Small for gestational age patients in real-life, French clinical practice: what is the difference between good and poor responders to growth hormone treatment?

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Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Statistics</th>
<th>Poor responders</th>
<th>Good responders</th>
<th>Good vs. poor responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight and/or height at birth</td>
<td>n (% [95% CI])</td>
<td>13 (76.5%) [52.7%, 90.4%]</td>
<td>22 (77.8%) [55.6%, 85.8%]</td>
<td>0.0000</td>
</tr>
<tr>
<td>SDS ≤−2</td>
<td></td>
<td>0.032 [0.035–0.10]</td>
<td>0.038 [0.035–0.10]</td>
<td>0.0845</td>
</tr>
<tr>
<td>Height SDS at birth</td>
<td>Mean (SD)</td>
<td>−1.6 (1.7) [−2.6, −0.6]</td>
<td>−1.2 (1.2) [−2.2, −0.2]</td>
<td>0.8126</td>
</tr>
<tr>
<td>Height SDS at treatment start</td>
<td>Mean (SD)</td>
<td>−3.2 (4.2) [−3.4, −3.0]</td>
<td>−2.8 (3.4) [−2.8, −3.1]</td>
<td>0.0006</td>
</tr>
<tr>
<td>Target height SDS</td>
<td>Mean (SD)</td>
<td>−1.0 (3.9) [−1.3, −0.4]</td>
<td>−1.6 (3.6) [−1.6, −1.6]</td>
<td>0.0857</td>
</tr>
<tr>
<td>Age at treatment start</td>
<td>Mean (SD)</td>
<td>9.7 (3.3) [9.3, 10.0]</td>
<td>9.4 (3.3) [9.1, 9.7]</td>
<td>0.0409</td>
</tr>
<tr>
<td>Growth velocity SDS 1 year before GH treatment</td>
<td>Mean (SD)</td>
<td>0.42 (0.43) [0.41, 0.44]</td>
<td>0.52 (0.43) [0.51, 0.53]</td>
<td>0.0446</td>
</tr>
<tr>
<td>GH dose at treatment initiation (mg/kg/day)</td>
<td>Mean (SD)</td>
<td>0.30 (0.067) [0.30, 0.068]</td>
<td>0.041 (0.061) [0.040, 0.045]</td>
<td>0.4270</td>
</tr>
<tr>
<td>GH dose at treatment initiation in classes (mg/kg/day)</td>
<td>n (% [95% CI])</td>
<td>0.40 (0.060) [0.39, 0.061]</td>
<td>0.039 (0.060) [0.038, 0.060]</td>
<td>0.4270</td>
</tr>
<tr>
<td>&lt;0.032 (0.035–0.10)</td>
<td></td>
<td>0.0% [0.0, 0.0]</td>
<td>0.0% [0.0, 0.0]</td>
<td>1.0000</td>
</tr>
<tr>
<td>&gt;0.032 (0.035–0.10)</td>
<td></td>
<td>3.9 (7.9) [3.2, 7.6]</td>
<td>3.2 (7.9) [3.0, 7.6]</td>
<td>0.0857</td>
</tr>
<tr>
<td>Growth velocity SDS in the first year of treatment</td>
<td>Mean (SD)</td>
<td>3.0 (1.2) [2.5, 3.4]</td>
<td>2.3 (1.3) [2.0, 2.6]</td>
<td>0.0780</td>
</tr>
<tr>
<td>Δ height SDS in the first year in the classes SDS ≤−1</td>
<td>n (% [95% CI])</td>
<td>9.0 (10) [8.4, 10.6]</td>
<td>9.2 (9.6) [8.9, 9.5]</td>
<td>0.0008</td>
</tr>
<tr>
<td>Δ height SDS in the first year in the classes SDS ≤−0.5</td>
<td>n (% [95% CI])</td>
<td>9.0 (10) [8.4, 10.6]</td>
<td>9.2 (9.6) [8.9, 9.5]</td>
<td>0.0008</td>
</tr>
<tr>
<td>GH treatment duration (months)</td>
<td>Mean (SD)</td>
<td>12.0 (9.3) [11.2, 12.8]</td>
<td>12.6 (9.3) [11.9, 13.3]</td>
<td>0.1341</td>
</tr>
<tr>
<td>GH cumulative dose (mg/kp)</td>
<td>Mean (SD)</td>
<td>55.5 (19.8) [45.1, 66.0]</td>
<td>59.0 (15.3) [48.4, 69.6]</td>
<td>0.3944</td>
</tr>
<tr>
<td>Δ change in, FAH, final adult height; GH; growth hormone; CI; confidence interval; SD; standard deviation; SDS; standard deviation score.</td>
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</tbody>
</table>

