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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 (C_{max}) 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

Steady State (after third injection)	**C_{max} (mean±SD)**	**AUC_{28d} (mean±SD)**	**t_{max}, median(range)**
Octreotide sc depot	29.3±7.1 ng/mL	3465±608 h·ng/mL	24 (2-24) hours
OCT-LAR	1.8±0.6 ng/mL	733±222 h·ng/mL	1 (0.5-360) hours

Relative bioavailability (using AUC_{28d}) 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.

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