Charting the Future of NET Therapy
New Evidence in Clinical Practice

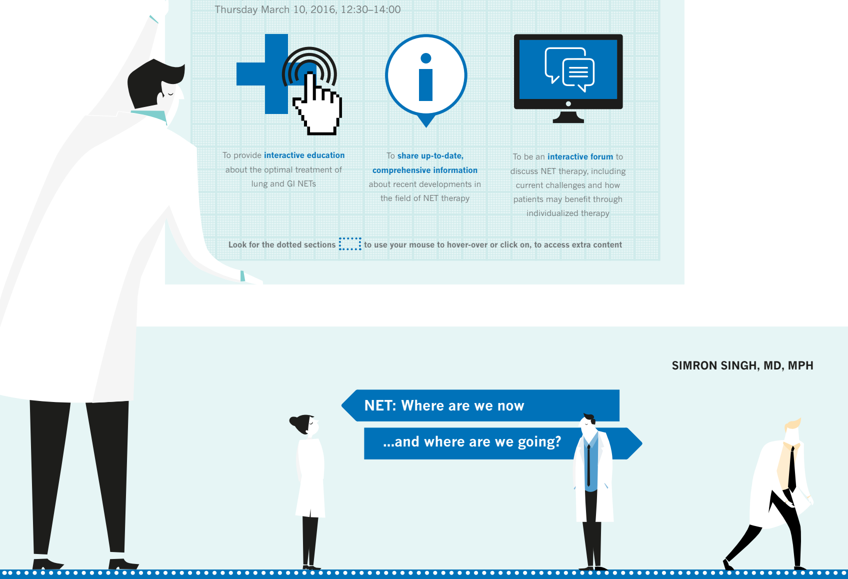
ENETS 2016
Thursday March 10, 2016, 12:30–14:00

To provide **interactive education** about the optimal treatment of lung and GI NETs

To **share up-to-date, comprehensive information** about recent developments in the field of NET therapy

To be an **interactive forum** to discuss NET therapy, including current challenges and how patients may benefit through individualized therapy

Look for the dotted sections ⬚ to use your mouse to hover-over or click on, to access extra content



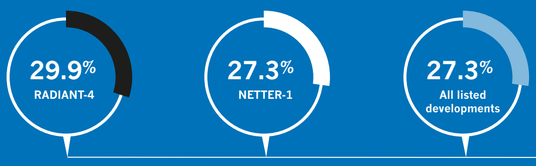
SIMRON SINGH, MD, MPH

NET: Where are we now

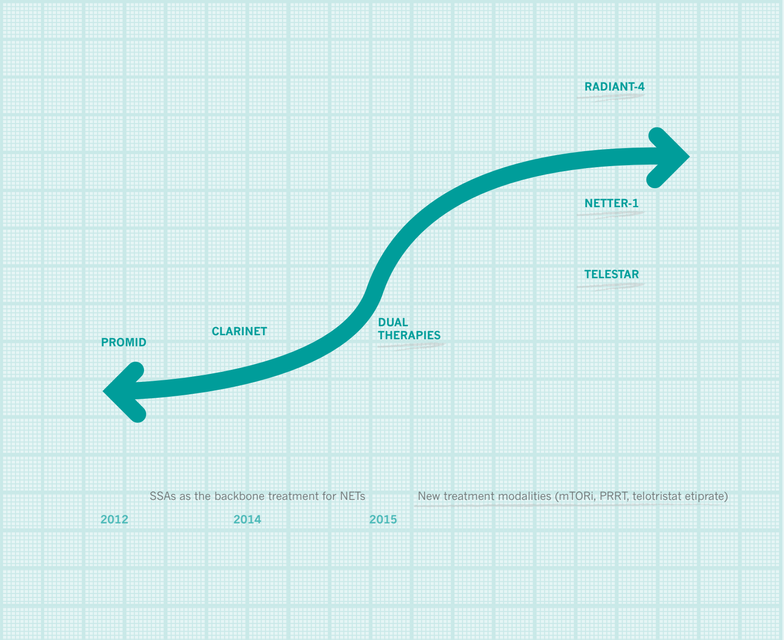
...and where are we going?

What development(s) over the last year will have the most significant impact on how you treat NETs?

