Lanreotide Autogel (Depot) Significantly Improves Tumor Progression-Free Survival in Patients with Non-functioning Gastroenteropancreatic Neuroendocrine Tumors: Results of the CLARINET Study

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Introduction

- Somatostatin analogs (SSAs) provide good symptom control in patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs).
- SSAs also inhibit tumor growth in various experimental tumor types by direct and indirect mechanisms.1
- To date, evidence is based mostly on retrospective and prospective open-label studies.2 Prior to CLARINET, PROMID was the only randomized placebo-controlled study conducted with somatostatin LAR in midgut NETs.3
- The randomized study of lanreotide depot Autogel (CLARINET) is the only randomized placebo-controlled study in a SSA in gastroenteropancreatic NETs (SSA-NETs), strengthening the evidence for progression-free survival (PFS) benefit.

CLARINET was a large 2-year international study (n=226, 14 countries) conducted with lanreotide Autogel (Depot) in US$ 212 mg (without dose titration). Patients had:

- well- or moderately differentiated non-functioning NETs
- ≥ 39% had Ki-67 ≥ 0.2%
- ≥ 48% had hepatic tumor load ≥ 10%.

Methods

Patients

- Key inclusion criteria:
  - adults with midgut tumor (IT and/or CR)
  - primary tumor localized in pancreas, rectum, head, or unknown origin
  - NET confirmed centrally using standardized and measurable criteria according to RECIST criteria version 1.0 and confirmed centrally.
- Key exclusion criteria:
  - metastatic disease and/or locally advanced inoperable tumor (or documented refusal to surgery)
  - primary tumor grade 3 and ≥ 2 protocol violations
  - bowel obstruction
  - tumor progression according to RECIST criteria version 1.0 and confirmed centrally.
- Secondary endpoints included patients alive and without tumor progression at 48 and 96 weeks, time to progression, overall survival (time from randomization to death due to any cause), interim biomarkers, safety. (If three secondary endpoints, data for overall survival and safety are presented here.)

Study endpoints

- Primary endpoint—PFS (time to death or disease progression confirmed centrally according to RECIST interval within 56 weeks of first study treatment).
- Secondary endpoint—PFS (primary endpoint) according to investigator assessment despite a central assessment of stable disease: lanreotide, 20 events and median of 24 months; placebo, 6 due to investigator decision (PD).

Results

- A total of 203 patients received treatment: lanreotide Depot 120 mg (n=101) vs. placebo (n=102) (Figure 2).
- Treatment groups were well-matched for baseline characteristics (Table 1).
- Lanreotide Depot significantly prolonged PFS vs. placebo:
  - median PFS not reached vs. 18 months, respectively (hazard ratio [HR] 0.47 [95% confidence interval (CI) 0.28–0.80]; p=0.0022; Figure 3). 4

Conclusions

- PFS substantially prolonged with lanreotide Depot 120 mg vs. placebo for metastatic well-differentiated GEP-NETS, with 53% relative risk reduction for progression or death in median overall survival.
- First randomized head-to-head trial with lanreotide Depot 120 mg vs. placebo:
  - significantly in patients with grade 1 and grade 2 tumors
  - significantly in patients with low and high HTL.
- Safety profile consistent with previous studies.
- CLARINET provides new evidence for the antiproliferative effects of lanreotide Depot, which may support its place in treatment algorithms.

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CLARINET investigators:

- B. de Roo, E. J. van der Lumpe, E. van den Lumpe, P. van der Lumpe, M. van der Lumpe, J. M. van der Lumpe, R. van der Lumpe, A. van der Lumpe, K. van der Lumpe, P. van der Lumpe, J. van der Lumpe, and H. van der Lumpe.

References


Table 1. Baseline demographic and disease characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lanreotide Depot (n=101)</th>
<th>Placebo (n=102)</th>
</tr>
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<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>57 (47–68)</td>
<td>59 (50–68)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>75 (74)</td>
<td>68 (67)</td>
</tr>
<tr>
<td>Primary tumor localization</td>
<td>49 (48)</td>
<td>37 (36)</td>
</tr>
<tr>
<td>- Liver</td>
<td>35 (34)</td>
<td>26 (25)</td>
</tr>
<tr>
<td>- Pancreas</td>
<td>28 (27)</td>
<td>28 (27)</td>
</tr>
<tr>
<td>Metastatic status, n (%)</td>
<td>94 (93)</td>
<td>92 (90)</td>
</tr>
<tr>
<td>- Metastatic</td>
<td>72 (71)</td>
<td>71 (70)</td>
</tr>
<tr>
<td>Time since diagnosis, mean (SD) in months</td>
<td>27.8 (39)</td>
<td>26.5 (37)</td>
</tr>
</tbody>
</table>
| No. of liver lesions, median | 9 | 10

Figure 2. Study design.

Figure 3. Median PFS in months.

Figure 4. Four-line graph comparing patients alive and with no progression (%).

Figure 5. No treatment difference for overall survival over 4 years.