Question # 1:
Can you review the most important recent advances and landmark clinical trials that support the use and approval of at least one SSA—lanreotide—as a foundational, anti-proliferative agent for GEP-NETs?

Question # 2:
What is our best understanding of the mechanism-of-action (MOA) for SSAs in the setting of GEP-NETs? What do we know? What do we still need to know?

Question # 3:
Can you discuss the design and results of the ELECT Trial, which evaluated the role of lanreotide for symptom relief in patients with functional (carcinoid syndrome) GEP-NETs?

Question # 4:
Based on evolving clinical experience, NCCN guidelines, and trials on SSAs, what is your perspective on how and when SSAs should be positioned, sequenced, and deployed across the continuum of patients with GEP-NETs?

Question # 5:
While there seems to be a consensus that progressive disease in GEP-NETs is a clear indication and trigger for SSA therapy, what criteria do you use to identify progressive disease in NETs?

Supported by an educational grant from Ipsen
Question # 6: In addition to functional NETs, what other clinical situations do you believe mandate early treatment with SSAs?

Question # 7: Given the very low toxic-to-therapeutic ratio for SSAs, some experts recommend very early, almost universal use of these agents, while others defer therapy for signs of progression and evidence of high volume disease. How do you weigh in on this controversy about early vs later use of SSAs for NETs?

Question # 8: Can you give us a couple of NET-focused case examples that will help guide our use of SSAs, including such agents as lanreotide, which is approved for its anti-tumor properties, in variable patient types with GEP-NETs?

Question # 9: What are the indications and triggers for deploying cytotoxic therapy, alone or in combination with other agents, including SSAs, in patients with GEP-NETs?

Question # 10: What is the role and rationale for using SSAs in combination with other therapies for GEP-NETs? If you start an SSA, do you continue it indefinitely?

Question # 11: What is the current and evolving role of PRRT for diagnosing and treating patients with GEP-NETs?

Question # 12: What is the evidence supporting the safety, efficacy, and foundational importance of SSAs in GEP-NETs? What did these trials—PROMID (octreotide) and CLARINET (lanreotide)—teach us? How are they different with respect to PFS?

Question # 13: What aggregate constellation of symptoms, tumor grade, progression, and/or clinical factors would be sufficient to trigger the use of SSAs in pancreatic or mid-gut GEP-NETs? How does the CLARINET data support these strategies in specific subgroups?

Question # 14: What do we know about the disease burden and epidemiology of gastric and pancreatic neuroendocrine tumors? How do you make decisions about how to sequence therapy for GEP-NETs? What is the role of SSAs?

Question # 15: What is the role of SSAs such as lanreotide in GEP-NETs? Is use of SSAs affected by low-volume vs. high volume disease? Should SSAs precede cytotoxic therapy?

Question # 16: What is the evidence supporting the safety, efficacy, and foundational importance of SSAs in GEP-NETs? What did these trials—PROMID (octreotide) and CLARINET (lanreotide)—teach us? How are they different with respect to PFS?

Question # 17: What aggregate constellation of symptoms, tumor grade, progression, and/or clinical factors would be sufficient to trigger the use of SSAs in pancreatic or mid-gut GEP-NETs? How does the CLARINET data support these strategies in specific subgroups?

Question # 18: Can you discuss two different patient types with GEP-NETs, one of whom you might deploy SSAs early, and one in whom you might wait for progression of disease prior to using this class of therapy?

Question # 19: How do you view SSAs as adjunctive or combination therapy with other modalities, including surgical resection, cytotoxic therapies, and other approaches?

Question # 20: What are the major challenges for determining a precise treatment roadmap for the individual patient with GEP-NETs? And where does precision-focused therapeutics enter into the treatment decision-making process?

Question # 21: What do we know about genetic drivers and profiles as they relate to aligning specific therapies with specific patient subgroups with GEP-NETs?

Question # 22: How do you determine how “aggressive”—i.e., liver-directed therapy in metastatic disease—to be in patients with GEP-NETs, and how do SSAs fit into these various modalities based on disease severity?

Question # 23: What do we think are the key take-home messages from the CLARINET trial, which evaluated the safety and efficacy of lanreotide on progression-free survival in GEP-NETs? How have its findings changed your practice strategy?

Question # 24: What evidence do we have to support combination therapy in GEP-NETs? Do you have a sequencing strategy that incorporates SSAs?

