Prospective observational study in patients with locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETS) treated with lanreotide depot/autogel in a US community oncology setting: interim analysis

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BACKGROUND
- Neuroendocrine tumors (NETs) are rare and serious form of cancer arising from cells throughout the endocrine system.

- Somatic analyses are recommended to control hormone-related symptoms associated with NETs and are a first-line option for the treatment of unresectable, metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) in the National Comprehensive Care Network (NCCN) treatment guidelines.

- While clinical trials provide valuable objective information on the efficiency and safety of therapeutic agents, patients enrolled in clinical trials are often highly selected and may not accurately reflect or completely represent the majority of patients who receive treatment in the community setting.

- Lanreotide depot/autogel was recently indicated for the treatment of patients with GEP-NETs, creating a need to understand real-world effectiveness of lanreotide depot/autogel in this population.

- In a phase 3 CLARINET study, estimated rates of progression-free survival at 24 months were 65.2% (95% CI 59.1-71.2) in lanreotide-treated patients and 33.1% (95% CI 23.9-42.8) in placebo-treated patients.

- The aim of this study is to provide real-world insights into the experience of patients receiving permanent dose adjustment for the treatment of locally advanced or metastatic well-differentiated GEP-NETs in the community setting.

OBJECTIVES
- Primary objective: estimate the probability of progression-free survival for patients with locally advanced/metastatic GEP-NETs being treated with lanreotide depot/autogel in a community setting.

- Secondary objectives/ endpoints:
  - Overall survival
  - Advance events (AEs)
  - Change in flushing and diarrhea
  - Patient satisfaction with treatment

METHODS
- This is a prospective, non-interventional study of GEP-NET patients treated with lanreotide depot/autogel for a 4-6 month observation period from initiation of treatment (NCT02717243).

- This pre-planned interim analysis describes the experience of the first 51 patients enrolled in a larger cohort who have 18 or more months of follow-up on lanreotide depot/autogel or an event (ie, death or disease progression).

Inclusion criteria
- Male or female aged 18 years of age
- Histologically confirmed locally advanced or metastatic, well-differentiated NET of the small bowel, stomach, colon, rectum, or pancreas or low or intermediate grade GEP-NETs (G1 or G2).
- NETs of unknown primary origin may be included if they can be excluded as the primary origin and can be a suspicion of NET origin.
- Treatment with lanreotide depot/autogel/autogel
- ECOG PS = 0-1.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0-1.

Exclusion criteria
- Poorly differentiated or high grade NETs (G2/GEP-NETs) or tumors with unknown grading
- Patients who have previously been treated with lanreotide depot/autogel prior to the start of the study cannot be progressed between lanreotide initiation and study entry.

Clinically defined disease progression
- Defined as at least 1 of the following:
  - Tumor growth (radiographic progression)
  - New sites of metastatic disease
  - Worsening clinical symptoms
  - Tumor-related death

AND
- In addition, one of the following:
  - Treatment modification/ dose increase, regimen change
  - Treatment discontinuation
  - Additional or other NET therapeutic intervention

Statistical considerations
- Outcomes include clinical-defined progression-free survival (defined above) and overall survival as well as changes in flushing and diarrhea, and satisfaction using the TSGC-Q.

- For time-to-event endpoints (clinically defined progression-free survival and overall survival), Kaplan-Meier curves were constructed and hazard ratio estimates were calculated along with 95% CI.

RESULTS
- Among the 51 patients with a year of follow-up, median age was 65 years, 64% were Caucasian, and 40% had CCOG performance status of 0-1.

- There were 37% of patients who had at least 1 AE experience prior to the study.

- The probability of clinically defined progression-free survival at 12 months was 49% (Figure 1).

- The probability of overall survival at 12 months was 59% (Figure 2).

- The top reasons for discontinuation were disease progression (13%) and AEs (40%).

- The main AEs reported were nausea (21%), fatigue (16%), and diarrhea (7%).

