Outcomes in growth hormone-treated Noonan syndrome children: impact of PTPN11 mutation status

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BACKGROUND & AIMS

- A higher prevalence of short stature is reported among Noonan syndrome (NS) patients with a PTPN11 mutation compared with NS patients with other mutations.1
- Norditropin® (somatropin; Novo Nordisk A/S) is approved for the treatment of short stature in children with NS.
- The effectiveness of growth hormone therapy (GHT) in treating short stature due to NS has previously been demonstrated, although data on the effect of PTPN11 mutation status on long-term GHT outcomes are discordant.1,2

Aim

- To assess the impact of PTPN11 mutation status on long-term effectiveness and safety outcomes in pre-pubertal NS patients receiving GHT.

RESULTS

- In total, 69 NS patients were included in the EAS: 49 patients (71%) were PTPN11-positive and 20 (29%) were PTPN11-negative.
- Baseline characteristics are shown in Table 1 and were similar between groups.

Table 1 Baseline characteristics (EAS, n=69)

<table>
<thead>
<tr>
<th>PTPN11+</th>
<th>PTPN11-</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>49</td>
</tr>
<tr>
<td>Mean (SD) age at GH start (years)</td>
<td>6.4 (3.3)</td>
</tr>
<tr>
<td>Mean (SD) baseline GH dose (mg/kg/day)</td>
<td>0.047 (0.015)</td>
</tr>
<tr>
<td>Mean (SD) HSDS (national reference)</td>
<td>-0.3 (0.8)</td>
</tr>
<tr>
<td>Mean (SD) HSDS (NS population)</td>
<td>-0.5 (0.8)</td>
</tr>
<tr>
<td>Mean (SD) BMI SDS</td>
<td>-0.6 (1.3)</td>
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</tbody>
</table>

- Growth outcomes
  - No statistically significant differences in HSDS and ΔHSDS over 4 years of GHT were observed between PTPN11+ and PTPN11- patients (Figures 1a and 1b).
  - The mean (standard deviation) ΔHSDS from baseline at 4 years was +1.3 (0.8) for PTPN11+ and +1.5 (0.7) for PTPN11- patients, based on general population reference data.
  - There were no significant differences between PTPN11+ and PTPN11- patients in the change in body mass index SD score from baseline (-0.02 vs -0.04, respectively).

- Safety
  - Of the SAS (n=113), 38 patients (33.6%) reported an adverse drug reaction or serious adverse event (SAE).
  - The most frequently reported events were headache (n=5 events reported in five patients) and arthralgia (n=3 events reported in three patients).
  - One SAE of atrial fibrillation was reported in a patient with a history of hypertrophic cardiomyopathy, although this was deemed unlikely related to GHT.

CONCLUSIONS

- After 4 years of GHT, growth outcomes were improved in GHT-naïve, pre-pubertal NS patients, irrespective of PTPN11 mutation status.
- Long-term safety data are reassuring regarding the safety of GHT in this population and are consistent with previous reports.3,4

REFERENCES


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