The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Wasif M. Saif,[1] Rohan Parikh,[2] David Ray,[3] James A. Kaye,[4] Samantha K. Kurosky,[2] Katharine Thomas,[5] Robert A Ramirez,[5]* Thorvardur Halfdanarson,[6] Thomas J.R. Beveridge,[3] Beloo Mirakhur,[3] Catherine A. Lubeck,[3] Saurabh Nagar,[2] Heloisa Soares[7]

[1]*Tufts University School of Medicine, Boston, MA, USA;* [2]*RTI Health Solutions, Research Triangle Park, NC, USA;* [3]*Ipsen Biopharmaceuticals, Basking Ridge, NJ, USA;* [4]*RTI Health Solutions, Waltham, MA, USA;* [5]*Ochsner Medical Center-Kenner, Neuroendocrine Tumor Program, Kenner, LA, USA;* [6]*Mayo Clinic, Rochester, MN, USA;* [7]*University of New Mexico Medical School, Albuquerque, NM, USA*

CLICK TO GO BACK TO KIOSK MENU

36

BACKGROUND

- Neuroendocrine tumors (NETs), a relatively rare group of neoplasms, are slow growing. Due to a paucity of symptoms in early stages, patients are often diagnosed at an advanced or metastatic stage.[1,2]
- The somatostatin analogs (SSAs) octreotide and lanreotide depot (lanreotide) are recommended as primary systemic therapy for patients with advanced or metastatic disease[3]; however, their indications differ.
- With differences in indication, administration, and the relatively recent approval of lanreotide (December 2014) by the United States (US) Food and Drug Administration, clinicians and patients may consider sequencing SSA therapy from long-acting octreotide to lanreotide. However, evidence of the feasibility of sequencing long-acting octreotide-treated patients to lanreotide and the resulting effectiveness and safety in real-world settings is limited.

OBJECTIVE

- To evaluate clinical outcomes among patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who transitioned from long-acting octreotide monotherapy to lanreotide monotherapy.

METHODS

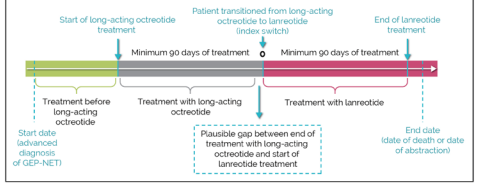
Study design and patient population

- We conducted a multicenter, noninterventional, retrospective medical record review of 91 patients who had a confirmed diagnosis of locally advanced or metastatic GEP-NET across six US-based sites.
- Patients aged ≥ 18 years who sequenced long-acting octreotide monotherapy with lanreotide monotherapy were included (minimum 90-day treatment on each drug; **Figure 1**).
- Patients were excluded if they had been enrolled in a clinical trial for GEP-NET, had a history of other malignant disease (except basal cell carcinoma or carcinoma in situ of the cervix), were being treated with an SSA in combination with other NET treatments other than immediate release (IR) subcutaneous octreotide, received other primary treatment (e.g., targeted therapy, chemotherapy) for GEP-NET, or had a familial NET syndrome.

Study measures and analyses

- Patient demographics and baseline clinical characteristics were collected.
- Treatment and outcome measures were observed during the periods of treatment with long-acting octreotide and lanreotide (**Figure 1**).
- Clinician-defined progressive disease was based on local tumor imaging, uncontrolled symptoms, biomarker progression, and/or clinical judgement.
- Clinical progression-free survival (PFS) was estimated using the Kaplan-Meier method starting at the date of transition to lanreotide.
  - Results were stratified by disease status at the time of transition (i.e., progressive disease, nonprogressive disease, or unknown status).
- Disease-related symptoms and other adverse events (AEs) were examined for each assessment period (**Figure 1**).
- Descriptive analysis was conducted for patient demographics, clinical characteristics, treatment, and outcome measures.

Figure 1. Study treatment periods



RESULTS

Patient demographics and clinical characteristics

- **Table 1** presents patient demographics and clinical characteristics for 91 patients included in the study.

