Acromegaly is a rare and serious disorder characterized by the chronic hypersecretion of growth hormone (GH) from a pituitary adenoma and subsequent hepatic overproduction of insulin-like growth factor 1 (IGF-1). Around 30-50% of patients with acromegaly also have hyperprolactinemia, which is associated with infertility, gonadal dysfunction, and reduced fertility. Current medical therapy for patients with acromegaly and hyperprolactinemia typically involves the combination of a somatostatin analogue and dopamine agonist to reduce GH/IGF-1 and prolactin levels, respectively. Pasireotide is a multi-receptor-targeted somatostatin analogue with high affinity for four of the five somatostatin receptor subtypes (sst), including sst5, which are the most prevalent sst on GH-secreting pituitary adenomas.

In a large, randomized, double-blind, Phase III trial in patients with acromegaly, pasireotide LAR was significantly superior to octreotide LAR at GH levels ≥2.5 µg/L and normal IGF-1 after 12 months of therapy. In this poster, we report the efficacy and safety of pasireotide LAR and octreotide LAR after 12 months of treatment in the subset of patients who had hyperprolactinemia at baseline.

### Methods

**Study Design**

Study naïve patients with active acromegaly (GH ≥5 µg/L or nadir ≥1 µg/L post-oral glucose tolerance test, and IGF-1 > upper limit of normal [ULN]) were eligible for enrollment into the 12-month study. Patients were either de novo or with a visible pituitary adenoma on gadolinium-enhanced pituitary MRI; a change of ≥20% was considered to be non-normalized.

**Assessments**

- **Mean prolactin, GH and IGF-1 levels** were assessed at baseline and at months 6, 9, and 12.
- **The proportion of patients achieving GH <2.5 µg/L and normal IGF-1, GH <2.5 µg/L, normal IGF-1, and normal prolactin levels** were assessed at month 12.
- **Changes from baseline in tumor volume at month 12 were evaluated by gadolinium-enhanced pituitary MRI; a change of ≥20% was considered significant.**

Safety was assessed throughout the study and was primarily based on the monitoring of all adverse events (AEs).

**Statistical Analysis**

This analysis included all the data collected during 12 months of treatment and the safety follow-up period.

The last available concurrent prolactin, GH, and IGF-1 values evaluated at the scheduled visit during the core study were used to compute the proportion of patients at month 12 achieving normal prolactin, GH <2.5 µg/L, normal IGF-1, and GH <2.5 µg/L and normal IGF-1.

**Patients**

- Of the 368 patients who were randomized to pasireotide LAR (n=176) or octreotide LAR (n=192), 59 (16.5%) had hyperprolactinemia at baseline:
- 29 and 30 patients in the pasireotide LAR and octreotide LAR treatment groups, respectively.

Baseline characteristics were similar between treatment arms (Table 1).

<table>
<thead>
<tr>
<th>Demographic variable</th>
<th>Pasireotide LAR, n=29</th>
<th>Octreotide LAR, n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years</td>
<td>49.2</td>
<td>49.5</td>
</tr>
<tr>
<td>Median female</td>
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<td>17.5</td>
</tr>
<tr>
<td>Race, n (%)</td>
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<tr>
<td>Caucasian</td>
<td>17 (58.6%)</td>
<td>18 (60.0%)</td>
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<td>Asian</td>
<td>8 (27.6%)</td>
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</tr>
<tr>
<td>Black</td>
<td>3 (10.3%)</td>
<td>2 (6.9%)</td>
</tr>
<tr>
<td>Other</td>
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<td>5 (16.7%)</td>
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<tr>
<td>Median time since diagnosis, months</td>
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<td>4.2</td>
</tr>
<tr>
<td>Previous surgery, n (%)</td>
<td>8 (28.0%)</td>
<td>7 (23.3%)</td>
</tr>
<tr>
<td>Median time since surgery months</td>
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<td>7.5</td>
</tr>
<tr>
<td>Mean GH level, µg/L</td>
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<td>33.6</td>
</tr>
<tr>
<td>Mean standardized IGF-1, µg/L</td>
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<td>3.1</td>
</tr>
<tr>
<td>Mean prolactin level, µg/L</td>
<td>83.5</td>
<td>55.9</td>
</tr>
</tbody>
</table>

**Results**

Efficacy of Treatment on Mean Prolactin, GH and IGF-1 Levels

- Following 12 months of treatment in patients with baseline hyperprolactinemia, 21/29 (72.4%) in the pasireotide LAR arm and 17/30 (56.7%) in the octreotide LAR arm had normal prolactin levels (Figure 1).

**Figure 1. Proportion of Patients with Normalized Prolactin Levels at Month 12, for Patients with Prolactin >ULN at Baseline**

- GH levels ≤2.5 µg/L at month 12 were observed in 34.5% of patients (n=10) who received pasireotide LAR and 43.3% of patients (n=13) who received octreotide LAR; the equivalent proportions of patients with normal IGF-1 levels were 24.1% (n=7) and 26.7% (n=8), respectively (Table 2).

**Table 2. GH and IGF-1 Response at Month 12 for Patients with Prolactin >ULN at Baseline**

- At month 12, mean prolactin levels had decreased by 65.7% in the pasireotide LAR arm and by 39.8% in the octreotide LAR arm (Figure 2A).

**Figure 2. Mean (±SE) (A) Prolactin, (B) GH and (C) IGF-1 Levels over Time in Patients with Prolactin >ULN at Baseline**

- GH levels ≤2.5 µg/L and normal IGF-1 levels were observed in 23.4% (n=7) and 21.7% (n=6), respectively (Figure 2B and 2C).

**Table 3. Prolactin >ULN at Baseline, Treated with (A) Pasireotide LAR and (B) Octreotide LAR**

- At month 12, tumor volume had decreased by a mean of 39.2% (median 33.2%; interquartile range 25.2–51.0%) in the pasireotide LAR treatment group and 39.6% (median 33.2%; interquartile range 25.0–58.9%) in the octreotide LAR treatment group. Any reduction or no change in tumor volume from baseline to month 12 was reported in 93.0% (n=192) and 91.3% (n=213) of patients in the pasireotide LAR and octreotide LAR treatment arms, respectively (Figure 3).

**Table 3. Prolactin >ULN at Baseline, Treated with (A) Pasireotide LAR and (B) Octreotide LAR**

**Safety and Tolerability**

- The most common AEs, regardless of relationship to study drug, for those patients with hyperprolactinemia (n=14) treated with pasireotide LAR were hyperglycemia (48.3% of patients (n=6)) and hyperprolactinemia (48.3% of patients (n=6)). The most common AEs related to pasireotide LAR were hyperglycemia-related AEs, compared with 13.3% of patients (n=4) who received octreotide LAR.

**Conclusion**

In this subset of patients with acromegaly and hyperprolactinemia, pasireotide LAR and octreotide LAR normalized prolactin levels in 72.4% and 56.7% of patients, respectively. Of note, a decrease in prolactin levels is not commonly reported with somatostatin analogue therapy. Mean GH and IGF-1 levels were also suppressed during treatment with pasireotide LAR and octreotide LAR. Most patients had a decrease in tumor volume, which may be particularly important in patients with hyperprolactinemia caused by compression of the pituitary stalks.

**References**


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**Slides and e-Prints**