Real-world data demonstrated a favourable safety profile of growth hormone treatment in patients with Noonan syndrome

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BACKGROUND & AIMS

• Growth hormone (GH) treatment improves height velocity and adult height in children with Noonan syndrome.1,2
• Noonan syndrome is commonly associated with cardiovascular (CV) anomalies, most commonly pulmonary stenosis and hypertrophic cardiomyopathy.3,4
• Concerns persist about the CV safety of GH treatment, despite data showing low rates of CV events and no change in left ventricular wall thickness.1,5
• This pooled analysis describes real-world evidence of the CV safety of GH treatment in patients with Noonan syndrome.

MATERIAL & METHODS

• Two non-interventional, multicentre studies (NordiNet® International Outcome Study (IOS) and ANSWER Program) evaluating long-term effectiveness and safety of Norditropin® (Novo Nordisk A/S, Denmark) as prescribed by treating physicians in the clinical setting across 24 countries.6
• Safety events were reported by treating physicians and included serious adverse events, serious adverse reactions (SARs; related to GH treatment) and non-serious adverse reactions (related to GH treatment).
• CV comorbidities reported at baseline and throughout the studies were also recorded.

RESULTS

Patient population and baseline characteristics

The safety analysis set (SAS) comprised 154 and 258 paediatric patients (naïve and non-naïve) with Noonan syndrome from the NordiNet® IOS and ANSWER Program (total n=412).

• Baseline characteristics were similar between patients in the SAS and those experiencing safety events (Table 1). An exception was height standard deviation score, which was lower in the latter group (p=0.322).

Table 1 Baseline characteristics

| SAS comprising No (n of patients) | Patients with safety events (n of patients) | Total n of patients (n of patients) | Total n of patients
|---|---|---|---|
| Female, % | 4 | 34 | 38 | 24.3%
| Age, years, mean (SD) | 404 | 404 | 404 | 404 |
| Height SDS,* mean (SD) | 371 | 371 | 742 | -1.22 (1.98) |
| Weight SDS,* mean (SD) | 368 | 368 | 736 | 0.040 (0.019) |
| Body mass index (BMI), mean (SD) | 22 | 22 | 44 | 22.7 (3.7) |
| Body mass index (BMI) SDS,* mean (SD) | 22 | 22 | 44 | 22.7 (3.7) |
| Bone age/chronological age, mean (SD) | 163 | 163 | 326 | 0.87 (0.10) |
| GH dose at baseline, µg/kg/d, mean (SD) | 162 | 162 | 324 | -1.13 (1.98) |
| GH dose at baseline, mean (SD) | 404 | 404 | 808 | -1.13 (1.98) |
| GH-naïve at baseline, % | 286 | 286 | 572 | 9.7 (4.1) |
| GH-naïve at baseline, mean (SD) | 412 | 412 | 824 | 21.5 (2.2) |
| Mean GH dose during study, µg/kg/d, mean (SD) | 412 | 412 | 824 | 21.5 (2.2) |

† Mean GH dose during study, µg/kg/d, <5 years, mean (SD) | 412 | 412 | 824 | 21.5 (2.2) |

 †Mean GH dose during study, µg/kg/d, ≥5 years, mean (SD) | 412 | 412 | 824 | 21.5 (2.2) |

Table 2 Summary of safety events

| Preferred term | NSAR (n of patients) | SAR (n of patients) | Total n of patients (n of patients) | Total n of patients
|---|---|---|---|---|
| Infections | 4 | 15 | 19 | 8.0%
| Bacterial | 2 | 2 | 4 | 1.6%
| Viral | 2 | 2 | 4 | 1.6%
| Gastrointestinal | 2 | 2 | 4 | 1.6%
| Cardiac | 1 | 2 | 3 | 1.2%
| Neurological | 1 | 1 | 2 | 0.8%
| Other* | 4 | 4 | 8 | 3.3%

GH treatment was well tolerated in patients with Noonan syndrome, including those with existing CV comorbidities and those receiving concomitant medications. Further studies are warranted to assess the CV safety of GH treatment in patients with Noonan syndrome.

CONCLUSIONS

• GH treatment is well tolerated in patients with Noonan syndrome, including those with existing CV comorbidities and those receiving concomitant medications.
• All CV complications were reported as comorbidities and may have been pre-existing at baseline.
• Further studies are warranted to assess the CV safety of GH treatment in patients with Noonan syndrome.