Table 1. Patient demographics and clinical characteristics

Total patient sample, (N)	91	
Sex, (n, %)		
Female	54	59.3%
Race, (n, %)		
White	83	91.2%
Black/African American	5	5.5%
Others/don't know	3	3.3%
Clinical stage at initial diagnosis, (n, %)		
Stage I/II/III	6	6.6%
Stage IV	65	71.4%
Don't know	20	22.0%
Primary tumor site of NET, (n, %)		
Small intestine	58	63.7%
Pancreas	13	14.3%
Colon/appendix	7	7.7%
Other primary tumor sites	7	7.7%
Unknown origin/don't know	6	6.6%
Age at diagnosis of locally advanced or metastatic GEP-NET		
Mean (SD)	57.7	10.9
Common site(s) of distant metastases at locally advanced or metastatic GEP-NET, (N, %)[a]		
Liver	65	71.4%
Lymph node(s)	34	37.4%
Peritoneal cavity	8	8.8%
Functional status at locally advanced or metastatic GEP-NET, (N, %)		
Functional disease	55	60.4%
Total duration of follow-up, months[b]		
Mean (SD)	70.6	41.3

SD = standard deviation.

[a]A patient may have multiple sites of distant metastases.

[b]Length of follow-up is the duration of time between the date of locally advanced or metastatic GEP-NET diagnosis and death or end of patient record.

Treatment with long-acting octreotide and reason(s) for transition

- After initial GEP-NET diagnosis, patients began treatment with long-acting octreotide after a mean (SD) of 17.0 (24.7) months and took long-acting octreotide for a mean (SD) of 38.4 (32.8) months.
- The most common known reasons for transition were progressive disease (n=20; 22.0%), formulary change (n=14; 15.4%), and patient preference (n=9; 9.9%). The reason for transition was not documented for more than one-third of patients (n=33; 36.3%).
- At the time of their transition to lanreotide, more than half of patients (n = 52; 57.1%) had nonprogressive disease, 28 (30.8%) patients had clinically defined progressive disease (19 [67.9%] patients assessed based on imaging), and the remainder had unknown disease status.

Treatment with lanreotide and tumor assessment

- At the end of study follow-up, 67 (73.6%) patients were still receiving lanreotide treatment, and the Kaplan-Meier estimated median (95% confidence interval [CI]) duration was 24.7 (16.7-59.9) months.
- Clinician-defined progressive disease was observed for 22 (24.2%) patients after initiating lanreotide monotherapy (20 of 22 [90.9%] patients were assessed based on imaging) (**Figure 2**).
  - The median (95% CI) clinical PFS after treatment with lanreotide was estimated to be 23.7 months (20.2, not estimable) (**Figure 3a**).
- Among patients with progressive disease at the time of transition to lanreotide (n = 28), 13 (46.4%) experienced subsequent clinician-defined disease progression while receiving lanreotide monotherapy (11 of 13 [84.6%] patients were assessed based on imaging) (**Figure 2**).
  - Among patients who had progressive disease at the time of transition to lanreotide, the median (95% CI) clinical PFS was estimated to be 15.2 months (11.4, not estimable) (**Figure 3b**).
- **Figures 4a and 4b** present the proportion of patients with disease-related symptoms and other AEs during each assessment period.

Figure 2. Proportion of patients with clinician-defined progressive disease while on lanreotide monotherapy

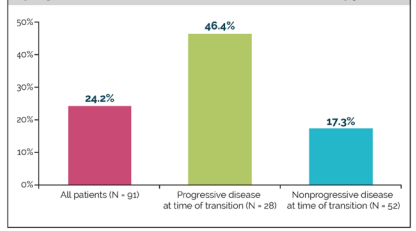
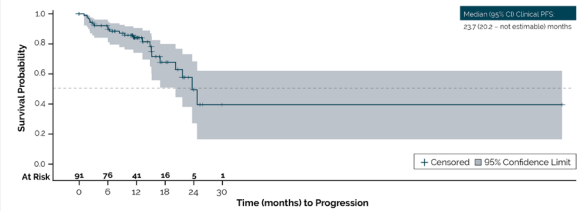