The majority of the delegates reported that over the last year the RADIANT-4 study, NETTER-1 study, and all listed developments would have the most significant impact on how they treat NETs

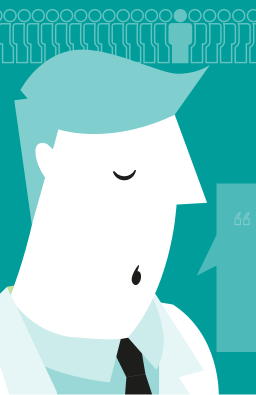


Key updates


RADIANT-4
NETTER-1
TELESTAR
PROMID
CLARINET
DUAL THERAPIES
SSAs as the backbone treatment for NETs
New treatment modalities (mTORi, PRRT, telotristat etiprate)
2012
2014
2015

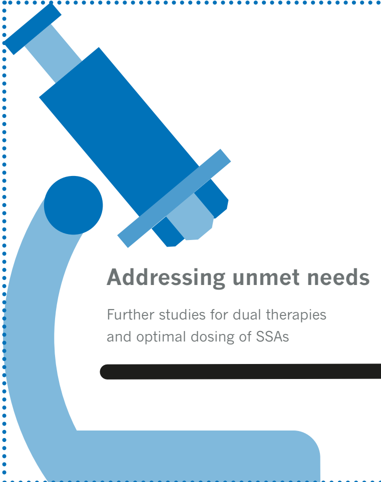
NET Patient Survey

NET affects the day-to-day lives of a large number of patients



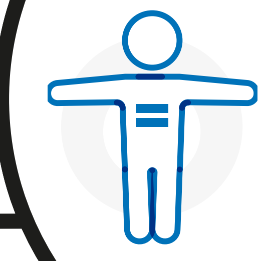
> **When we take data from the past year, we need to move towards a patient-centered care model. Designing care around what the patient wants (understanding their experience and listening to them) will be one of the largest advancements in the treatment of neuroendocrine cancers**

> **Despite great data and advancements, and great publications and agents, the impact of NET on patients' lives remains substantial and we need to start integrating both of these areas towards improved patient-centered care**



Addressing unmet needs

Further studies for dual therapies and optimal dosing of SSAs



The right treatment for the right patient at the right time!

Tolerability

Resistance

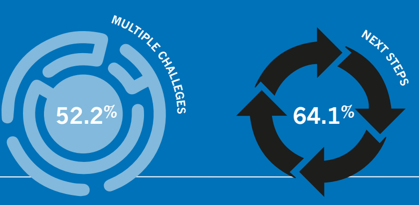
Guidelines

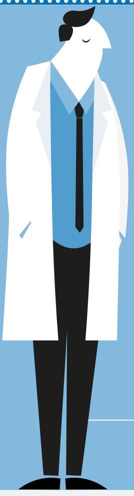
Collaboration

Patient Experience

Which of the following do you view as the greatest challenge facing patients with NET?

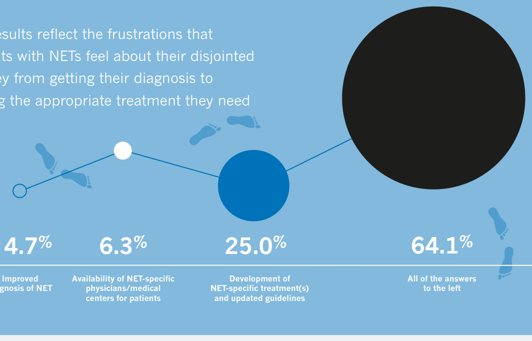
Over half the delegates considered that there were multiple challenges facing patients with NET and multiple important next steps for NET therapy





Which of the following do you view as the most important next step(s) for NET therapy?

The results reflect the frustrations that patients with NETs feel about their disjointed journey from getting their diagnosis to getting the appropriate treatment they need



Case-based presentation: Lung NET

NICOLA FAZIO, MD

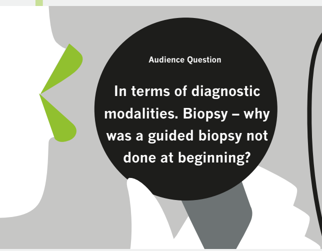
Dr Fazio presented a clinical case of a patient with lung atypical carcinoid who presented with metachronous liver metastases 7 years after the initial tumor was radically resected

BEST PRACTICE
The expert faculty discussed the best way to follow up with patients

GUIDELINES & EXPERIENCE
Although there is currently no clear evidence, there are guidelines and clinical experience

5-YEAR FOLLOW UP
The guidelines state, follow up should continue for 5–10 years. With atypical carcinoids, possible relapse within first 5 years should be considered

CT SCAN
For this case, the patient was followed up with 7 month CT scans for the first 5 years followed by yearly CT scans



Audience Question

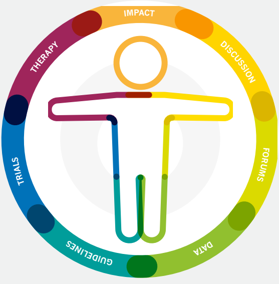
In terms of diagnostic modalities. Biopsy – why was a guided biopsy not done at beginning?

