Phase I, Open-Label, Randomized, Pharmacokinetic/Pharmacodynamic (PK/PD) Study of Octreotide Subcutaneous (sc) Depot Versus Octreotide Long-Acting Repeatable (OCT-LAR) in Healthy Volunteers

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Background: The LAR formulation of octreotide, the most widely used somatostatin analogue, must be reconstituted prior to intramuscular injection. Octreotide sc depot is a new ready-to-use formulation for sc administration. This phase I study compared the PK/PD of octreotide sc depot to OCT-LAR.

Methods: Healthy adult male/female volunteers received a single dose of octreotide sc 200 μg and were subsequently randomly assigned 1 week later to three injections of octreotide sc depot 30 mg/month (n=14) or OCT-LAR 30 mg/month (n=14). Blood samples were collected pre- and post-injection and at prespecified time points during the study. Adverse events (AEs) were recorded.

Results: Octreotide sc depot exhibited a steady, rapid increase to peak concentrations (Cmax) followed by a slow, exponential decrease through day 28. OCT-LAR displayed a burst concentration peak and rapid decline to undetectable values that rebounded by day 7, stabilized from day 10, and finally decreased around day 21.

Table. Comparison of PK Parameters

<table>
<thead>
<tr>
<th>Steady State (after third injection)</th>
<th>Cmax (mean±SD)</th>
<th>AUC₂₈d (mean±SD)</th>
<th>tmax, median(range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octreotide sc depot</td>
<td>29.3±7.1 ng/mL</td>
<td>3465±608 h·ng/mL</td>
<td>24 (2-24) hours</td>
</tr>
<tr>
<td>OCT-LAR</td>
<td>1.8±0.6 ng/mL</td>
<td>733±222 h·ng/mL</td>
<td>1 (0.5-360) hours</td>
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</table>

Relative bioavailability (using AUC₂₈d) of octreotide sc depot versus OCT-LAR was 487% (90% CI: 411–578). Octreotide sc depot provided more rapid and greater IGF-1 suppression than OCT-LAR after injection during weeks 1-2, although IGF-1 levels remained similar during weeks 3-4; AUC for IGF-1 suppression was similar in both groups. In accordance with the known safety profile of octreotide, the most frequent AEs for both octreotide sc depot and OCT-LAR were mild to moderate gastrointestinal events. Local tolerability was generally good; local discomfort was mild and transitory when it did occur.

Conclusions: Octreotide sc depot provides greater octreotide bioavailability with a more rapid onset and similar duration of effect compared with OCT-LAR in healthy volunteers and offers enhanced convenience as it may be supplied in a convenient, prefilled syringe with a thinner needle. Phase III studies of octreotide sc depot in patients with neuroendocrine tumors and acromegaly are planned.

Previously presented at the 16th European Congress of Endocrinology (ECE); May 3-7, 2014; Warsaw, Poland.