Figure 3. Clinical PFS

A) Clinical PFS



B) Clinical PFS by Disease Status at Time of Transition to Lanreotide

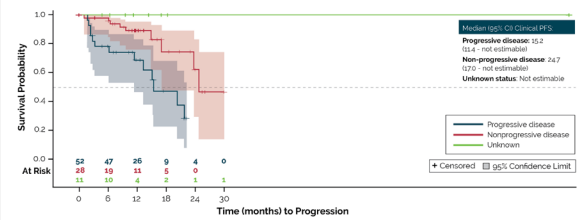
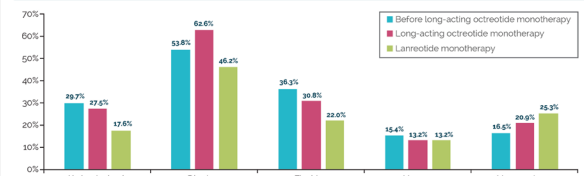
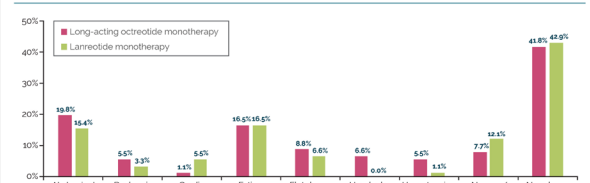


Figure 4. Disease-related symptoms and other AEs reported during different phases of therapy

A) Symptoms[a]



B) AEs[a]



[a]Includes data recorded for at least 5.0% of patients during either of the treatment phases (i.e., before long-acting octreotide monotherapy [only for symptoms], during long-acting octreotide monotherapy, or during lanreotide monotherapy). Duration of long-acting octreotide monotherapy was relatively longer as compared with the observed duration of lanreotide monotherapy.

LIMITATIONS

- Patients included in the study were selected by convenience sample, so study findings may not be generalizable to the overall population of patients with locally advanced or metastatic GEP-NET.
- The type and frequency of testing to assess tumor status in a real-world practice may differ (and is typically more variable) from those required in a clinical trial protocol. Therefore, PFS estimates from this study should be compared with clinical trial estimates with these limitations in mind.
- Evaluation of progression in this study was not restricted to tumor imaging only and assessment through symptoms, biochemical tests, and/or clinical judgement was allowed. However, more than 90% of patients were determined to have progressive disease using tumor imaging.
- The requirement for 90 days of lanreotide treatment after transition could have introduced immortal time bias into survival estimates.

CONCLUSION

- This retrospective medical record review assessed the feasibility of sequencing from long-acting octreotide monotherapy to lanreotide monotherapy among patients with locally advanced GEP-NET across multiple sites in the US.
- After receiving long-acting octreotide for an average of 38 months, the median clinical PFS for lanreotide monotherapy was estimated to be 23.7 months (95% CI, 20.2 to not estimable).
- Our study suggests that patients with locally advanced or metastatic GEP-NETs previously treated with long-acting octreotide monotherapy can be safely transitioned to lanreotide monotherapy.
  - The clinical PFS observed among patients who had either nonprogressive or progressive disease at the time of transition from long-acting octreotide to lanreotide reinforces the possibility of sequencing lanreotide after long-acting octreotide.

References

1. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol. 2008 Jun 20;26(18):3063-72.
2. Öberg KE. The management of neuroendocrine tumours: current and future medical therapy options. Clin Oncol. 2012 May 31;24(4):282-93.
3. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology (NCCN guidelines). Neuroendocrine tumors version 2. 2018. Available at https://www.nccn.org/professionals/physician_gls/pdf/ neuroendocrine.pdf. Accessed July 16, 2018.

Contact Information

David Ray, Pharm.D., MBA
Ipsen Biopharmaceuticals, Inc.
106 Allen Road, 3rd Floor
Basking Ridge, NJ 07920 USA
E-mail: david.ray@ipsen.com

*Dr. Ramirez was unable to review the abstract, but meets all ICMJE authorship criteria to qualify as an author of this poster.

Presented at the North American Neuroendocrine Tumor Society (NANETS), Seattle, Washington, USA, October 4–6, 2018.