Question # 25: How do you decide whether to continue SSAs in the face of disease progression? And how does the relatively low toxicity of SSAs affect your decision?
Question # 26: How should the pathological characteristics of GEP-NETs guide initial and long-term therapy? What suboptimal approaches do you see in the general oncology community in these specialized patient populations?

Alexandria Phan, MD
Associate Professor
Houston Methodist Cancer Center
Director, GI Medical Oncology
Houston, Texas

Question # 27: What are the unique characteristics of the CLARINET study, and how do the results of this trial compare to other SSA trials so we can optimally position lanreotide and other SSAs at the front lines of GEP-NETs management?

Question # 28: Do the SSA trials help guide us on the timing of treatment for GEP-NET patients who have asymptomatic, indolent disease? What are your recommendations for early treatment in this large subgroup of NET patients who not yet manifested progression?

Question # 29: How do you approach the controversy about how to sequence therapeutic options in patients with GEP-NETs?

Question # 30: What do you want to communicate to the general oncologist about the heterogeneity of GEP-NETs and the role of NETs and referral centers for partnering in therapeutic decisions?

Pamela L. Kunz, MD
Assistant Professor of Medicine
Department of Oncology
Stanford University Medical Center
Stanford, California

Question # 31: What is the role for “NET Centers of Excellence?” Why are these centers critical for optimizing care for patients with GEP-NETs?

Question # 32: How is the epidemiology and prevalence of GEP-NETs changing and what are the implications for GI oncologists in terms of detecting and managing these tumors?

Question # 33: How do the classification strategies, pathological features, Ki-67 index, and clinical factors influence management and treatment decisions for patient with GEP-NETs?

Question # 34: How do you manage patients with well-differentiated pancreatic vs. non-pancreatic NETs? And what considerations apply to selecting SSAs?

Question # 35: Why do SSAs play a foundational role in the early treatment of GEP-NETs? In which patient subgroups are they especially important? And how do we select between lanreotide and octreotide when SSAs are indicated?

Question # 36: Can you take us through a real world case scenario of a patient with GEP-NETs and guide us through selection of an SSA?

Question # 37: In which patient subgroups with GEP-NETs would you start lanreotide or octreotide at the time of initial diagnosis?

Question # 38: What would be your sequential approach—included targeted, liver-directed tumor ablative and embolization techniques—to a patient with pancreatic GEP-NETs and hepatic metastases at the time of diagnosis?

Question # 39: Should SSAs almost always be a part of combination therapy in patients with advanced GEP-NETs? What is the rationale for this approach?

Question # 40: What do we still need to learn about SSA selection, sequencing, and combination therapy in order to optimize multi-agent approaches to GEP-NETs treatment?

Michael A Choti, MD MBA FACS
Professor and Chair
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UT Southwestern Medical Center
Dallas, Texas

Question # 41: What is the current status of surgical treatment as a mainstay for management of GEP-NETs? What surgical strategies are used to optimize clinical outcomes?

Question # 42: Can you provide specific guidance about liver-directed therapies—with both surgical and radio-ablation techniques—in patients with GEP-NET metastatic liver disease?

Question # 43: What are the other surgical challenges when managing NETs? Especially as these relate to managing both the primary tumor and the metastatic sites of the disease in the setting of pancreatic NET?

Question # 44: If a pancreatic NET is discovered incidentally, will you always deploy a surgical approach as a primary modality for management?

Question # 45: As a GI surgical oncologist, where do you see SSAs as part of multimodal management of GEP-NETs? How do the results of the CLARINET and PROMID trials influence your therapeutic approach in patients with metastatic versus resectable disease?

Question # 46: What is the current role of liver-directed, targeted radiographic-based approaches to metastatic NETs? And what is the role and timing for PRRT?
Question # 47: Is there a role for liver transplantation for GEP-NETs?

Michael Morse, MD
Professor of Medicine
Division of Oncology
Duke University School of Medicine
Durham, North Carolina

Question # 48: How do you classify GEP-NETs tumors and why is precise classification essential for optimizing therapeutic intervention?

Question # 49: In your view, what are the clinical, pathological or symptomatic triggers for deploying SSAs in pancreatic or mid-gut GEP-NETs in functional vs. non-functional tumors?

Question # 50: Why have the barriers to using SSAs in patients with NETs and low-volume disease been lowered? On the basis of what evidence and landmark trial data have therapeutic approaches changed?

Question # 51: In patients with metastatic NETs, how do you apportion, sequence, and align the available surgical, pharmacologic, and targeted radiotherapeutic approaches? Where do SSAs fit into this multimodal scheme?