- The most common AEs leading to discontinuation included hypoglycemia (9%) and pneumonitis (6%).

LIMITATIONS
- This study captures a convenience sample from the US Oncology patient population, which may limit generalizability to other populations.

- The 12-16 month duration of this interim analysis may lack the long-term follow-up needed to identify prognostic events in an incipient disease such as GEP-NETs.

CONCLUSION
- This interim analysis provides the first prospectively collected real-world outcomes of patients treated with lanreotide depot/autogel for GEP-NETs.

- Interim results suggest lanreotide depot/autogel is effective in disease control and most patients are satisfied with free treatment.

References

Conflicts of interest
- The authors have indicated they have no conflicts of interest to disclose.

Acknowledgements
- The authors would like to thank the patients participating in this study. The authors have acknowledged the contributions of the following: new, n.a., no prior authorship statement at the time of publication.

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BACKGROUND

- Neuroendocrine tumors (NETs) are a rare and serious form of cancer arising from cells throughout the endocrine system.1
- Somatostatin analogs are recommended to control hormone-related symptoms associated with NETs and as a first-line option for the treatment of unresectable, metastatic gastroenteropancreatic (GEP) NETs in the National Comprehensive Care Network (NCCN) treatment guidelines.2
- While clinical trials provide valuable objective information on the efficacy and safety of therapeutic agents, patients enrolled in clinical trials are often highly selected and may not accurately reflect or completely represent the majority of patients who receive treatment in the community setting.
- Lanreotide depot/autogel was recently indicated for the treatment of patients with GEP-NETs, creating a need to understand real-world effectiveness of lanreotide depot/autogel in this population.
  - In the phase 3 CLARINET study, estimated rates of progression-free survival at 24 months were 65.1% (95% confidence interval [CI]: 56.0, 74.1) in lanreotide-treated patients and 33.0% (95% CI: 23.0, 43.3) in placebo-treated patients.3
- The aim of this study is to provide real-world insights into the experience of patients receiving lanreotide depot/autogel for the treatment of locally advanced or metastatic well-differentiated GEP-NETs in the community setting.

OBJECTIVES

- Primary objective: estimate the probability of progression-free survival for patients with locally advanced, metastatic GEP-NETs being treated with lanreotide depot/autogel in a community setting.
- Secondary objectives/endpoints:
  - Overall survival
  - Adverse events (AEs)
  - Change in flushing and diarrhea
  - Patient satisfaction with treatment (Treatment Satisfaction Questionnaire for Medication [TSQM-g])

METHODS

- This is a prospective, non-interventional study of GEP-NET patients treated with lanreotide depot/autogel for a 24-month observation period from initiation of treatment (NCT02730104).
- This pre-planned interim analysis describes the experience of the first 50 patients (total planned sample is 100 patients) who have had 1 year of follow-up on lanreotide depot/autogel or an event (i.e., death or disease progression).

Inclusion criteria

1. Male or female ≥18 years of age.
2. Histologically confirmed locally advanced or metastatic, well-differentiated NET of the small bowel, stomach, colon/rectum, or pancreas (low or intermediate grade; i.e., G1 or G2).
   a. NETs of unknown primary origin may be included if lung can be excluded as the primary origin and there is suspicion of GEP-NET origin.
3. Treatment with lanreotide depot/autogel (SSA-naive patients with prior treatment with octreotide LAR are permitted).

Exclusion criteria

1. Poorly differentiated or high grade (i.e., G3) GEP-NETs or tumors with unknown grading.
2. Patients who have previously initiated treatment with lanreotide depot/autogel prior to the start of the study cannot have progressed between lanreotide initiation and study entry.

