N=134)
Upto 5 years.	76 (56.72)
Upto 7 years	47 (35.07)
Upto 6 years	11 (8.21)
More than 7 years	0
Data presented as n (%). OS, overall survival.	



- The majority of physicians (56.72%) reported an average overall survival of up to 5 years for their patients with metastatic NETs. This timeframe likely reflects the typical progression and management of the disease.
- A significant number of physicians (35.07%) indicated that their patients' average overall survival extends up to 7 years, suggesting that some patients experience longer-term survival with appropriate treatment and management strategies.
- A smaller percentage of physicians (8.21%) reported an average OS of up to 6 years, indicating variability in patient outcomes and treatment responses among different practices.

Question 10: What % of your patients take TKI as first line for NET?

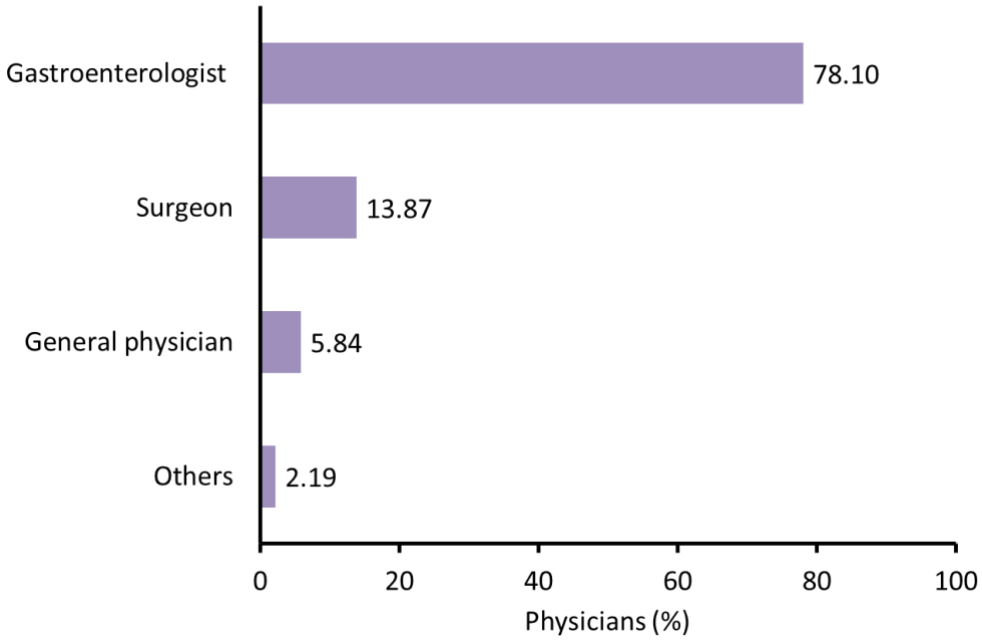
Options	Number of physicians (N=134)
Upto 10%	62 (46.27)
Upto 20%	46 (34.33)
Upto 30%	16 (11.94)
More than 30%	10 (7.46)
Data presented as n (%). TKI, tyrosine kinase inhibitor.	



- A significant proportion of physicians (46.27%) reported that up to 10% of their NET patients are prescribed TKIs as their initial treatment. This suggests that TKIs may be considered in a moderate number of cases but not as a predominant first-line option.
- Additionally, 34.33% of physicians indicated that up to 20% of their patients receive TKIs as first-line therapy, indicating a broader but still selective use among NET patients.
- For a smaller subset of physicians, TKIs are used more extensively, with 11.94% prescribing them to up to 30% of their patients as initial treatment.
- Moreover, 7.46% of physicians using TKIs in more than 30% of cases. This suggests a minority of physicians rely more heavily on TKIs as a primary therapeutic option for NETs.

Question 11: In your clinical practice, from which speciality you get NET referrals?