This study was sponsored by Ipsen

The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Wasif M. Saif,[1] Rohan Parikh,[2] David Ray,[3] James A. Kaye,[4] Samantha K. Kurosky,[2] Katharine Thomas,[5] Robert A Ramirez,[5] Thorvardur Halfdanarson,[6] Thomas J.R. Beveridge,[3] Beloo Mirakhur,[3] Catherine A. Lubeck,[3] Saurabh Nagar,[2] Heloisa Soares[7]

[1]Tufts University School of Medicine, Boston, MA, USA; [2]RTI Health Solutions, Research Triangle Park, NC, USA; [3]Ipsen Biopharmaceuticals, Basking Ridge, NJ, USA; [4]RTI Health Solutions, Waltham, MA, USA; [5]Ochsner Medical Center-Kenner, Neuroendocrine Tumor Program, Kenner, LA, USA; [6]Mayo Clinic, Rochester, MN, USA; [7]University of New Mexico Medical School, Albuquerque, NM, USA

BACKGROUND

- Neuroendocrine tumors (NETs), a relatively rare group of neoplasms, are slow growing. Due to a paucity of symptoms in early stages, patients are often diagnosed at an advanced or metastatic stage.[1,2]
- The somatostatin analogs (SSAs) octreotide and lanreotide depot (lanreotide) are recommended as primary systemic therapy for patients with advanced or metastatic disease[3]; however, their indications differ.
- With differences in indication, administration, and the relatively recent approval of lanreotide (December 2014) by the United States (US) Food and Drug Administration, clinicians and patients may consider sequencing SSA therapy from long-acting octreotide to lanreotide. However, evidence of the feasibility of sequencing long-acting octreotide-treated patients to lanreotide and the resulting effectiveness and safety in real-world settings is limited.

OBJECTIVE

- To evaluate clinical outcomes among patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who transitioned from long-acting octreotide monotherapy to lanreotide monotherapy.

METHODS

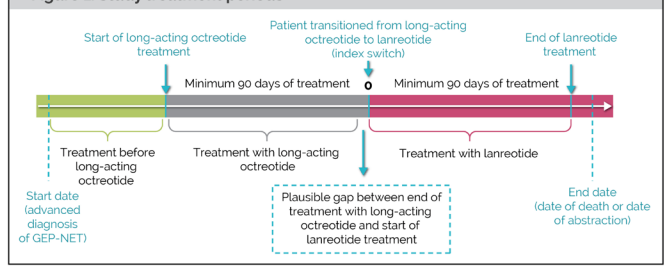
Study design and patient population

- We conducted a multicenter, noninterventional, retrospective medical record review of 91 patients who had a confirmed diagnosis of locally advanced or metastatic GEP-NET across six US-based sites.
- Patients aged ≥ 18 years who sequenced long-acting octreotide monotherapy with lanreotide monotherapy were included (minimum 90-day treatment on each drug; **Figure 1**).
- Patients were excluded if they had been enrolled in a clinical trial for GEP-NET, had a history of other malignant disease (except basal cell carcinoma or carcinoma in situ of the cervix), were being treated with an SSA in combination with other NET treatments other than immediate release (IR) subcutaneous octreotide, received other primary treatment (e.g., targeted therapy, chemotherapy) for GEP-NET, or had a familial NET syndrome.

Study measures and analyses

- Patient demographics and baseline clinical characteristics were collected.
- Treatment and outcome measures were observed during the periods of treatment with long-acting octreotide and lanreotide (**Figure 1**).
- Clinician-defined progressive disease was based on local tumor imaging, uncontrolled symptoms, biomarker progression, and/or clinical judgement.
- Clinical progression-free survival (PFS) was estimated using the Kaplan-Meier method starting at the date of transition to lanreotide.
  - Results were stratified by disease status at the time of transition (i.e., progressive disease, nonprogressive disease, or unknown status).
- Disease-related symptoms and other adverse events (AEs) were examined for each assessment period (**Figure 1**).
- Descriptive analysis was conducted for patient demographics, clinical characteristics, treatment, and outcome measures.