Question # 52: What is the optimal approach to a patient with hepatic metastases in the setting of a confirmed GEP-NET?

Question # 53: Can you take us through the sequencing of radiological, pharmacological, SSA, and cytotoxic therapies in a patient with advanced or metastatic GEP-NET?

Question # 54: What is the role of cytotoxic therapy in NETs? And how do you select among the options? And should SSAs be continued in the face of progressive disease?

Johanna Bendell, MD
Director, GI Oncology Research
Associate Director, Drug Development Unit
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee

Question # 55: What classification system do you employ to make clinically actionable decisions for treating NETs? And what does the natural history of NETs look like? Can you provide an overview of treatment approaches across the continuum of disease?

Question # 56: In your view, what are the clinical, pathological or symptomatic triggers for deploying lanreotide and other SSAs in pancreatic or mid-gut GEP-NETs in functional vs. non-functional tumors? What are the effects of these agents on PFS?

Professor Andrea Frilling, MD, PhD, FACS, FRCS, FEBS
Professor of Surgery
Chair in Endocrine Surgery
Consultant Surgeon
Department of Surgery and Cancer
Imperial College London
London, United Kingdom

Question # 57: What are the current NCCN guidelines for use of lanreotide in GEP-NETs?

Question # 58: What is the role of surgical treatment for GEP-NETs? And how does the clinical histology and stage of the tumor impact your surgical strategy?

Question # 59: What is the role for adjuvant SSAs such as lanreotide and octreotide in patients with NETs who have undergone a primary surgical procedure?

Question # 60: What is role and approval status of lanreotide for treatment of NETs in Europe?

Question # 61: Are surgical approaches to advanced and metastatic NETs in the U.S. and Europe aligned, or are there important differences in surgical strategies? Please explain.

Question # 62: What is the current status of adjuvant treatment in GEP-NETs?

Mauro Cives, MD
Department of GI Oncology
H. Lee Moffitt Cancer Center and Research Institute
Tampa, Florida

Question # 63: What do we know about the disease burden, incidence and epidemiology of gastric and pancreatic neuroendocrine tumors?

Question # 64: How do you recommend sequencing and selecting among the major pillars of multi-modal therapy for NETs—surgical intervention, pharmacologic therapy (SSAs), and radiotherapy—both as individual and/or combination strategies?

Question # 65: When should SSA therapy be started in GEP-NETs, and what is the role of combination therapy using an SSA plus cytotoxic therapy?
Question # 66: How does the classification and pathology of a GEP-NETs tumor determine what our optimal therapeutic choices should be? And what is the status of SSAs for delaying progression of NETs?

Question # 67: Should surgical excision of a GEP-NETs tumor—either primary resection or resection of metastases—always be accompanied by adjunctive pharmacologic therapy? When and under what circumstances?

Question # 68: What are the clinical or pathological parameters for use of everolimus therapy?

Question # 69: What are the indications for antiangiogenesis therapy for patients with GEP-NETs?

Question # 70: How do you sequence the various therapies that are available for GEP-NETs?

Question # 71: Based on recent trials evaluating strategies for extending PFS, what does the current roadmap look like as it relates to use of lanreotide and octreotide for GEP-NETs? Should SSAs be started at diagnosis or at signs of progression?

Question # 72: In your view, what are the clinical, pathological, or symptomatic triggers for deploying and sequencing specific interventions in GEP-NETs?

Question # 73: What is your systematic approach to evaluating and initiating treatment in the newly diagnosed GEP-NETs patient?

Question # 74: How do you decide whether to start an SSA early, at the time of initial diagnosis, or wait, until signs of progression in the setting of GEP-NETs? What factors make you tilt one way or another?

Question # 75: How do you risk-stratify your patients with GEP-NETs so your treatments are optimally aligned with their likelihood of benefiting from SSAs?

Question # 76: How have the specific results emanating from the CLARINET and PROMID trials helped us make decisions about the choice and timing for SSAs at the front lines of GEP-NETs care?

Question # 77: Can the SSAs be compared based on MOA and/or extrapolating from cross-trial comparisons, despite the limitations and pitfalls of such analyses?

Question # 78: Do you advise patients to continue SSAs when they have had progression while on this therapy? Does it depend on the degree of progression or other factors?

Question # 79: What are the unresolved therapeutic issues in the management of GEP-NETs? What do we still need to know?