Introduction

• Optimization and individualization of growth hormone (GH) treatment in children born small for gestational age (SGA), with growth retardation, is an issue.
• Prediction models, to assess the statal response to treatment, have been developed from large observational studies. A good response to GH treatment is defined as final adult height (FAH) standard deviation score (SDS) >−2.
• Based on available data, the known criteria for a good response in GH deficiency (GHD) are: age and height at treatment start, target height, GH dose and first year treatment response.
• The best predictors in the SGA model during 3 years of follow-up were: GH dose, weight at the start of treatment, mid-parental height SDS and age at treatment start (for age, there was an inverse association).

Results

• Of the 291 patients, 183 were GH-naïve.
• The mean (SD) treatment duration was 4.4 (2.2) years and for the 90 patients who reached FAH, it was 5.3 (2.2) years.
• To date, 51 GH-naïve patients have completed the study (good responders: 31; poor responders: 20).
• Patient characteristics are presented in Table 1.
• A significant difference was observed for the following characteristics in good versus poor responders (data are shown in Table 1):
  - Height SDS at treatment start: p=0.0006.
  - Age (years) at treatment start: p=0.0490.
  - Growth velocity SDS 1 year before treatment: p=0.0446.
• A positive trend was observed for the following characteristics:
  - Target height SDS: p=0.0857.
  - Growth velocity SDS in the first year of treatment: p=0.0780.
• Change in height SDS ≥ −0.5 (% patients): p=0.0845.
• Good responders were taller and younger at the beginning of treatment, with better growth velocity in the year preceding treatment.
• There was a trend towards greater growth velocity in the first year of treatment in good responders compared with poor responders.

Conclusion

• Prospective, observational French registry data show that some of the criteria for a good response to treatment in GHD could also be applicable to patients born SGA, treated with Norditropin®, and useful for clinical practice.
• Nevertheless, the observational design of the study, and the small sample size of patients, could limit the power of analysis.
• Further investigations with more patients completing the study, and additional observational studies, are needed.

References

Conflict of interest disclosures
MN, RC, BL and JPS are members of the Scientific Committee of, and investigators for, the SGA Registry. EH and BV are employees of Novo Nordisk.

This study was supported by Novo Nordisk and is registered at ClinicalTrials.gov (NCT01571853). The authors thank the investigators and patients participating in this study. The authors take full responsibility for the content of the poster but are grateful to Watermedias Medical (supported by Novo Nordisk) for writing assistance. Presented at the 57th Meeting of the European Society for Paediatric Endocrinology, Athens, Greece, 27–29 September 2018.

Methods

• Between 2005 and 2010, 291 children born SGA, treated with Norditropin® (somatropin), Novo Nordisk A/S, were included in a prospective, observational French registry which followed all patients treated with Norditropin® for this indication.
• All patients participated in follow-up until they reached FAH.
• The study is ongoing.
• Of the 90 patients who completed the study, 51 were GH-naïve and were stratified as good and poor responders according to observed FAH SDS ≥ −2, respectively.
• The criteria that were addressed and compared can be seen in Table 1.
• Analysis was descriptive. Student’s t-test was used to compare mean quantitative data (standard deviation [SD] p-value) and Wilcoxon’s test was used to establish 95% intervals for proportions of qualitative data.