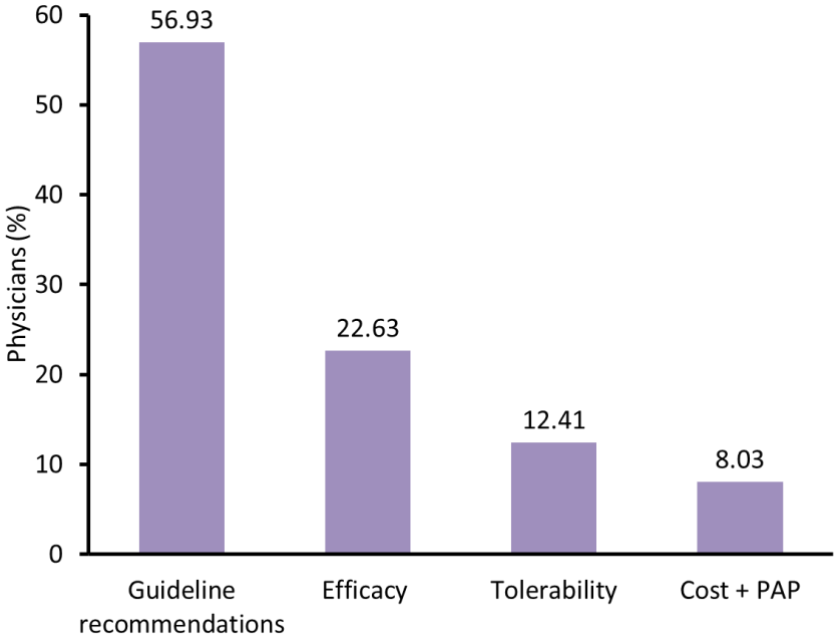
Options	Number of physicians (N=137)
Gastroenterologist	107 (78.10)
Surgeon	19 (13.87)
General physician	8 (5.84)
Others	3 (2.19)
Data presented as n (%).	



- A significant majority, comprising 78.10% physicians, indicates their pivotal role in the diagnosis and treatment of NETs, particularly those affecting the gastrointestinal tract. Their expertise is crucial in navigating the complexities of gastrointestinal NETs.
- Representing 13.87%, surgeons play a critical role in the surgical management of NETs, performing procedures such as tumor resections and contributing essential skills in the comprehensive treatment approach.
- With 5.84%, general physicians contribute to the initial evaluation and referral process for patients suspected or diagnosed with NETs, underscoring their role in primary care coordination.

Question 12: In treatment, what are your key reasons for using octreotride in NET patients?

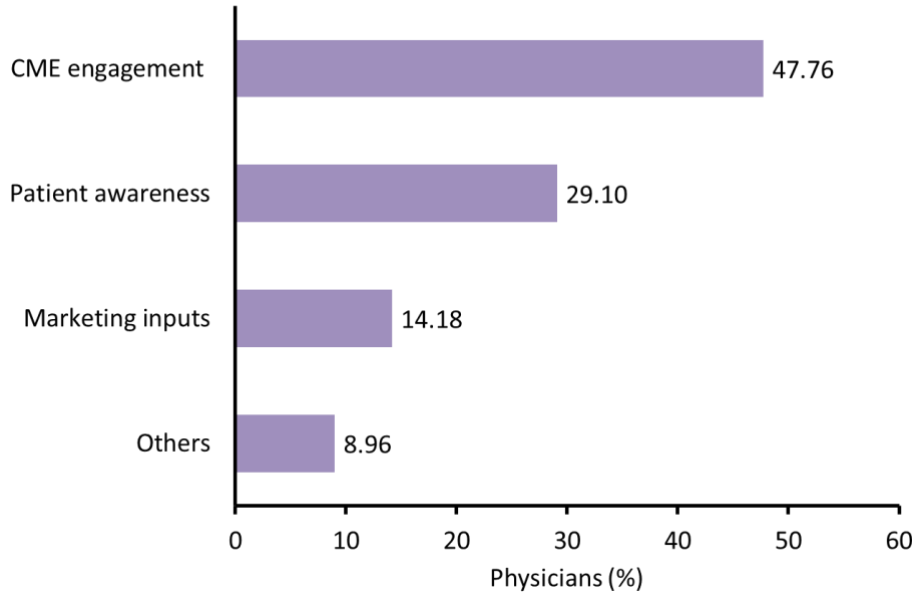
Options	Number of physicians (N=137)
Guideline recommendations	78 (56.93)
Efficacy	31 (22.63)
Tolerability	17 (12.41)
Cost + PAP	11 (8.03)
Data presented as n (%). PAP, papanicolaou.	



- Majority of physicians (56.93%) reported adherence to guideline recommendations as a primary reason for using octreotide in NET patients.
- About 22.63% of physicians chose efficacy as a reason for using octreotide.
- This highlights the perception among some physicians that octreotide effectively controls symptoms or slows disease progression in NET patients.
- Around 17 physicians (12.41%) indicated tolerability as a factor.
- Octreotide's favorable tolerability profile could make it a preferred choice, especially in maintaining patient compliance and quality of life.
- 11 physicians (8.03%) considered cost and possibly patient assistance programs (PAP) as reasons.