Presented at the North American Neuroendocrine Tumor Society (NANETS), Seattle, Washington, USA, October 4–6, 2018. This study was sponsored by Ipsen.
Clinically defined disease progression
• Defined as at least 1 of the following:
  - Tumor growth (radiographic progression)
  - New sites of metastatic disease
  - Worsening clinical symptoms
  - Tumor-related death

AND
• In addition, one of the following:
  - Treatment modification (dose increase, regimen change)
  - Treatment discontinuation
  - Additional or other NET therapeutic intervention

Statistical considerations
• Outcomes included clinically defined progression-free survival (defined above) and overall survival, as well as changes in flushing and diarrhea, and satisfaction (using the TSOM-9).
• For time-to-event endpoints (clinically defined progression-free survival and overall survival), Kaplan-Meier curves were constructed and Kaplan-Meier estimates were calculated along with 95% CIs.

RESULTS
• Among the 70 patients with 1 year of follow-up, median age was 65 years. 84% were Caucasians, and 96% had ECOG performance status of 0 or 1 (Table 1).
  - There were 35% of patients who had octreotide LAR experience prior to the study.

Table 1. Demographics and baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>64.2 (10.5)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>29 (41.4)</td>
</tr>
<tr>
<td>Male</td>
<td>41 (58.6)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>42 (60.0)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (2.9)</td>
</tr>
<tr>
<td>Black</td>
<td>2 (2.9)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>ECOG / Performance Status, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>27 (44.1)</td>
</tr>
<tr>
<td>1</td>
<td>25 (44.1)</td>
</tr>
<tr>
<td>2</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Pending</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Code, n (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>30 (42.9)</td>
</tr>
<tr>
<td>2</td>
<td>11 (17.1)</td>
</tr>
<tr>
<td>Prior Chemotherapy, n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6 (9.3)</td>
</tr>
<tr>
<td>No</td>
<td>64 (90.7)</td>
</tr>
<tr>
<td>Flushing at Screening, n (%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>58 (82.9)</td>
</tr>
<tr>
<td>Yes</td>
<td>12 (17.1)</td>
</tr>
<tr>
<td>P-Moderate</td>
<td></td>
</tr>
<tr>
<td>P-Mild</td>
<td></td>
</tr>
<tr>
<td>P-Moderate</td>
<td></td>
</tr>
<tr>
<td>Diarrhea at Screening, n (%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>57 (81.4)</td>
</tr>
<tr>
<td>Yes</td>
<td>13 (18.6)</td>
</tr>
<tr>
<td>P-Moderate</td>
<td></td>
</tr>
<tr>
<td>P-Moderate</td>
<td></td>
</tr>
</tbody>
</table>

*Includes treatment with lanreotide depot/autogel and octreotide LAR.
ECOG, Eastern Cooperative Oncology Group 19; n, no.; P, present; SD, standard deviation.

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- The probability of clinically defined progression-free survival at 12 months was 92% (Figure 1).

![Figure 1. Probability of progression-free survival](image)

- The probability of overall survival at 12 months was 96% (Figure 2).

![Figure 2. Probability of overall survival](image)

- Largely, flushing and diarrhea remained stable at 1-year, and at 1-year follow-up on treatment, >80% of patients were at least somewhat satisfied with the drug (Tables 2 and 3).

| Table 2. Change in flushing and diarrhea at 12 months of follow-up |
|-------------------------|-------------------------|-------------------------|-------------------------|
|                         | Bartter                  | Stable                  | Worse                   |
| Flushing, n (%)         | 2 (10.0)                 | 2 (10.0)                | 0                       |
| Diarrhea, n (%)         | 2 (10.0)                 | 2 (10.0)                | 1 (5.0)                 |

For flushing: n=78 patients. For diarrhea: n=77 patients.
### Table 3. Summary of the worst score of satisfaction (TSQM-9) over the study period

