Background

- Metastatic neuroendocrine tumors (NETs) are rare and no prospective trials specific to lung NETs have been reported.1
- Surgical resection remains the mainstay for lung NETs; other approved treatment options for advanced lung NETs are limited, with no standard therapeutic regimens.2
- For advanced lung NETs:
  - Currently, recommendations for most treatment options rely on data available for well-differentiated digestive NETs or a few retrospective studies in lung NETs, while emphasizing that the disease parameters differ.2,4
  - The mTOR inhibitor everolimus was recently approved as a treatment option for lung NET in the US and EU based on one placebo-controlled phase 3 trial (RADAR 4) in a mixed population of patients with advanced progressive gastrointestinal and lung NETs.5

Somatostatin analogs (SSAs) are among targeted treatments that have recently demonstrated increased progression-free survival (PFS) among patients with NETs, particularly those with gastroenteropancreatic NETs.5–7

Objective

- The large multinational phase 3 CLARINET study demonstrated antitumor efficacy with the SSA lanreotide autogel (also known as autogel) vs. placebo for metastatic gastroenteropancreatic NETs.8,9
- Patients with lung NETs were not included in CLARINET, and prospective randomized studies of SSA therapies for these particular NET subtypes are currently lacking.
- High levels of expression of the somatostatin receptors SSTR2A and SSTR2B in lung NETs recently demonstrated increased progression-free survival (PFS) among patients with a best overall response of PR or CR at any time prior to randomization.
- The open-label period will last until 6 months after the data cut-off date.

Methods

Patients

- 216 patients with lung NET will be enrolled from around 80 sites across the USA, Canada, and Europe.

Table 1. Key inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>Adult patients (18 years) with metastatic and/or unresectable, pathologically well-differentiated, typical or atypical lung NETs</td>
<td>Previous SSA treatment (&gt;3 days of short-acting SSA or ≥2 doses of long-acting SSA within 6 weeks of randomization)</td>
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<td>Malignant index &lt;200 mitoses/mm² for typical tumor, or &lt;100 mitoses/mm² and/or foci of necrosis for atypical tumor</td>
<td>More than 1 course of Ctx (cytotoxic Ctx, MIT, or IFNa) for lung NET at any time prior to randomization</td>
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<tr>
<td>Positive somatostatin-receptor imaging (grade 2 or higher on Krenning scale)</td>
<td>CTx treatment (cytotoxic Ctx, MIT, or IFNa) for lung NET within 4 weeks of randomization</td>
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<td>ECOG performance status score of 0</td>
<td>PRRT at any time prior to randomization</td>
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<tr>
<td>Negative pregnancy test, non-lactating and using acceptable method of birth control (as applicable)</td>
<td>Functional disease requiring SSA treatment for symptom management</td>
</tr>
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- The double-blind period will continue until progressive disease (PD) centrally assessed/death (or withdrawal from the study treatment for unacceptable toxicity or any other reason) or until the date of data cut-off/primary study analysis (when 175 PD according to central review or death events are reached).
- Patients with centrally assessed PD on placebo may opt to enter the open-label extension period.
- Patients without centrally assessed PD on lanreotide depot 120 mg at the data cut-off date of double-blind period may opt to enter the open-label extension period.
- The open-label period will last until 6 months after the data cut-off date.
- All patients who experience PD will be followed to document survival, quality of life (QoL), and subsequent anti-cancer treatments; eligible patients who do not choose to receive open-label lanreotide will also be followed.

Discussion

- Treatment of advanced lung NETs continues to be an area of unmet need; the role of SSAs and other molecular targeted therapies on these diverse and clinically challenging tumors requires further research.
- Results from ongoing phase 3 clinical trials such as this will provide the data needed to help evaluate the efficacy and safety of potential new treatment options for advanced lung NETs.
- SPINET is the first prospective, placebo-controlled, randomized study designed to assess the effect of lanreotide depot/autogel 120 mg on typical and atypical carcinoid lung NETs.

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References