Figure 1. Study treatment periods



RESULTS

Patient demographics and clinical characteristics

- **Table 1** presents patient demographics and clinical characteristics for 91 patients included in the study.

Table 1. Patient demographics and clinical characteristics

Total patient sample, (N)	91	
Sex, (n, %)		
Female	54	59.3%
Race, (n, %)		
White	83	91.2%
Black/African American	5	5.5%
Others/don't know	3	3.3%
Clinical stage at initial diagnosis, (n, %)		
Stage I/II/III	6	6.6%
Stage IV	65	71.4%
Don't know	20	22.0%
Primary tumor site of NET, (n, %)		
Small intestine	58	63.7%
Pancreas	13	14.3%
Colon/appendix	7	7.7%
Other primary tumor sites	7	7.7%
Unknown origin/don't know	6	6.6%
Age at diagnosis of locally advanced or metastatic GEP-NET		
Mean (SD)	57.7	10.9
Common site(s) of distant metastases at locally advanced or metastatic GEP-NET, (N, %)[a]		
Liver	65	71.4%
Lymph node(s)	34	37.4%
Peritoneal cavity	8	8.8%
Functional status at locally advanced or metastatic GEP-NET, (N, %)		
Functional disease	55	60.4%
Total duration of follow-up, months[b]		
Mean (SD)	70.6	41.3

SD = standard deviation.

[a]A patient may have multiple sites of distant metastases.

[b]Length of follow-up is the duration of time between the date of locally advanced or metastatic GEP-NET diagnosis and death or end of patient record.

Presented at the North American Neuroendocrine Tumor Society (NANETS), Seattle, Washington, USA, October 4–6, 2018.

This study was sponsored by Ipsen

The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Wasif M. Saif,[1] Rohan Parikh,[2] David Ray,[3] James A. Kaye,[4] Samantha K. Kurosky,[2] Katharine Thomas,[5] Robert A Ramirez,[5] Thorvardur Halfdanarson,[6] Thomas J.R. Beveridge,[3] Beloo Mirakhur,[3] Catherine A. Lubeck,[3] Saurabh Nagar,[2] Heloisa Soares[7]

[1]Tufts University School of Medicine, Boston, MA, USA; [2]RTI Health Solutions, Research Triangle Park, NC, USA; [3]Ipsen Biopharmaceuticals, Basking Ridge, NJ, USA; [4]RTI Health Solutions, Waltham, MA, USA; [5]Ochsner Medical Center-Kenner, Neuroendocrine Tumor Program, Kenner, LA, USA; [6]Mayo Clinic, Rochester, MN, USA; [7]University of New Mexico Medical School, Albuquerque, NM, USA

Treatment with long-acting octreotide and reason(s) for transition

- After initial GEP-NET diagnosis, patients began treatment with long-acting octreotide after a mean (SD) of 17.0 (24.7) months and took long-acting octreotide for a mean (SD) of 38.4 (32.8) months.
- The most common known reasons for transition were progressive disease (n=20; 22.0%), formulary change (n=14; 15.4%), and patient preference (n=9; 9.9%). The reason for transition was not documented for more than one-third of patients (n=33; 36.3%).
- At the time of their transition to lanreotide, more than half of patients (n = 52; 57.1%) had nonprogressive disease, 28 (30.8%) patients had clinically defined progressive disease (19 [67.9%] patients assessed based on imaging), and the remainder had unknown disease status.

Treatment with lanreotide and tumor assessment

- At the end of study follow-up, 67 (73.6%) patients were still receiving lanreotide treatment, and the Kaplan-Meier estimated median (95% confidence interval [CI]) duration was 24.7 (16.7-59.9) months.
- Clinician-defined progressive disease was observed for 22 (24.2%) patients after initiating lanreotide monotherapy (20 of 22 [90.9%] patients were assessed based on imaging) (**Figure 2**).
  - The median (95% CI) clinical PFS after treatment with lanreotide was estimated to be 23.7 months (20.2, not estimable) (**Figure 3a**).
- Among patients with progressive disease at the time of transition to lanreotide (n = 28), 13 (46.4%) experienced subsequent clinician-defined disease progression while receiving lanreotide monotherapy (11 of 13 [84.6%] patients were assessed based on imaging) (**Figure 2**).
  - Among patients who had progressive disease at the time of transition to lanreotide, the median (95% CI) clinical PFS was estimated to be 15.2 months (11.4, not estimable) (**Figure 3b**).

