Small for gestational age patients with premature treatment discontinuation: their journey in French, real-life settings

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Objective

This study examined the journey of patients born small for gestational age (SGA) who prematurely discontinued treatment with Norditropin® (somatropin; Novo Nordisk A/S) in a French, real-life cohort.

Introduction

• Premature discontinuation of growth hormone (GH) treatment by patients born SGA is usually linked to safety or ineffectiveness.
• However, this population has not been extensively studied compared to those patients who continue treatment until they reach final adult height (FAH).
• All patients participated in follow-up visits until they reached FAH.

Methods

• Between 2005 and 2010, 291 children born SGA, treated with Norditropin®, were included in a prospective, observational French registry which followed all patients treated with Norditropin® for this indication.

Results

• Of the 291 patients:
  - 183 were GH-naïve.
  - 96 patients reached FAH, including 51 who were GH-naïve (56.6%).
  - 69 patients discontinued prematurely, including 37 who were GH-naïve (53.6%).
  - 23 patients were lost to follow-up.
  - 109 patients are still being studied.
• Patients with premature treatment discontinuation represented 23.71% of the total population (N=291).
• Treatment discontinuation occurred mainly during the third and fourth year of treatment (33.3% and 27.5% of patients discontinuing, respectively).
• Mean (standard deviation [SD]) follow-up duration was 3.4 (1.7) years.
• Patient characteristics are shown in Table 1.
• A significant difference or positive trend was observed for the following characteristics (median values) in patients discontinued prematurely versus completers (Table 1):
  - Age at treatment initiation: p=0.0579.
  - Age at last visit: p=0.0001.
  - Treatment duration: p=0.0001.
• During the first year of follow-up, the change in height of patients with premature discontinuation was comparable to that of completers.

Table 1 • Patient characteristics: study completers and discontinuing patients

<table>
<thead>
<tr>
<th>Study completers (N=90)</th>
<th>Pts with premature tt discontinuation (N=69)</th>
<th>Discontinuing patients vs. study completers p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at tt initiation (years)</td>
<td>9.5 [5.4; 11.2]</td>
<td>6.5 [4.4; 10.9]</td>
</tr>
<tr>
<td>Dose at inclusion (mg/kg/d)</td>
<td>0.040 [0.034; 0.048]</td>
<td>0.043 [0.035; 0.055]</td>
</tr>
<tr>
<td>Pts with dose &gt;0.035±10%</td>
<td>53.4% (47/88)</td>
<td>60.7% (37/61)</td>
</tr>
<tr>
<td>T1 duration (years)</td>
<td>4.8 [3.7; 6.2]</td>
<td>3.0 [2.1; 3.9]</td>
</tr>
<tr>
<td>Duration of temporary tt discontinuation (years)</td>
<td>0.08 [0.04; 0.44]</td>
<td>0.32 [0.04; 1.00]</td>
</tr>
<tr>
<td>Pts with at least one tt discontinuation during the study (%)</td>
<td>20.0% (18/90)</td>
<td>27.5% (19/69)</td>
</tr>
<tr>
<td>Gain in height SDS between inclusion and T1 end</td>
<td>1.26 [0.77; 1.81]</td>
<td>1.12 [0.67; 1.68]</td>
</tr>
<tr>
<td>Height SDS at last visit</td>
<td>–1.6 [–2.2; –1.1]</td>
<td>–1.8 [–2.4; –1.3]</td>
</tr>
<tr>
<td>Patients with height SDS at last visit ≥2</td>
<td>65.6% (59/90)</td>
<td>62.3% (43/69)</td>
</tr>
<tr>
<td>Target height SDS</td>
<td>–1.2 [–1.7; –0.7]</td>
<td>–0.8 [–1.6; –0.1]</td>
</tr>
<tr>
<td>GH dose prescribed at the end of Pts (mg/kg/d)</td>
<td>0.039 [0.036; 0.041]</td>
<td>0.048 [0.031; 0.052]</td>
</tr>
<tr>
<td>Age at study end (years)</td>
<td>15.4 [14.4; 16.4]</td>
<td>15.1 [13.3; 15.2]</td>
</tr>
</tbody>
</table>

• A number of criteria were analysed, comparing patients who discontinued treatment prematurely with study completers (Table 1).
• Statistical analysis: Student’s t-test was used to compare mean quantitative data (standard deviation [SD] [p-value]) and Wilson’s test was used to establish 95% intervals for proportions of qualitative data.

Conclusions

• French, real-life data show that around one fifth of patients born SGA, treated with GH, stopped treatment prematurely and that the median time for discontinuation was the third year.
• The main reasons for stopping treatment prematurely were safety issues, poor adherence/treatment fatigue and satisfaction with attained height. An increased understanding of these reasons for premature treatment discontinuation is needed.
• The link between first year height gain and good long-term statural response should be investigated further.

Conflict of interest disclosures

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

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