Introduction

- Recombinant human GH was first approved in 1985 as a safe and effective treatment for short stature in patients with GH deficiency (GHD) and more recently in patients with Turner syndrome (TS) and early small for gestational age (SGA) babies.
- Despite a favourable safety profile, concerns have been raised over a potential link between GH therapy and increased morbidity and mortality.1-5
- NordiNet® IOS is a non-interventional study assessing the long-term effectiveness and safety of GH (norditropin®) treatment in everyday clinical practice.

Results

- Baseline demographic and clinical characteristics are displayed in Table 1.
- In this study, a total of 428 AEs were reported for 372 patients.
- The overall proportion of patients with one, two, or three or more AEs were 91.1% (n=339), 6.7% (n=25) and 2.2% (n=9), respectively. The proportions of patients with one, two or three or more AEs according to risk group are shown in Figure 1.
- Overall IRs were 3.74 events/1000 PYE for ADRs, 3.77 events/1000 PYE for SADRs, and 1.08 events/1000 PYE for SAEs.
- IRs of ADRs, SADRs and SAEs were significantly higher in the intermediate-risk and high-risk groups in comparison to the low-risk group (Figure 2).
- Following the first AE, 50.4% of all patients remained on the same GH dose; proportionally more patients in the low-risk group (56.8%) and intermediate-risk group (52.0%) than in the high-risk group (28.0%) remained on the same GH dose after the AE.
- The proportion of all patients discontinuing treatment after the first AE was 25.1% with proportionally more patients in the high-risk group (46.0%) than in the low-risk (17.3%) or intermediate-risk (25.5%) groups discontinuing after the AE.

SAEs of interest

- Neoplasms/malignancies were more frequent in the intermediate-risk (15 events reported in 13 of 5336 patients [0.2%]) and high-risk (24 events reported in 10 of 5336 patients [0.2%]) groups than in the low-risk group (three events, one event each in three of 10,164 patients [0.1%]).
- One cardiovascular event was reported in the low-risk group (in one of 10,164 patients [<0.1%]), eight cardiovascular events were reported in the intermediate-risk group (five cardiac events in three of 5336 patients [0.1%] and one vascular event in each of three 5336 patients [<0.1%]), and no cardiovascular events were reported in the high-risk group.
- The total number of reported nervous system disorders was 15 in the low-risk group (one event each in 10 of 16,104 patients [0.1%]), 37 in the intermediate-risk group (in 24 of 5336 patients [0.4%]), and 13 in the high-risk group (in 10 of 5336 patients [0.2%]).

Table 1. Baseline demographic and clinical characteristics by risk group.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Low-risk group</th>
<th>Intermediate-risk group</th>
<th>High-risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>10,164 (62.1)</td>
<td>6341 (62.4%)</td>
<td>3823 (37.6%)</td>
<td>5388 (52.6)</td>
</tr>
<tr>
<td>Sex, male/female, %</td>
<td>62.5/37.5</td>
<td>67.5/32.5</td>
<td>54.0/46.0</td>
<td>64.5/35.4</td>
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<tr>
<td>Mean age at treatment start, years (SD)</td>
<td>8.81 (3.66)</td>
<td>9.33 (3.77)</td>
<td>7.93 (3.28)</td>
<td>8.31 (2.25)</td>
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<tr>
<td>Mean height SDS at baseline (SD)</td>
<td>-2.59 (0.91)</td>
<td>-2.47 (0.92)</td>
<td>-2.79 (0.86)</td>
<td>-2.56 (1.29)</td>
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<tr>
<td>Mean duration of GH treatment, years (SD)</td>
<td>3.79 (2.81)</td>
<td>3.28 (2.81)</td>
<td>3.84 (2.82)</td>
<td>4.63 (3.24)</td>
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<tr>
<td>Mean GH dose until first event, µg/kg/day (SD)</td>
<td>34.98 (9.02)</td>
<td>32.46 (6.91)</td>
<td>39.8 (10.57)</td>
<td>33.75 (11.18)</td>
</tr>
</tbody>
</table>

Conclusions

- These results are consistent with previous reports from NordiNet® IOS and reconfirm the overall favourable safety profile of GH treatment.
- Patients in the intermediate-risk and high-risk groups seemed to be more likely to have a second AE than those in the low-risk group.
- A low proportion of patients with three or more AEs were reported across all risk groups.

Methods

- Safety data were analysed from 16,359 patients enrolled in NordiNet® IOS and treated with GH between 1998 and 2016.
- Patient diagnoses were based on physician’s decision and were classified according to Medical Dictionary for Regulatory Activities (MedDRA) preferred terms System Organ Class (SOC) classification. "Neoplasms benign, malignant and unspecified (incl cysts and polyps), nervous system disorders and cardiovascular disorders.

Statistical analyses

- Patient-years of exposure (PYE) were calculated from initiation of GH treatment to the end of GH treatment or patient’s final visit.
- Incidence rates (IRs) defined as number of events/1000 PYE for adverse drug reactions (ADRs), serious ADRs (SADRs), and serious AEs (SAEs) were calculated, and comparisons, according to risk group in relation to the low-risk group, were carried out using Poisson regression (log-linear model).
- The proportions of patients with one, two and three or more AEs were calculated.
- Incidence of AEs of interest are presented using descriptive statistics only.

References