Spanish ECOS Study Analysis: Socioeconomic Data, Adherence and Growth Outcomes with Case Studies

Maria Dolores Rodríguez-Arnao,[1] Amparo Rodríguez Sánchez,[1] Ignacio Díez López,[2] Joaquín Ramírez Fernández,[3] Jose Antonio Bermúdez de la Vega,[4] Virginia Ballano,[5] Jenny Alvarez Nieto,[6] Ekaterina Koledova,[7] on behalf of the ECOS/Spain investigator group

[1]Pediatric Endocrinology Unit, Pediatric Service, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]Pediatric Endocrinology Unit, Pediatric Service, Hospital Universitario Araba, Araba/Alava, Spain; [3]Pediatric Endocrinology Unit, Pediatric Service, Hospital Universitario Príncipe de Asturias, Madrid, Spain; [4]Pediatric Endocrinology, Centro Nuevas Tecnologias, Sevilla, Spain; [5]Regional Clinical Operations, Merck, Madrid, Spain; [6]Medical Affairs, Merck, Madrid, Spain; [7]Global Medical, Safety & CMO, Merck KGaA, Darmstadt, Germany

INTRODUCTION

- The ECOS observational study in Spain (NCT01376921) aims to evaluate adherence to recombinant human growth hormone (r-hGH) therapy prescribed via the easypod™ electromechanical auto-injector device.

- The easypod™ device administers pre-set doses of Saizen® r-hGH and stores accurate records of each dose and injection taken, which can then be shared with healthcare providers for the evaluation of adherence.[1]

- Although the easypod™ device makes the administration of r-hGH easier and more comfortable for the patient,[2] other factors can affect adherence, leading to poor outcomes with respect to height velocity and final height. These factors include family socioeconomic status, education level and support, and treatment duration.[3,4,5]

OBJECTIVES

- To assess the use and acceptability of easypod™ and adherence to r-hGH therapy.
- To assess the overall socioeconomic background of caregivers responsible for administering injections.
- To highlight differences in individual patient's dosing patterns.

METHODS

- Adherence was determined categorically and also as the percentage adherence over time, defined as the number of days with injections received divided by the number of days with injections planned.
- Accurate individual adherence data were transcribed directly from a patient's easypod™, whereas socioeconomic, demographic, auxological and diagnostic data were obtained from medical notes.

RESULTS

Patient Demographics

- The Spanish cohort consisted of 280 children, of whom 240 were included in the final analysis set (52% male) (**Table 1**).

Table 1. Demographic Data Full Analysis Set (n=240)

| Characteristics	
Age at inclusion into study (years)	9.0 (8.6, 9.4)
Gender	Male 125 (52%)
Ethnicity	Caucasian 225 (93.75%) African 1 (0.42%) Asian 3 (1.25%) Other 8 (3.35) Missing 3 (1.25%)
Height before r-hGH treatment (cm)	111.6 (109.4, 113.9)
Growth velocity before r-hGH treatment (cm/year)	4.5 (4.2, 4.7)
Treatment only with Saizen easypod™	Yes 234 (97.5%) No 2 (0.83%) Missing 4 (1.67%)
Parent marital status at baseline	Married/cohabiting 191 (79.58%) Separated/divorced 11 (4.58%) Single 2 (0.83%) Widowed 5 (2.8%) Not known/missing 31 (12.92%)
Employment status at baseline – Father/legal guardian	Employed 185 (77.08%) Home maker 0 (0.00%) Unemployed 9 (3.75%) Other 2 (0.83%) Not known 37 (15.42%) Missing 7 (2.92%)
Employment status at baseline – Mother	Employed 151 (62.92%) Home maker 30 (12.50%) Unemployed 17 (7.08%) Not known 39 (16.25%) Missing 3 (1.25%)
Educational status of person performing majority of injections	University degree 75 (31.25%) Primary education 84 (35.00%) Other 23 (9.58%) Not known 53 (22.08%) Missing 5 (2.08%)

Data are n(%) or mean (95% confidence interval)

- The majority of patients were Caucasian (93.8%), with a diagnosis of growth hormone deficiency (GHD, 60.0%), small for gestational age (SGA, 35.8%), Turner Syndrome (TS, 3.3%) or chronic renal failure (CRF, 0.83%).

- Despite high overall adherence (median 98.8%, mean 94.5% [95% confidence interval (CI) 92.8, 96.3]), growth responses varied and patterns of missed doses proved highly individual and, in some cases, fluctuated over time, possibly reflecting changes in caregiver or other life circumstances.

- Almost 80% of injection-giving carers were employed, while 31.0% had degree level education, 35.0% had only had school level education, 9.5% had 'other' education and for 22% this was not recorded.

Case Studies in Dosing Behaviour

- Because the cohort data shown above are not sufficiently granular to probe the relationship between adherence and patient growth, representative cases were solicited from Spanish ECOS Investigators.