Figure 2. Proportion of patients with clinician-defined progressive disease while on lanreotide monotherapy

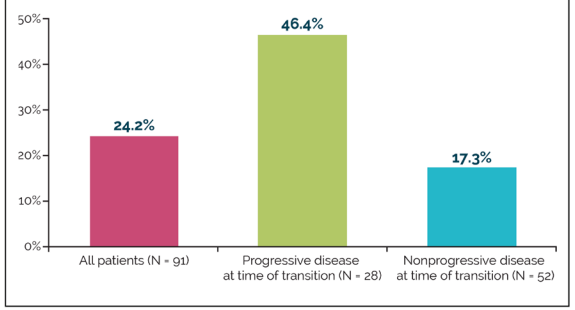
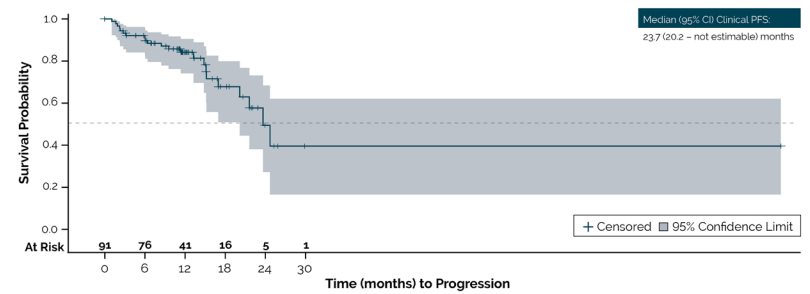
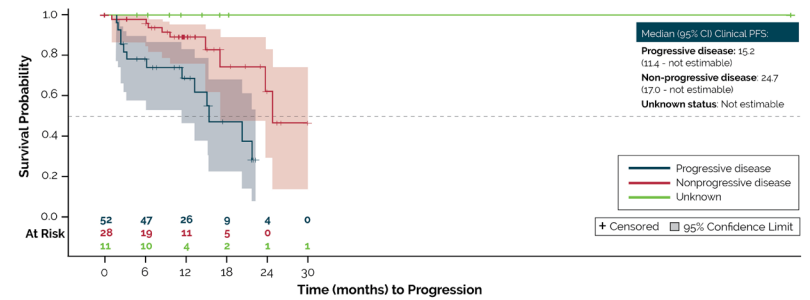


Figure 3. Clinical PFS

A) Clinical PFS



B) Clinical PFS by Disease Status at Time of Transition to Lanreotide



The sequencing of lanreotide (LAN) after octreotide LAR (OCT) for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

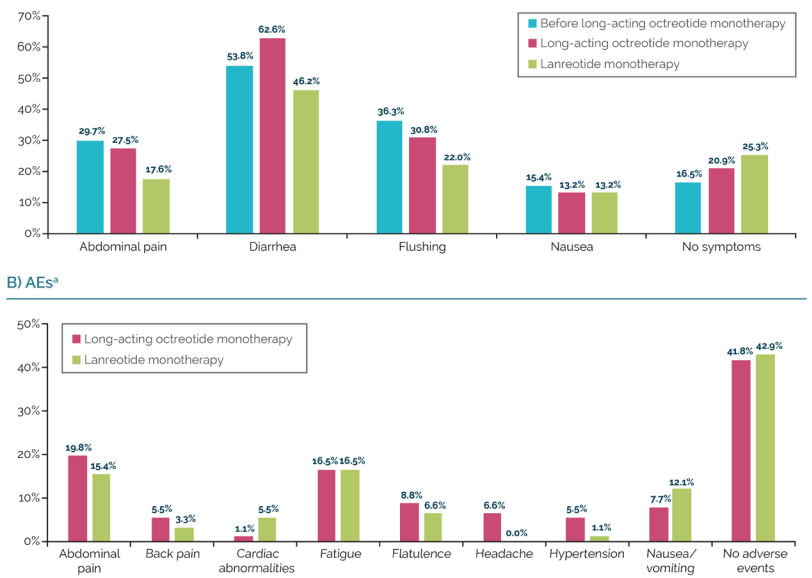
Wasif M. Saif,[1] Rohan Parikh,[2] David Ray,[3] James A. Kaye,[4] Samantha K. Kurosky,[2] Katharine Thomas,[5] Robert A Ramirez,[5]* Thorvardur Halfdanarson,[6] Thomas J.R. Beveridge,[3] Beloo Mirakhur,[3] Catherine A. Lubeck,[3] Saurabh Nagar,[2] Heloisa Soares[7]

