Growth hormone dosing patterns in short children born small for gestational age

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Introduction

- Short children born small for gestational age (SGA), defined as weight and/or length <–2 standard deviation (SD) below the mean for the gestational age, who fail to catch up in height by 2 years of age are at high risk of short stature in later life.[1]
- Growth hormone (GH) therapy is beneficial in the majority of short children born SGA, with long-term GH therapy allowing 85% to reach an adult height within the normal range (>–2 standard deviation score [SDS]) and 98% to reach an adult height within their target height range.[2]
- In Europe, GH is approved for short (height standard deviation score [SDS] <–2.5) children born SGA who fail to show catch-up growth by 4 years of age.[3] A dose of 35 µg/kg/day is usually recommended until final height is reached and if there is an inadequate response, re-evaluation is indicated, including consideration of compliance, GH dose and diagnosis.[4]
- GH dose has been evaluated as an important response factor in children born SGA.[2,5]

Methods

- We have investigated the patterns of GH dose used for the treatment of short children born SGA enrolled in NordiNet® International Outcome Study (IOS), a non-interventional study evaluating the long-term effectiveness and safety of Norditropin® in a real-life clinical setting.[6]
- GH dose at baseline and average dose during treatment year 1–4 and entire treatment period, and duration of GH treatment were calculated. Descriptive statistics were applied on age, height SDS and insulin-like growth factor I (IGF-I) SDS.
- The proportions of patients with low (<30 µg/kg/day), medium (30–50 µg/kg/day) and high (≥50 µg/kg/day) GH dose were analysed, as were the proportions with a GH dose decrease or increase of >10%, or no change (–10% to +10% of previous dose) from baseline dose within the first year of treatment.

Results

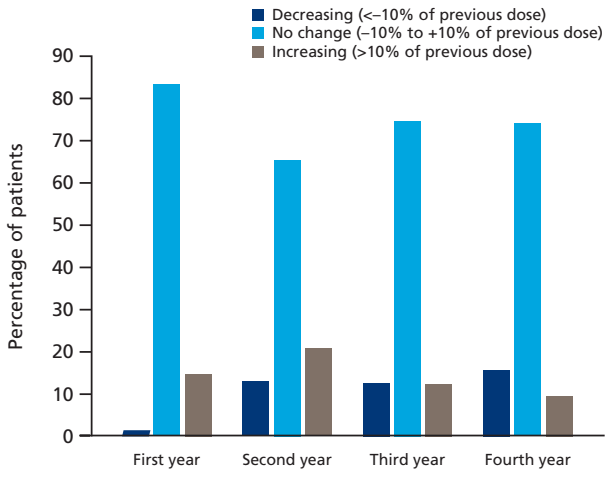
- Overall, 2652 children born SGA were analysed, of which 53.7% were male.
- Baseline demographics (mean [SD]) are provided in Table 1. Baseline demographics were similar between genders (Table 1).
- The majority (77.1%) of children born SGA evaluated were in the medium dose group (n=2044). Similar proportions of children born SGA were in the low (11.2%; n=296) and high (11.8%; n=312) dose groups.
- For the majority of children born SGA, GH dose did not change through 4 years of treatment (Figure 1).
- Within the first year of treatment, GH dose decreased for 1.7% and increased for 14.8% of patients, and did not change for 83.5% of patients. Results were similar in subsequent treatment years, with an increase in GH dose in 21.0%, 12.6% and 9.7% of patients in the second, third and fourth year of treatment, respectively (Figure 1).
- Baseline height SDS significantly correlated with GH dose (p<0.0001). Mean (SD) height SDS was –2.8 (1.0), –2.9 (0.8), and –3.1 (0.9) in the low, medium and high dose groups, respectively (Table 1).
- Baseline height SDS was lower in patients with increasing first year GH dose (–3.1±1.1) than for those with no change (–2.8 [0.8]; n=2061) (p=0.003) or decreasing (–2.3 [0.7]) dose (p=0.005) (Figure 2).

Table 1 Baseline demographics and patient characteristics. Data are mean (SD).

	Female (n=1229)	Male (n=1423)	All (n=2652)
Baseline demographics			
Age at treatment start (years)	7.7 (3.1)	7.9 (3.4)	7.8 (3.3)
Baseline height SDS	–2.9 (0.8)	–2.8 (0.8)	–2.9 (0.8)
Low dose, 25.8 (8.1) µg/kg/day (n=296)	–2.8 (0.8)	–2.8 (1.1)	–2.8 (1.0)
Medium dose, 37.3 (4.8) µg/kg/day (n=2044)	–2.9 (0.8)	–2.8 (0.8)	–2.9 (0.8)
High dose, 59.0 (9.4) µg/kg/day (n=312)	–3.2 (1.0)	–3.0 (0.8)	–3.1 (0.9)
Baseline IGF-I SDS	–0.8 (1.4)	–0.7 (1.7)	–0.7 (1.5)
Patient characteristics			
GH dose during treatment period (µg/kg/day)	38.8 (10.0)	38.4 (10.0)	38.6 (10.0)
GH dose (µg/kg/day)			
Baseline	37.6 (12.0)	37.7 (12.7)	37.6 (12.3)
Year 1	38.9 (11.3)	38.7 (12.0)	38.8 (11.7)
Year 2	40.5 (11.3)	39.7 (12.2)	40.1 (11.8)
Year 3	40.8 (11.4)	40.1 (12.1)	40.4 (11.8)
Year 4	40.3 (11.8)	39.4 (11.9)	39.8 (11.8)
Exposure time (years)	3.2 (2.3)	3.5 (2.5)	3.4 (2.4)

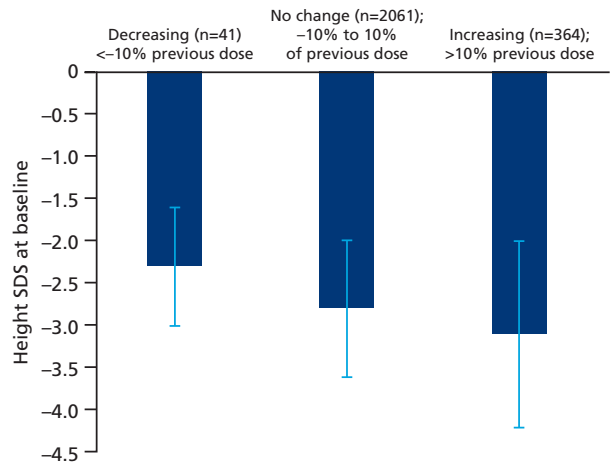
GH, growth hormone; IGF-I, insulin-like growth factor I; SDS, standard deviation score

Figure 1 Percentage of patients with decreasing, no change, or increase in GH dose by year of treatment.



GH, growth hormone

Figure 2 Baseline height SDS for patients by change in GH dose during first year of treatment.



GH, growth hormone; SDS, standard deviation score

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Conclusions

- Based on our analysis in 2652 short children born SGA enrolled in NordiNet® IOS, GH doses prescribed by clinicians tend to remain unchanged over time.
- During an average treatment period of 3.4 years, children with the lowest height SDS are more likely to receive GH in the higher dose range in everyday clinical practice. Also, GH dose is more likely to increase in children with the lowest height SDS.
- Further investigation is warranted in order to assess the impact of GH dose adjustment on treatment outcomes in short children born SGA.

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