Adult height of patients enrolled in PATRO Children, an ongoing observational study of the long-term safety and effectiveness of Omnitrope®

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Introduction

- Omnitrope® is a recombinant human growth hormone (rhGH, somatropin) approved by the European Medicines Agency in 2006, with approval granted on the basis that it matches the reference medicine (Genotropin®, Pfizer) in terms of safety, efficacy and quality.
- Replacement GH therapy stimulates linear growth and increases growth rate in children with growth hormone deficiency (GHD).[1]
- rhGH therapy is also approved for paediatric use in other indications, such as children with Turner Syndrome (TS) and Prader-Willi Syndrome (PWS), short children born small for gestational age (SGA), and children with chronic renal insufficiency (CRI).[1] GH therapy is also approved for the treatment of idiopathic short stature (ISS) in the United States, Canada and Brazil.
- The PAtients TReated with Omnitrope (PATRO) children study is an ongoing, long-term, post-marketing surveillance programme for Omnitrope®.

Objectives

- The main objective of PATRO Children is to assess the long-term safety of rhGH, particularly in terms of diabetogenic potential and risk of malignancies (and all potential risks in PWS patients).
- The effect of rhGH treatment on growth and adult height (AH) is assessed as a secondary objective of the study.
- Here we present data on AH achievement as of January 2019.

Methods

- PATRO Children is an international, longitudinal, non-interventional study, conducted in hospitals and specialised endocrinology clinics across 14 different countries.[2]
- The study population includes infants, children and adolescents receiving Omnitrope® therapy according to country-specific prescribing information.

Table 1. Patient characteristics (effectiveness population)

Characteristic	N (%)
All patients	5777 (100.0)
Male	3418 (59.2)
Female	2359 (40.8)
rhGH-näive	4912 (85.0)
Pre-treated	861 (14.9)
Missing	4
GHD patients	3482 (60.3)
Male	2348 (67.4)
Female	1134 (32.6)
rhGH-näive	2966 (85.2)
Pre-treated	513 (14.7)
Missing	3
SGA patients	1570 (27.2)
Male	834 (53.1)
Female	736 (46.9)
rhGH-näive	1353 (86.2)
Pre-treated	216 (13.8)
Missing	1
TS patients	285 (4.9)
Male	–
Female	285 (100.0)
rhGH-näive	228 (80.0)
Pre-treated	57 (20.0)
PWS patients	201 (3.5)
Male	95 (47.3)
Female	106 (52.7)
rhGH-näive	167 (83.1)
Pre-treated	34 (16.9)
ISS patients	185 (3.2)
Male	106 (57.3)
Female	79 (42.7)
rhGH-näive	152 (82.2)
Pre-treated	33 (17.8)
CRI patients	54 (0.9)
Male	35 (64.8)
Female	19 (35.2)
rhGH-näive	46 (85.2)
Pre-treated	8 (14.8)

CRI, chronic renal insufficiency; GHD, growth hormone deficiency; ISS, idiopathic short stature; PWS, Prader-Willi syndrome; rhGH, recombinant human growth hormone; SGA, small for gestational age; TS, Turner syndrome

- Auxological data may be recorded at each visit. Height velocity (HV, cm/year), height standard deviation score (HSDS), and HVSDS are derived from height measurements and country-specific reference tables.
- It is anticipated that patients will be treated with Omnitrope® until they achieve AH. Patients are considered to have reached AH if they discontinue the study due to reaching AH/bone age maturity, or reaching near AH according to the opinion of their treating physician.