[1]Tufts University School of Medicine, Boston, MA, USA; [2]RTI Health Solutions, Research Triangle Park, NC, USA; [3]Ipsen Biopharmaceuticals, Basking Ridge, NJ, USA; [4]RTI Health Solutions, Waltham, MA, USA; [5]Ochsner Medical Center-Kenner, Neuroendocrine Tumor Program, Kenner, LA, USA; [6]Mayo Clinic, Rochester, MN, USA; [7]University of New Mexico Medical School, Albuquerque, NM, USA

CLICK TO GO BACK TO KIOSK MENU

- **Figures 4a and 4b** present the proportion of patients with disease-related symptoms and other AEs during each assessment period.

Figure 4. Disease-related symptoms and other AEs reported during different phases of therapy



[a]Includes data recorded for at least 5.0% of patients during either of the treatment phases (i.e. before long-acting octreotide monotherapy [only for symptoms], during long-acting octreotide monotherapy, or during lanreotide monotherapy). Duration of long-acting octreotide monotherapy was relatively longer as compared with the observed duration of lanreotide monotherapy.

LIMITATIONS

- Patients included in the study were selected by convenience sample, so study findings may not be generalizable to the overall population of patients with locally advanced or metastatic GEP-NET.
- The type and frequency of testing to assess tumor status in a real-world practice may differ (and is typically more variable) from those required in a clinical trial protocol. Therefore, PFS estimates from this study should be compared with clinical trial estimates with these limitations in mind.
- Evaluation of progression in this study was not restricted to tumor imaging only and assessment through symptoms, biochemical tests, and/or clinical judgement was allowed. However, more than 90% of patients were determined to have progressive disease using tumor imaging.
- The requirement for 90 days of lanreotide treatment after transition could have introduced immortal time bias into survival estimates.

CONCLUSION

- This retrospective medical record review assessed the feasibility of sequencing from long-acting octreotide monotherapy to lanreotide monotherapy among patients with locally advanced GEP-NET across multiple sites in the US.
- After receiving long-acting octreotide for an average of 38 months, the median clinical PFS for lanreotide monotherapy was estimated to be 23.7 months (95% CI, 20.2 to not estimable).
- Our study suggests that patients with locally advanced or metastatic GEP-NETs previously treated with long-acting octreotide monotherapy can be safely transitioned to lanreotide monotherapy.
  - The clinical PFS observed among patients who had either nonprogressive or progressive disease at the time of transition from long-acting octreotide to lanreotide reinforces the possibility of sequencing lanreotide after long-acting octreotide.

References

1. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol. 2008 Jun 20;26(18):3063-72.
2. Öberg KE. The management of neuroendocrine tumours: current and future medical therapy options. Clin Oncol. 2012 May 31;24(4):282-93.
3. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology (NCCN guidelines). Neuroendocrine tumors version 2. 2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ neuroendocrine.pdf. Accessed July 16, 2018.

Contact Information

David Ray, Pharm.D., MBA
Ipsen Biopharmaceuticals, Inc.
106 Allen Road, 3rd Floor
Basking Ridge, NJ 07920 USA
E-mail: david.ray@ipsen.com

*Dr. Ramirez was unable to review the abstract, but meets all ICMJE authorship criteria to qualify as an author of this poster.

Presented at the North American Neuroendocrine Tumor Society (NANETS), Seattle, Washington, USA, October 4–6, 2018.

This study was sponsored by Ipsen