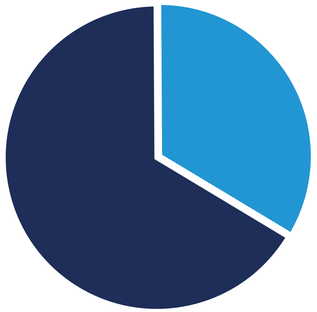
P1-132

Growth hormone treatment was effective in most children with short stature born small for gestational age and no safety concerns were identified.

66%

Achieved height standard deviation score within normal range by the last study visit



34%

Did not achieve height standard deviation score within normal range by the last study visit

Use of growth hormone therapy in short patients born small for gestational age: data from real-life French clinical practice

Régis Coutant,[1] Bruno Leheup,[2] Marc Nicolino,[3] Jean-Pierre Salles[4]

[1]University Hospital Angers, Angers, France; [2]Medical School and University Hospital of the University of Lorraine, Nancy, France; [3]Lyon University Pediatric Hospital, Lyon, France; [4]Children's Hospital, Toulouse University Hospital, Toulouse, France

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BACKGROUND & AIMS

- In France, prescription of growth hormone (GH) therapy is subject to exception drug status,[1] as data on final height and tolerability of long-term exposure to GH are lacking.
- A national registry monitoring the long-term exposure to supraphysiological doses of GH in children born small for gestational age (SGA) was created to address this absence of data and, in turn, improve quality and safety of care for children born SGA.

MATERIAL & METHODS

- The registry data were collected as an observational, non-interventional, longitudinal study (ClinicalTrials.gov, NCT01578135) (**Figure 1**).

Figure 1 Methods and endpoints

GH-naïve and non-naïve SGA children

126 sites in France

Inclusion period was between 2005 and 2010, with follow-up until 2018, or until final adult height*

Primary endpoints:
- Proportion of patients with normal HSDS (>–2) at last visit and with normal final adult HSDS at last visit.

Secondary endpoints:
- Change from baseline in height and HSDS.
- Factors associated with normal HSDS at last visit.†
- Safety endpoints (frequency of AEs and AEs of special interest).

* †Determined by the investigator as height velocity <2 cm/year; or bone age >14 years for girls and >16 years for boys.
†Analysed by multivariate logistic regression analysis with stepwise elimination.
AE, adverse event; GH, growth hormone; HSDS, height standard deviation score; SGA, small for gestational age.

RESULTS

Baseline characteristics

- Of the 1406 registered patients, every fifth child was randomly selected for the long-term follow-up as a representative subpopulation (n=291), for efficacy and safety analyses. The baseline characteristics between these two groups were similar (**Table 1**).

Table 1 Baseline characteristics

Variable	Registered patients, n=1406	Randomly selected subpopulation, n=291
Male/female, n (%)	726 (51.6)/680 (48.4)	157 (54.0)/134 (46.0)
Age at study inclusion, years, mean (SD), [min; max]	8.79 (3.53), [1.46; 18.37]	8.08 (3.32), [1.74; 16.80]
HSDS, mean (SD)	–2.55 (0.95)	–3.07 (0.86)

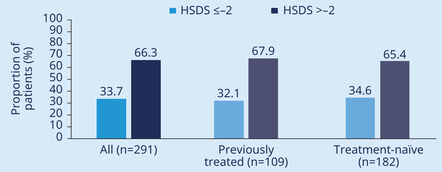
HSDS, height standard deviation score; SD, standard deviation.

RESULTS

Effectiveness

- Normal height standard deviation score (HSDS) was reached by 66.3% of patients at last visit. The proportion of patients reaching normal HSDS was similar between previously treated and treatment-naïve patients (**Figure 2**).
  - Among the 24.7% of patients who achieved final adult height at last visit, 66.7% reached normal HSDS.

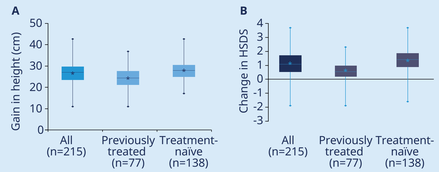
Figure 2 Proportion of patients reaching normal HSDS at last visit*



*Defined as the time at which they had reached adult height or treatment was interrupted/discontinued. HSDS, height standard deviation score.

- Median (interquartile range) change from baseline in height and HSDS was 27.0 (23.5; 29.7) cm and 1.10 (0.54; 1.71), respectively (**Figure 3**).

Figure 3 Median (Q1; Q3) change in height (A) and HSDS (B) from inclusion to visit 5†



†After visit 5, there were small numbers of patients and therefore these data are not shown. The time point of visit 5 is specific to each patient and took place approximately 54 months after treatment initiation.
Data shown are median, Q1 (the middle number between the smallest value and the median), Q3 (the middle number between the highest value and the median) range, and mean HSDS, height standard deviation score; Q, quartile; *, mean.

- Four factors were significantly associated with achieving normal HSDS (**Table 2**).

Table 2 Factors associated with achieving normal HSDS

	OR	95% CI	*P*-value
HSDS at treatment initiation (taller better)	5.65	3.22; 9.92	<0.0001
Age at treatment initiation (younger better)	0.88	0.79; 0.98	0.0166
Treatment duration* (longer better)	1.20	1.04; 1.38	0.0116
Presence of chronic disease (absence better)	0.43	0.21; 0.87	0.0188

*Excluding periods of discontinuation.
OR >1 means associated with greater odds of outcome. OR = 1 means there is no association. OR <1 means associated with lower odds of outcome.
CI, confidence interval; HSDS, height standard deviation score; OR, odds ratio.

Safety

- There were 287 adverse events (AEs) reported in 149 (51.2%) patients (**Table 3**).

Table 3 Proportions of patients who reported different types of AEs

Type of AEs	n (%) of patients
Non-serious AEs	201 (70.0)
AEs considered possibly/probably related to GH treatment	112 (39.1)
SAEs considered possibly/probably related to GH treatment	6 (7.0)

AE, adverse event; GH, growth hormone; SAE, serious adverse event.

- The most frequent AEs were increased insulin-like growth factor I (IGF-I; 17.2%) headache (9.3%), and arthralgia (4.5%), with most (n=71/100) of these events reported in treatment-naïve patients.
- Sixteen (5.5%) of the 291 patients discontinued treatment prematurely, most commonly due to increased IGF-I (n=4).
- Five AEs of special interest were reported, none of which were considered related to GH treatment.
  - Two tumours or tumour-like lesions:
    - Malignant nephroblastoma with a fatal outcome.
    - Benign renal cyst.
  - Two cardiovascular events:
    - Left ventricular hypertrophy.
    - Tricuspid valve incompetence.
  - One cerebrovascular event:
    - Ventriculo-cardiac shunt due to hydrocephalus.

CONCLUSIONS

- GH therapy was effective in most short children born SGA.
- No new safety concerns were observed with use of GH therapy.
- The likelihood of achieving normal HSDS with GH therapy increased with greater baseline HSDS, younger age at start of treatment, longer duration of GH treatment and absence of a chronic disease; reinforcing the importance of early identification and treatment of short patients born SGA.

REFERENCES

1. Haute Autorité de Santé. Transparency Committee Summary (Norditropin). October 2020. www.has-sante.fr/upload/docs/application/pdf/2021-03/norditropine_07102020_summary_ct18683.pdf.

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