<table>
<thead>
<tr>
<th>Question</th>
<th>Extremely Dissatisfied (1 of 3)</th>
<th>Very Dissatisfied (2 of 3)</th>
<th>Dissatisfied (3 of 3)</th>
<th>Satisfied (1 of 3)</th>
<th>Very Satisfied (2 of 3)</th>
<th>Extremely Satisfied (3 of 3)</th>
<th>Total N</th>
</tr>
</thead>
<tbody>
<tr>
<td>How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?</td>
<td>1.0 (4)</td>
<td>1.0 (4)</td>
<td>4.0 (4)</td>
<td>6.0 (4)</td>
<td>6.0 (4)</td>
<td>7.0 (4)</td>
<td>45</td>
</tr>
<tr>
<td>How satisfied or dissatisfied are you with the way the medication relieves your symptoms?</td>
<td>1.0 (4)</td>
<td>1.0 (4)</td>
<td>3.1 (4)</td>
<td>3.3 (4)</td>
<td>4.0 (4)</td>
<td>7.0 (4)</td>
<td>45</td>
</tr>
<tr>
<td>How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?</td>
<td>1.0 (4)</td>
<td>1.0 (4)</td>
<td>2.1 (4)</td>
<td>6.0 (4)</td>
<td>4.0 (4)</td>
<td>8.0 (4)</td>
<td>45</td>
</tr>
<tr>
<td>How easy or difficult is it to use the medication in its current form?</td>
<td>0.0 (4)</td>
<td>1.0 (4)</td>
<td>4.0 (4)</td>
<td>11.0 (4)</td>
<td>6.0 (4)</td>
<td>12.0 (4)</td>
<td>45</td>
</tr>
<tr>
<td>How easy or difficult is it to plan when you will take the medication each time?</td>
<td>0.0 (4)</td>
<td>0.0 (4)</td>
<td>2.0 (4)</td>
<td>4.0 (4)</td>
<td>13.0 (4)</td>
<td>13.0 (4)</td>
<td>45</td>
</tr>
<tr>
<td>How convenient or inconvenient is it to take the medication as prescribed?</td>
<td>1.0 (4)</td>
<td>1.0 (4)</td>
<td>4.0 (4)</td>
<td>6.0 (4)</td>
<td>4.0 (4)</td>
<td>10.0 (4)</td>
<td>45</td>
</tr>
<tr>
<td>Taking all things into account, how satisfied or dissatisfied are you with the medication?</td>
<td>0.0 (4)</td>
<td>0.0 (4)</td>
<td>4.0 (4)</td>
<td>9.0 (4)</td>
<td>9.0 (4)</td>
<td>9.0 (4)</td>
<td>45</td>
</tr>
</tbody>
</table>

All patients answered all questions, i.e., no missing data.

- The top reasons for discontinuation were disease progression (10%) and AE (4%).
- The main AE reported thus far were nausea (10%), fatigue (4%), and abdominal pain (4%).
- The most common AE leading to discontinuation included hypoglycemia (2%) and pneumonitis (2%).

### LIMITATIONS

- This study captures a convenience sample from the US Oncology patient population, which potentially may limit its generalizability to other populations.
- The 12-month duration of this interim analysis may lack the long-term follow-up needed to identify progressive events in an indolent disease such as GEP-NETs.

### CONCLUSION

- This interim analysis provides the first prospectively collected real-world outcomes of patients treated with lanreotide depot/autogel for GEP-NETs.
- Interim results suggest lanreotide depot/autogel is effective in disease control and most patients are satisfied with their treatment.

### References


### Conflicts of interest

ASP, member of advisory board for Ipsen; Advanced Accelerator Applications, Eisai, Teva, and CHF; MED consultant/advisor for Ipsen; MS, employee of Ipsen; stock ownership in Ipsen and Johnson & Johnson research funding from Ipsen; BM, DR, and KA, employees of Ipsen DM, DC.

### Acknowledgements

The authors thank the investigators and patients participating in this study. The authors thank Nicola Codazzi of The Medacycle Group, New Hope, PA, for providing post-presentation support, which was sponsored by Ipsen in accordance with Good Publication Practice guidelines.