Question 13: In below options, what according to you can be improved or added to increase brand penetration?

Options	Number of physicians (N=134)
CME engagement	64 (47.76)
Patient awareness	39 (29.10)
Marketing inputs	19 (14.18)
Others	12 (8.96)
Data presented as n (%). CME, continuing medical education.	



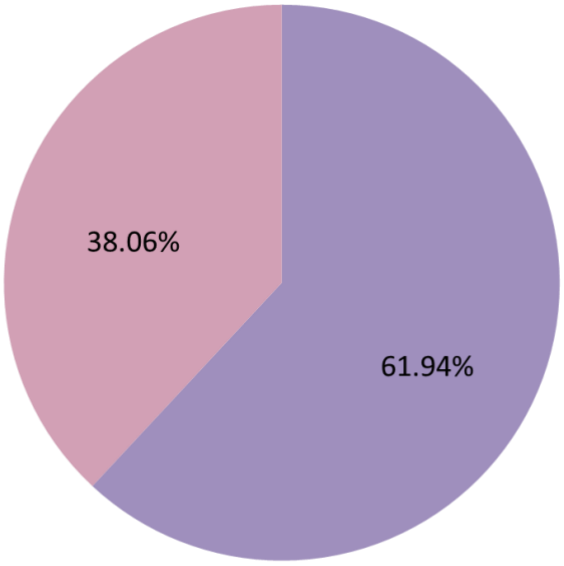
- The factor with the highest engagement was Continuing Medical Education (CME), with 64 physicians (47.76%) indicating that enhancing CME engagement could significantly improve brand penetration. This suggests that nearly half of the respondents believe that providing more educational opportunities and resources could foster greater familiarity and preference for the brand among medical professionals.
- Patient awareness was the second most frequently cited factor, with 39 physicians (29.10%) recognizing it as a key area for improvement. This indicates a substantial portion of the respondents consider increasing patient

knowledge and awareness of the brand to be crucial for better market penetration.

- Marketing inputs were identified by 19 physicians (14.18%) as an area that could benefit from enhancements. This reflects the view that more robust and targeted marketing strategies could help in reaching a broader audience and strengthening brand presence.
- Finally, 8.96% physicians mentioned other factors that were not specifically listed in the survey. These could include a variety of suggestions unique to individual experiences and perspectives that were not captured by the primary categories.

Question 14: In Scientific engagement programs, you like the interaction to be of what type?

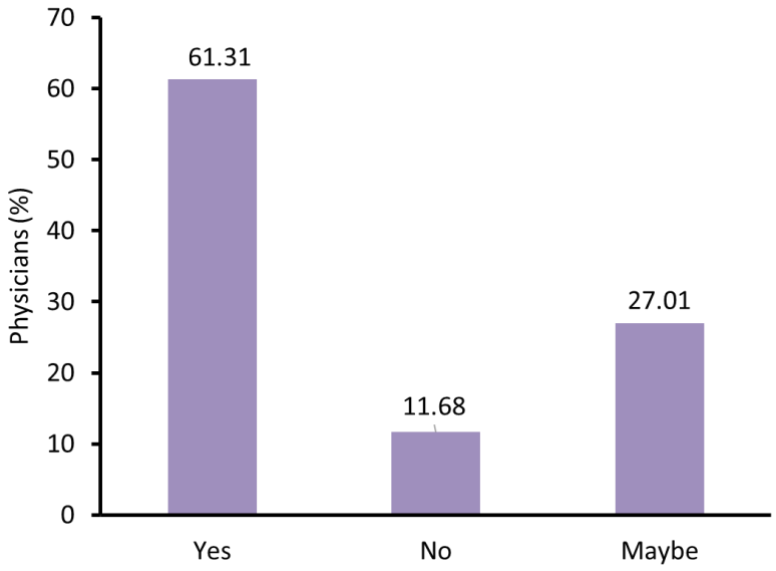
Options	Number of physicians (N=134)
Virtual platform	83 (61.94)
Digital platform	51 (38.06)
Data presented as n (%).	