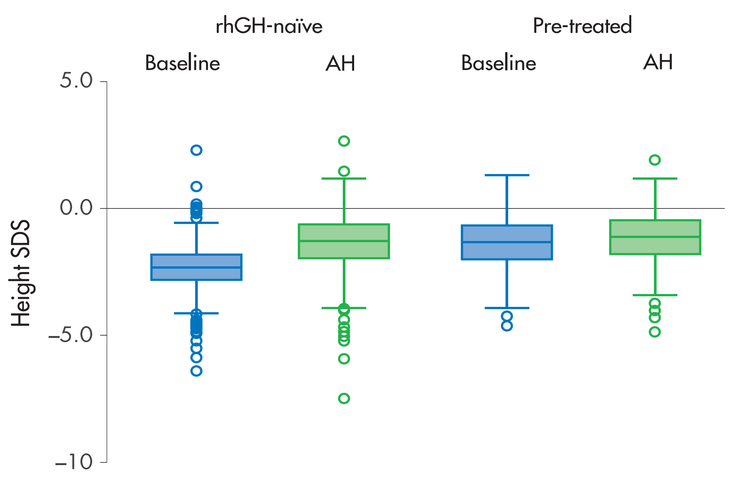
Results

- As of January 2019 (approximately 13 years since the study start), 5777 patients were enrolled in the study and included in the effectiveness population (all patients with a documented height measurement at the start of Omnitrope® treatment and at least one measurement of height during Omnitrope® treatment) [Table 1].
- Overall, 4912 patients (85.0%) were rhGH-naïve at study entry and 861 (14.9%) had previously received rhGH treatment.
- To date, 1209 patients (20.9%) (male, n=626; female, n=583) have reached AH according to the opinion of their treating physician. Of these, 925 patients (76.5%) were rhGH-naïve at study entry and 283 (23.4%) were not.
- Of the patients who reached AH, 772 (63.9%) had GHD, and 309 (25.6%) were born SGA.

GHD patients

- Among GHD patients who reached AH, 479 (62.0%) were male and 293 (38.0%) were female.
- Mean (SD) Omnitrope® treatment duration in the study was 4.1 (1.9) years and 3.3 (2.0) years in rhGH-naïve (n=614) and pre-treated (n=157) GHD patients, respectively.
- In rhGH-naïve patients, mean (SD) baseline HSDS was −2.34 (0.88); at AH, mean (SD) HSDS was −1.32 (1.10)]. In pre-treated patients, mean (SD) baseline HSDS was −1.29 (1.11); at AH, mean (SD) HSDS was −1.16 (1.07) [Figure 1].

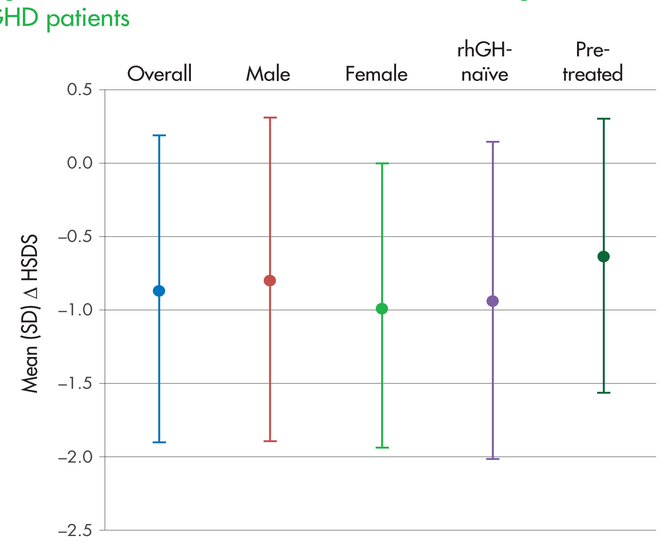
Figure 1. HSDS at baseline and adult height in rhGH-naïve and pre-treated GHD patients



AH, adult height; GHD, growth hormone deficiency; HSDS, height standard deviation score; rhGH, recombinant human growth hormone; SD, standard deviation

- Mean (SD) HSDS at AH was −0.99 (1.14) in GHD patients with multiple pituitary hormone deficiencies (n=64), −1.30 (1.09) in patients with isolated GHD (n=635), and −1.40 (0.99) in GHD patients with neurosecretory dysfunction (n=45).
- Mean (SD) HSDS at AH was −1.30 (1.06) in patients who were pubertal at baseline (n=278) and −1.27 (1.11) in patients who were pre-pubertal (n=476).
- The mean (SD) difference in AH achieved and estimated target height was −4.55 (7.20) cm.
- Figure 2 shows the difference between AH SDS and target height SDS for different categories of GHD patients.