Not all pathologists agree with early biopsy, and not all radiologists agree to perform a biopsy without excluding other sites first

It was acknowledged that Ki-67 is not often used by pathologists to classify the tumor but is used by the clinician to make the right decision

Case-based presentation: Lung NET

Click the scenario ① ② ③ ④ ⑤



Clinical Scenario 1

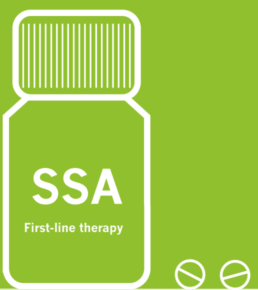
The patient received everolimus 10 mg/day vs. placebo within RADIANT-4 trial

Patient characteristics
Female
55-years old
PS = 0 (ECOG)
Asymptomatic
No comorbidity

Tumor characteristics
Bilobar liver-only mets
SRS/^{68}Ga PET: +++ (liver only)
Well-differentiated NET
Ki-67 10%

Advanced lung well-differentiated NET: First-line therapy?

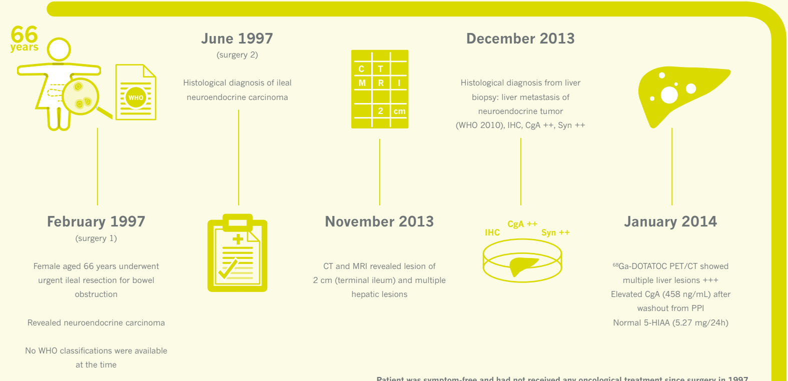
The majority of the audience would initiate SSAs as first-line therapy to this patient



> **Further research is required to define how patient and tumor characteristics may influence treatment decisions**

DIEGO FERONE, MD, PHD

Case-based presentation: GI NET with a complicated history



June 1997
(surgery 2)

Histological diagnosis of ileal neuroendocrine carcinoma

December 2013

Histological diagnosis from liver biopsy: liver metastasis of neuroendocrine tumor (WHO 2010), IHC, CgA ++, Syn ++

February 1997
(surgery 1)

Female aged 66 years underwent urgent ileal resection for bowel obstruction

Revealed neuroendocrine carcinoma

No WHO classifications were available at the time

November 2013

CT and MRI revealed lesion of 2 cm (terminal ileum) and multiple hepatic lesions

January 2014

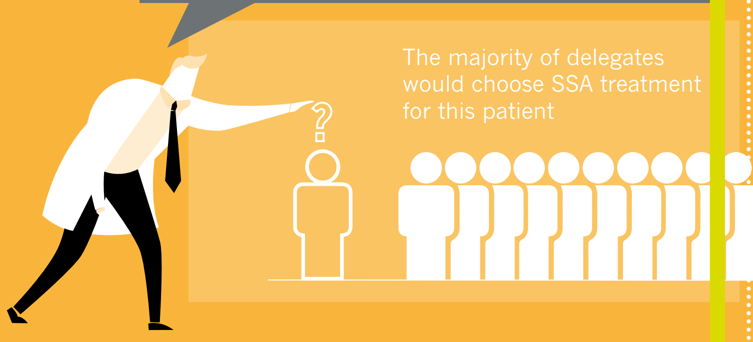
^{68}Ga-DOTATOC PET/CT showed multiple liver lesions +++
Elevated CgA (458 ng/mL) after washout from PPI
Normal 5-HIAA (5.27 mg/24h)

Patient was symptom-free and had not received any oncological treatment since surgery in 1997

Question from the Chair

How would you approach treatment if the Ki-67 was high?