- Approximately 61.94% of physicians preferred scientific engagement programs to be conducted on virtual platforms.
- This indicates a clear preference among a majority of physicians for virtual platforms, which could be due to convenience, accessibility, or specific features offered.
- However, 38.06% of physicians reported a preference for scientific engagement programs on digital platforms.
- While fewer in number compared to virtual platforms, these physicians likely favor digital platforms for their own reasons, such as specific functionalities or compatibility with their workflow.

Question 15: Would you prefer a International Speaker engagement program in near future on NETs diagnosis and treatment?

Options	Number of physicians (N=137)
Yes	84 (61.31)
No	16 (11.68)
Maybe	37 (27.01)
Data presented as n (%).	



- Majority of physicians (61.31%) reported that they would prefer an International Speaker engagement program in the near future on NETs diagnosis and treatment.
- About 11.68% indicated they would not prefer attending such a program.
- Around 27% are unsure or undecided about attending.

6 SUMMARY

The study on octreotide therapy across diverse medical conditions highlights its significant role in managing various disorders, including acromegaly, NETs, and conditions associated with hormone hypersecretion. Octreotide's mechanism involves binding to somatostatin receptors to inhibit hormone release, offering therapeutic benefits in symptom control and disease management. The retrospective analysis involving 137 physicians revealed insights into treatment patterns and patient outcomes. The majority of physicians reported using octreotide for NETs, emphasizing its efficacy in controlling symptoms and potentially influencing disease progression. Common investigations for NET diagnosis included DOTA scan, and the average duration of octreotide treatment varied by the type and stage of NET.

7 DISCUSSION

The findings underscore octreotide's established efficacy and safety profile across a spectrum of medical conditions, reinforcing its role as a cornerstone therapy in managing hormone hypersecretion and tumor growth in NETs. The study's results align with existing literature, supporting octreotide's use based on guideline recommendations and its perceived efficacy by healthcare providers. However, challenges remain in optimizing treatment duration and patient outcomes, particularly in advanced stages of disease where longer-term therapy may be necessary. Insights into referral patterns and treatment preferences highlight opportunities for multidisciplinary collaboration and tailored therapeutic approaches.

8 CLINICAL RECOMMENDATIONS

- Emphasize early use of octreotide in managing NETs to potentially improve overall survival and quality of life.
- Tailor treatment duration and intensity based on disease stage and patient response to optimize outcomes.

- Foster collaboration among gastroenterologists, surgeons, and general physicians for comprehensive NET management.
- Enhance patient understanding of octreotide therapy benefits and potential side effects to improve adherence and treatment outcomes.

9 CONSULTANT OPINION

Consultant opinion underscores the importance of integrating octreotide into comprehensive treatment strategies for NETs, advocating for continued research to refine therapeutic guidelines and improve patient outcomes. Consultants emphasize the role of evidence-based medicine in guiding octreotide use across different disease stages and patient demographics, with a focus on personalized medicine to address individual patient needs effectively.

10 MARKET OPPORTUNITIES

- Explore additional therapeutic applications beyond current FDA-approved indications, potentially targeting rare diseases and conditions with unmet medical needs.
- Capitalize on increasing global prevalence of NETs and other hormone-related disorders, particularly in emerging markets.
- Invest in medical education and awareness programs to enhance healthcare provider knowledge and patient engagement regarding octreotide therapy benefits.

11 MARKET POSITIONING

- Highlight octreotide's proven efficacy and safety profile compared to alternative therapies in managing hormone hypersecretion and tumor growth.
- Emphasize patient-reported outcomes and quality of life improvements to differentiate octreotide in the competitive landscape.
- Form strategic alliances with healthcare providers and medical societies to strengthen market presence and expand therapeutic applications.
- Invest in research and development to innovate new formulations and delivery methods, enhancing treatment convenience and patient adherence.

REFERENCES

1. Debnath D, Cheriyath P. Octreotide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544333/

2. Rosenberg JM. Octreotide: a synthetic analog of somatostatin. Drug Intell Clin Pharm. 1988;22(10):748-54.

3. Borna RM, Jahr JS, Kmiecik S, Mancuso KF, Kaye AD. Pharmacology of Octreotide: Clinical Implications for Anesthesiologists and Associated Risks. Anesthesiol Clin. 2017;35(2):327-339.

4. Chaudhry R, Singh B, Subhas P. OCTREOTIDE IN GASTROENTEROLOGY. Med J Armed Forces India. 1997;53(4):293-294.

5. Costa F, Gumz B. Octreotide - A Review of its Use in Treating Neuroendocrine Tumours. Eur Endocrinol. 2014;10(1):70-74.