P3-P200

Small for gestational age patients with premature treatment discontinuation: their journey in French, real-life settings

Jean-Pierre Salles;[1] Régis Coutant;[2] Bruno Leheup;[3] Marc Nicolino;[4] Evguenia Hacques;[5] Béatrice Villette[5]

[1]Hôpital des Enfants, CHU, Toulouse, France; [2]CHU, Angers, France; [3]CHRU, Université de Lorrainé, Nancy, France; [4]Hôpital Mère-Enfant, Groupement Hospitalier Est, Lyon, France; [5]Novo Nordisk, La Défense, France

Objective

This study examined the journey of patients born small for gestational age (SGA) who prematurely discontinued treatment with Norditropin® (somatropin; Novo Nordisk A/S) in a French, real-life cohort.

Introduction

- Premature discontinuation of growth hormone (GH) treatment by patients born SGA is usually linked to safety or ineffectiveness.
- However, this population has not been extensively studied compared to those patients who continue treatment until they reach final adult height (FAH).

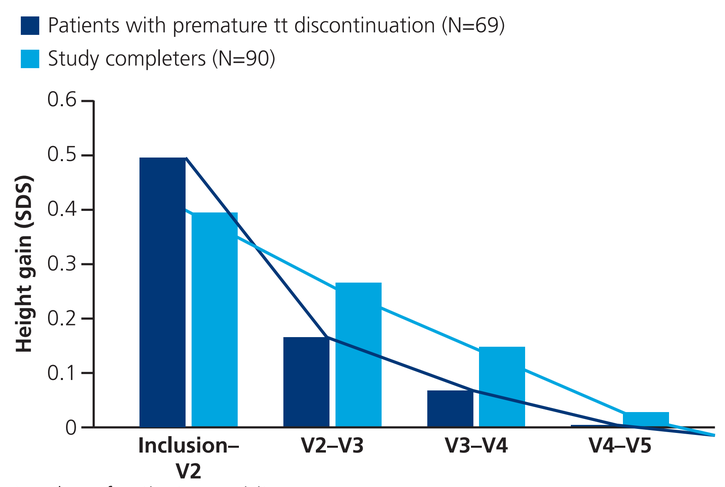
Methods

- Between 2005 and 2010, 291 children born SGA, treated with Norditropin®, were included in a prospective, observational French registry which followed all patients treated with Norditropin® for this indication.
- All patients participated in follow-up visits until they reached FAH.
- A number of criteria were analysed, comparing patients who discontinued treatment prematurely with study completers (**Table 1**).
- Statistical analysis: Student's t-test was used to compare mean quantitative data (standard deviation [SD]) (*p*-value) and Wilson's test was used to establish 95% intervals for proportions of qualitative data.

Results

- Of the 291 patients:
  - 183 were GH-naïve.
  - 90 patients reached FAH, including 51 who were GH-naïve (56.6%).
  - 69 patients discontinued prematurely, including 37 who were GH-naïve (53.6%).
  - 23 patients were lost to follow-up.
  - 109 patients are still being studied.
  - Patients with premature treatment discontinuation represented 23.71% of the total population (N=291).
  - Treatment discontinuation occurred mainly during the third and fourth year of treatment (33.3% and 27.5% of patients discontinuing, respectively).
  - Mean (standard deviation [SD]) follow-up duration was 3.4 (1.7) years.
- Patient characteristics are shown in **Table 1**.
- A significant difference or positive trend was observed for the following characteristics (median values) in patients discontinued prematurely versus completers (**Table 1**):
  - Age at treatment initiation: *p*=0.0579.
  - Age at last visit: *p*=<0.0001.
  - Treatment duration: *p*=<0.0001.
- During the first year of follow-up, the change in height of patients with premature discontinuation was comparable to that of completers.
- During the second year of treatment, growth slowed considerably and continued to decline during follow-up.
- During the fourth year of treatment, 42% of the patients who subsequently stopped treatment early remained on treatment versus 83% of study completers.
- **Figure 1** shows the annual height gain from the beginning of treatment up to visit 5 (fourth year of follow-up) in patients who discontinued prematurely and study completers.
- Height standard deviation score at last visit was –1.6 [–2.2; –1.1] for study completers and –1.8 [–2.4; –1.3] for patients who discontinued treatment (*p*=0.1252).
- The most common reasons for premature treatment discontinuation were related to:
  - Safety (adverse event or doubts about the safety of GH treatment): 13 cases. The adverse events that caused premature treatment discontinuation were non-serious.
  - Poor adherence or treatment fatigue: nine cases.
  - Eight subjects stopped treatment because they were satisfied with the stature they had attained.

Figure 1 ♦ Height gain (SDS) between each follow-up visit



SDS, standard deviation score; tt, treatment; V, visit.

Conclusions

- French, real-life data show that around one fifth of patients born SGA, treated with GH, stopped treatment prematurely and that the median time for discontinuation was the third year.
- The main reasons for stopping treatment prematurely were safety issues, poor adherence/ treatment fatigue and satisfaction with attained height. An increased understanding of these reasons for premature treatment discontinuation is needed.
- The link between first year height gain and good long-term statural response should be investigated further.

Table 1 ♦ Patient characteristics: study completers and discontinuing patients

	Study completers (N=90)	*Pts with premature tt discontinuation (N=69)*	*Discontinuing patients vs. study completers p-value*
Age at tt initiation (years)	9.5 [5.4; 11.2]	6.5 [4.4; 10.9]	0.0579
Dose at inclusion (mg/kg/d)	0.040 [0.034; 0.048]	0.043 [0.035; 0.055]	0.6243
Pts with dose >0.035±10%	53.4% (47/88)	60.7% (37/61)	0.3804
Tt duration (years)	4.8 [3.7; 6.2]	3.0 [2.1; 3.9]	0.0001
Duration of temporary tt discontinuation (years)	0.08 [0.04; 0.44]	0.32 [0.04; 1.00]	0.1489
Pts with at least one tt discontinuation during the study (%)	20.0% (18/90)	27.5% (19/69)	0.2650
Gain in height SDS between inclusion and tt end	1.26 [0.77; 1.81]	1.12 [0.67; 1.68]	0.4389
Height SDS at last visit	–1.6 [–2.2; –1.1]	–1.8 [–2.4; –1.3]	0.1252
Patients with height SDS at last visit >–2	65.6% (59/90)	62.3% (43/69)	0.6732
Target height SDS	–1.2 [–1.7; –0.7]	–0.8 [–1.6; –0.1]	0.1002
GH dose prescribed at the end of FU (mg/kg/d)	0.039 [0.036; 0.041]	0.044 [0.031; 0.052]	0.4562
Age at study end (years)	15.4 [14.4; 16.4]	13.1 [9.3; 15.2]	<0.0001

Values are shown as median [Q1; Q3] unless otherwise stated.
FU, follow-up; GH, growth hormone; Pts, patients; SDS, standard deviation score; tt, treatment; Q, quartile.

Conflict of interest disclosures

JPS, RC, BL and MN are members of the Scientific Committee of, and investigators for, the SGA Registry; EH and BV are employees of Novo Nordisk.

This study was supported by Novo Nordisk and is registered at ClinicalTrials.gov (NCT01578135). The authors thank the investigators and patients participating in this study. The authors take full responsibility for the content of the poster but are grateful to Watermeadow Medical (supported by Novo Nordisk) for writing assistance.
Presented at the 57th Meeting of the European Society for Paediatric Endocrinology, Athens, Greece, 27–29 September 2018.