Figure 2. Difference between adult HSDS and target HSDS in GHD patients

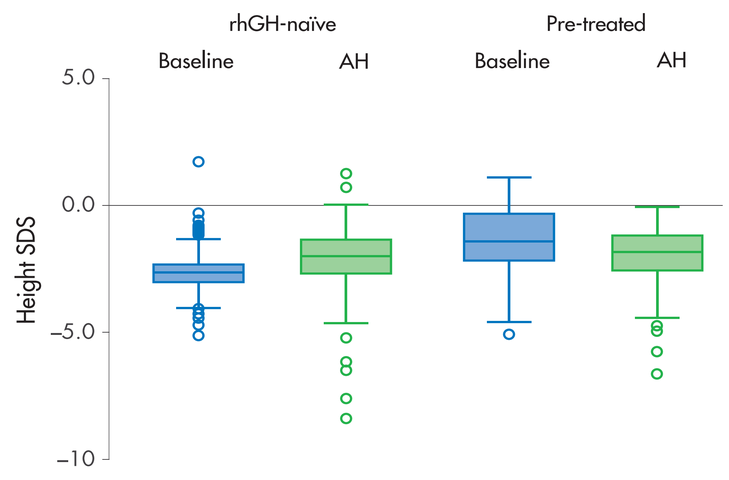


GHD, growth hormone deficiency; HSDS, height standard deviation score; rhGH, recombinant human growth hormone; SD, standard deviation

SGA patients

- In SGA patients who reached AH, 123 (39.8%) were male and 186 (60.2%) were female.
- Mean (SD) Omnitrope® treatment duration in the study was 4.4 (2.1) years and 3.6 (2.0) years in rhGH-naïve (n=291) and pre-treated (n=90) SGA patients, respectively.
- In rhGH-naïve patients, mean (SD) baseline HSDS was −2.63 (0.82); at AH, mean (SD) HSDS was −2.08 (1.20). In pre-treated patients, mean (SD) baseline HSDS was −1.37 (1.23); at AH, mean (SD) HSDS was −2.04 (1.19) [Figure 3].

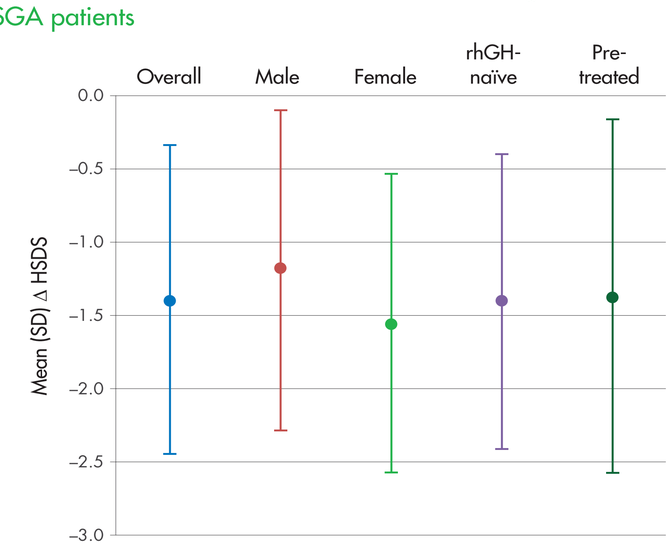
Figure 3. HSDS at baseline and adult height in rhGH-naïve and pre-treated SGA patients



AH, adult height; HSDS, height standard deviation score; rhGH, recombinant human growth hormone; SD, standard deviation; SGA, small for gestational age

- Mean (SD) HSDS at AH was −2.17 (1.34) in patients who were pubertal at baseline (n=107) and −2.02 (1.11) in patients who were pre-pubertal (n=199).
- The mean (SD) difference in AH achieved and estimated target height was −6.82 (6.97) cm.
- The mean (SD) difference between AH SDS and target height SDS for different categories of SGA patients are shown in Figure 4.

Figure 4. Difference between adult HSDS and target HSDS in SGA patients



HSDS, height standard deviation score; rhGH, recombinant human growth hormone; SD, standard deviation; SGA, small for gestational age

Conclusions

- Based on this analysis, Omnitrope® treatment improves AH of rh-GH naïve children with GHD and SGA in real-life clinical practice.
- PATRO Children is an ongoing study, and will continue to provide further long-term data on AH with Omnitrope® treatment in these and other approved indications.

References

1. European Medicines Agency. Omnitrope® Summary of Product Characteristics. Available from: www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000607/WC500043695.pdf.
2. Pfäffle R, Schwab KO, Marginean O, et al. Design of, and first data from, PATRO Children, a multicentre, noninterventional study of the long-term efficacy and safety of Omnitrope® in children requiring growth hormone treatment. *Ther Adv Endocrinol Metab* 2013; 4: 3–11.

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