Growth hormone (GH) dosing patterns in children with isolated GH deficiency and multiple pituitary hormone deficiency enrolled in the NordiNet® International Outcome Study

Introduction
• Growth hormone deficiency (GHD) may be either isolated growth hormone deficiency (IGHD) or included in multiple pituitary hormone deficiency (MPHD) where levels of other pituitary hormones are also decreased or absent.
• Current treatment guidelines for patients with IGHD or MPHD recommend treatment with growth hormone (GH) at least until completion of linear growth.
• To guide treatment optimisation for patients with IGHD and MPHD, it is important to monitor GH treatment in clinical practice, where treatment and outcomes may vary from randomised controlled trials.
• Data from observational studies support the benefits of GH treatment; after 2 years, height gains in patients with IGHD or MPHD are similar and 75% achieve final height within their target height range.
• The NordiNet® International Outcome Study (IOS) captures data on patients treated with GH (Nordropthrop® somatropin, second generation GH, Novo Nordisk A/S, Denmark) in a real-life clinical setting and may help guide treatment optimisation.

 Aim and methods
• We investigated GH dosing patterns in children with IGHD and MPHD over a 7-year period, using data from the NordiNet® IOS (NCT00960128), a non-interventional study evaluating the long-term effectiveness and safety of Nordropthrop®.
• Average GH dose during the full treatment period and duration of GH treatment were calculated and categorised as low (0–25 μg/kg/day), medium (25–40 μg/kg/day) and high (>40 μg/kg/day). The proportions of patients with low, medium and high average GH dose were analysed, as were the proportions with a decrease or an increase of >10%, or no change in GH dose from baseline within the first and second year of treatment (as this is the time period during which doctors closely monitor growth and adverse events, and thus adjust the dose as needed).
• Descriptive statistics were applied on age, body mass index (BMI) standard deviation score (SDS), height SDS and insuline-like growth factor-1 (IGF-1) SDS for all patients and by diagnosis, gender, and dose group.
• Linear regression was performed to analyse the relationship between baseline height SDS or BMI SDS at treatment start and GH dose during the full treatment period.

Results
• Overall, data from 6297 patients were analysed, 5033 (66.4%) boys with IGHD and 794 (10.0%) boys with MPHD. Baseline demographics are shown in Table 1.
• At baseline, across both indications, boys were older and taller than girls. Furthermore, all patients with IGHD were younger and shorter, and had higher baseline IGF-1 SDS than patients with MPHD (Table 1).
• Average GH dose during the full treatment period was higher in patients with IGHD than MPHD, whilst average mean doses during the full treatment period were similar between boys and girls (Table 2).
• The majority (76.7%) of all patients were in the medium-dose group at baseline (Table 1). At baseline, the medium-dose group comprised over three-quarters (78.6%) of all patients with IGHD and almost two-thirds (63.6%) of all patients with MPHD. Of the remaining patients with IGHD, 11.2% were in the low-dose group and 10.2% were in the high-dose group. For MPHD these proportions were 28.3% and 8.1%, respectively.

Table 1. Baseline characteristics of boys and girls with IGHD and MPHD.

<table>
<thead>
<tr>
<th>Table 2. Mean doses (μg/kg/day) for boys and girls with IGHD and MPHD across the treatment period.</th>
<th>Boys</th>
<th>IGHD</th>
<th>Girls</th>
<th>IGHD</th>
<th>Boys</th>
<th>MPHD</th>
<th>Girls</th>
<th>MPHD</th>
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<tbody>
<tr>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Full treatment period</td>
<td>3055</td>
<td>31.9 (4.0)</td>
<td>1848</td>
<td>32.4 (4.6)</td>
<td>477</td>
<td>29.8 (5.0)</td>
<td>317</td>
<td>28.7 (6.4)</td>
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<td>Year 1</td>
<td>3000</td>
<td>31.3 (0.0)</td>
<td>1912</td>
<td>31.6 (7.2)</td>
<td>487</td>
<td>29.8 (5.1)</td>
<td>330</td>
<td>29.4 (4.6)</td>
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<tr>
<td>Year 2</td>
<td>3200</td>
<td>32.4 (0.0)</td>
<td>1619</td>
<td>32.9 (7.4)</td>
<td>415</td>
<td>33.0 (7.2)</td>
<td>289</td>
<td>30.5 (5.0)</td>
</tr>
<tr>
<td>Year 3</td>
<td>2655</td>
<td>32.5 (0.0)</td>
<td>1353</td>
<td>33.2 (7.8)</td>
<td>341</td>
<td>30.2 (7.3)</td>
<td>235</td>
<td>30.0 (7.2)</td>
</tr>
<tr>
<td>Year 4</td>
<td>2094</td>
<td>32.2 (7.0)</td>
<td>1073</td>
<td>33.0 (8.0)</td>
<td>279</td>
<td>29.9 (5.6)</td>
<td>181</td>
<td>29.0 (7.2)</td>
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<tr>
<td>Year 5</td>
<td>1994</td>
<td>31.8 (4.0)</td>
<td>749</td>
<td>32.4 (4.1)</td>
<td>210</td>
<td>29.9 (10.0)</td>
<td>145</td>
<td>27.4 (10.0)</td>
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<tr>
<td>Year 6</td>
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<td>31.4 (9.0)</td>
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<td>32.5 (7.8)</td>
<td>150</td>
<td>28.2 (8.9)</td>
<td>102</td>
<td>26.9 (10.1)</td>
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<tr>
<td>Year 7</td>
<td>804</td>
<td>31.1 (8.1)</td>
<td>359</td>
<td>31.9 (8.7)</td>
<td>107</td>
<td>27.9 (8.9)</td>
<td>84</td>
<td>27.2 (9.6)</td>
</tr>
</tbody>
</table>

Figure 1 Change in GH dose during first and second year of treatment in patients with IGHD and MPHD.

Figure 2 Mean (SD) GH dose by age, diagnosis and sex: a) boys with IGHD; b) girls with IGHD; c) boys with MPHD; d) girls with MPHD.

Conclusions
• Patients with MPHD received lower mean GH doses than patients with IGHD.
• Significant inverse correlations were observed between GH dose and baseline height SDS or BMI SDS in both cohorts of IGHD and MPHD patients.
• The majority of patients with IGHD or MPHD received a GH dose of 25–40 μg/kg/day during the analysis period.

References

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