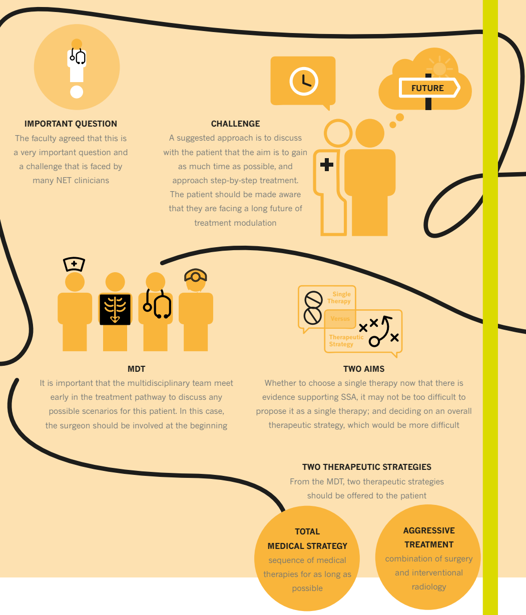
Decision point: What would you do? What therapy would you consider?



The majority of delegates would choose SSA treatment for this patient

Audience Question

If the patient asks about her prognosis, and asks 'Am I going to die?' how would you handle this?



IMPORTANT QUESTION
The faculty agreed that this is a very important question and a challenge that is faced by many NET clinicians

CHALLENGE
A suggested approach is to discuss with the patient that the aim is to gain as much time as possible, and approach step-by-step treatment. The patient should be made aware that they are facing a long future of treatment modulation

MDT
It is important that the multidisciplinary team meet early in the treatment pathway to discuss any possible scenarios for this patient. In this case, the surgeon should be involved at the beginning

TWO AIMS
Whether to choose a single therapy now that there is evidence supporting SSA, it may not be too difficult to propose it as a single therapy; and deciding on an overall therapeutic strategy, which would be more difficult

TWO THERAPEUTIC STRATEGIES
From the MDT, two therapeutic strategies should be offered to the patient

TOTAL MEDICAL STRATEGY
sequence of medical therapies for as long as possible

AGGRESSIVE TREATMENT
combination of surgery and interventional radiology

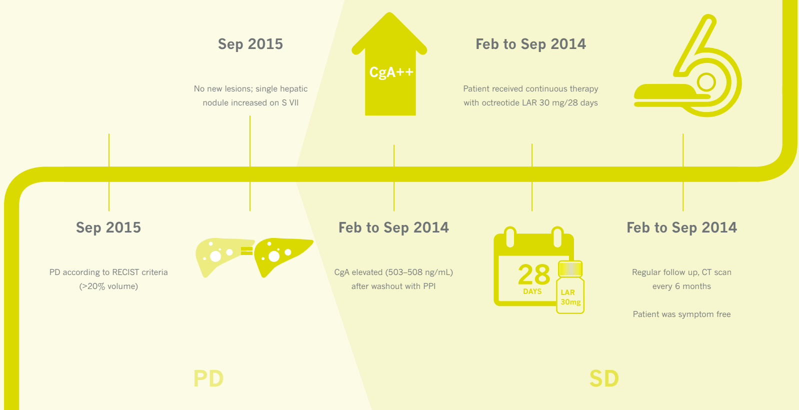
Audience Question

Should you not consider resection of the primary tumor before looking at systemic therapy?

> **"Dr Ferone shared that as the patient had already relapsed twice, it was the opinion of his MDT that surgery was not an option for the patient in this particular situation"**

> **"Another opinion from the Chair was that if they could, their MDT would discuss surgically removing the primary tumor based on retrospective data which shows that removal of the primary tumor from the small bowel improves survival**
>
> It should be discussed with the patient that this is not a curative strategy, and the aim would be to control the disease with therapy and turn it into a chronic disease with which the patient can live. The patient should be started on the least toxic treatment, and made aware that there are other treatment options available if needed"

Case-based presentation: GI NET with a complicated history



Sep 2015

No new lesions; single hepatic nodule increased on S VII

Feb to Sep 2014

Patient received continuous therapy with octreotide LAR 30 mg/28 days

Sep 2015

PD according to RECIST criteria (>20% volume)

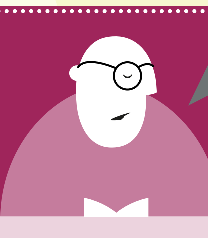
Feb to Sep 2014

CgA elevated (503–508 ng/mL) after washout with PPI

Feb to Sep 2014

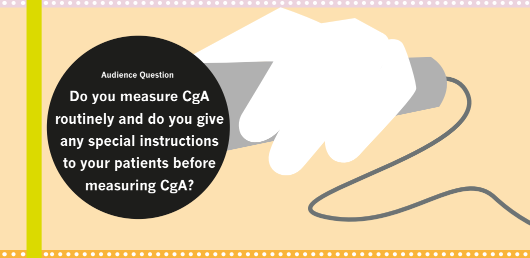
Regular follow up, CT scan every 6 months

Patient was symptom free



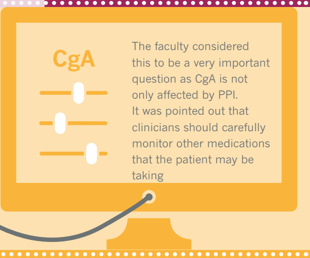
Question from the Chair

With regards to deciding whether the patient has progressed, do you always look at RECIST criteria or do you consider other factors such as biochemistry?



Audience Question

Do you measure CgA routinely and do you give any special instructions to your patients before measuring CgA?



The faculty considered this to be a very important question as CgA is not only affected by PPI.
It was pointed out that clinicians should carefully monitor other medications that the patient may be taking

Decision point: What would you do? Which therapy would you start?

The majority of the delegates opted for treatment with everolimus+SSA, with PRRT as second choice. No members of the audience voted for chemotherapy, which the faculty agreed with

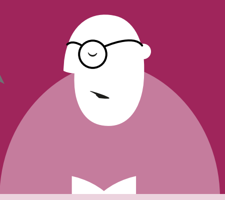
36.7% EVEROLIMUS + SSA

28.6% PRRT

CHEMOTHERAPY

Question from the Chair

It is interesting that 5% would opt to switch to a different SSA



Audience Question

When you start SSA treatment for a patient such as this who is symptom-free, do you need to try the short-acting SSA first before the long-acting SSA?

TOLERABILITY

It was agreed that patients are not routinely administered short-term treatment with a short-acting SSA prior to treatment with a long-acting SSA. Usually a dose test will be performed first to observe tolerability (local and general) over a few hours before administering treatment with a long-term SSA

In this case where there is persistence of the primary tumor another treatment strategy should be considered

For some patients a liver transplant may be a consideration, however, it is a complicated treatment route

Audience Question

Would a liver transplant have been a consideration in this patient?

Sep 2015

Increase of octreotide LAR dose up to 40 mg/28days

SD

March 2014

28
DAYS
LAR
40mg

Sep 2015

High dose of octreotide well tolerated by the patient

Question from the Chair

How do you decide whether to increase the dose or the frequency, or both?

Case-based presentation: GI NET with a complicated history

Audience Question

If you consider the following variable, for instance, results from the NETTER-1 trial with 60 mg octreotide that showed that patients progressed after 8 months. If you knew this, would you have done the same?

> **“Dr Ferone agreed that he would have made the same treatment decision as it is important to assess all patient characteristics”**

> **“Increasing octreotide dose is a valid treatment option for slowly progressive GI NETs”**

Question from the Chair

Perhaps you may wish to comment on how best to make the treatment decision and how to individualize treatment?

CONSIDERATION

The initial response should be considered, and the aggression and timing of progression. If progression was rapid or multifocal, PRRT therapy would have been a consideration

NORMALITY OF LIFE

The treatment strategy selected for this patient (increase in octreotide dose) had the best impact on their normality of life

Conclusions

Key themes from the discussions held in the symposium centered on the importance of...

- The impact of treatment upon the patient and their quality life
- The importance of the MDT in the treatment pathway
- The importance of functional imaging in diagnosis
- The consideration of all available clinical evidence when defining progression
- The importance of discussing treatment options with the patient

Meeting Feedback

465
DELEGATES attended the symposium

POSITIVE
★★★★★
FEEDBACK for the symposium

What was the major strength of this program?	What was the major weakness of this program?	What was the most important thing you learned from this program?
Integration of technology EXCELLENT real-life case discussions Using NEW DATA on the background of cases	TIME Clinical data presentation and discussion of treatment options must be more OBJECTIVE	Using medication in different situations See how MANY THINGS we don't know