- **Case study 1 (04 003)**
  – Male diagnosed with GHD
  – Age at start of treatment: 5 years 2 months
  – Duration of study treatment: 4 years 11 months
  – Tanner stage 1 throughout period of study
  – Adherence: >90% during the first year of treatment, rising to >95% from 2 years
  – The main documented reasons for the missed doses up to 4 years after starting treatment were forgetting to take the injection, nights away from home and technical problems with easypod™
  – During year 5, the patient had a physician-sanctioned temporary cessation of treatment ≥1 week
  – Speed of growth was as expected: height increased from the 10th percentile to the 50th percentile for age (**Figure 1**)
  – This patient developed puberty after the study period, and was taking gonadotropin-releasing hormone analogs as of November, 2015.

Figure 1. Patient Growth (04 003) During Study Compared With Height-for-age Percentiles

10th, 50th and 90th percentiles from Boys – Growth (Stature) – CDC, 2–20 years.
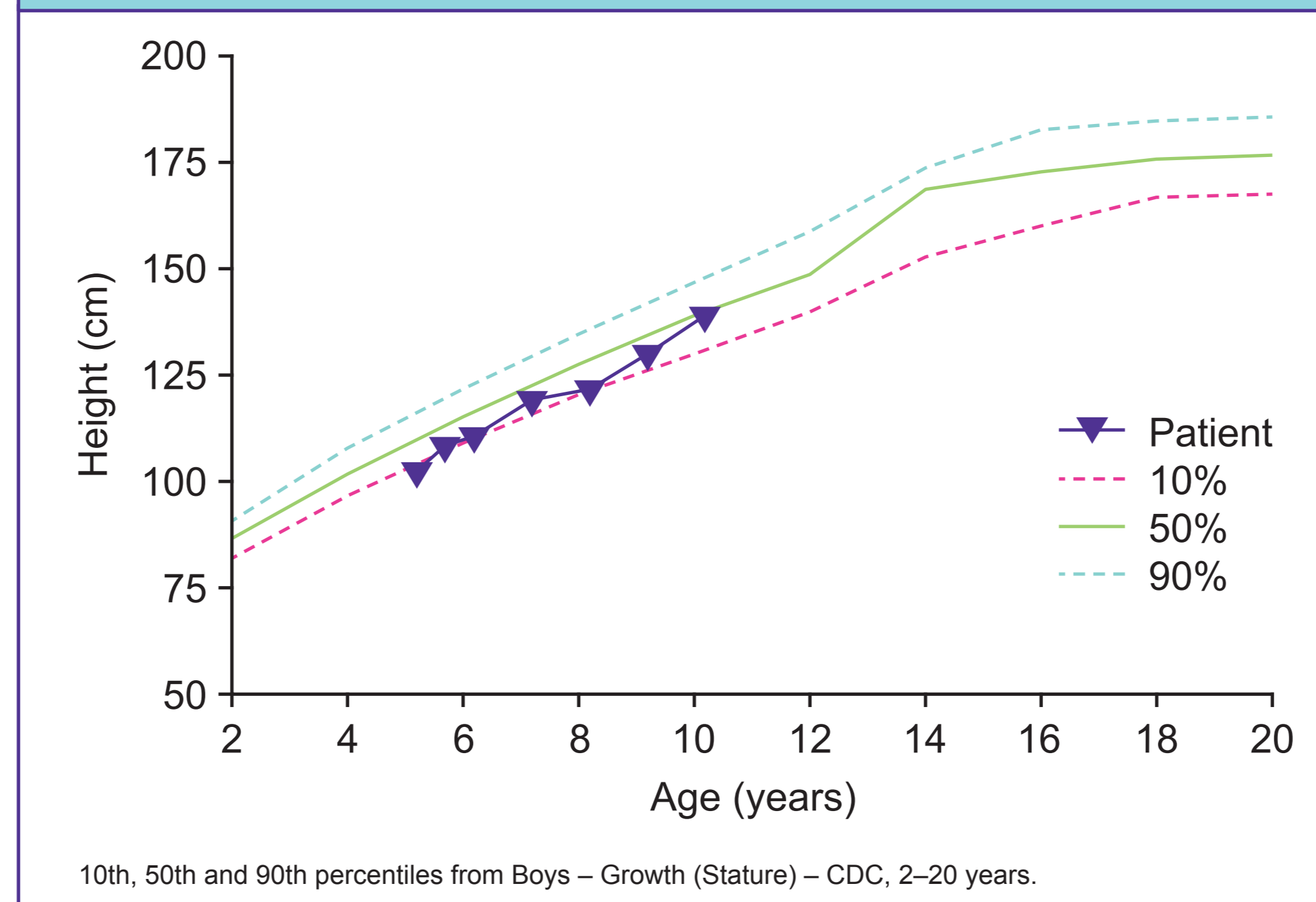
- **Case study 2 (39 006)**
  – Male diagnosed with GHD
  – Age at start of treatment: 4 years 6 months
  – Duration of study treatment: 4 years 8 months
  – Tanner stage 1 throughout the study
  – Adherence was >95% up to 3 years and >90% during years 4 and 5
  – The main documented reason for the missed doses during years 2–5 were nights away from home and technical problems with easypod™
  – During years 4 and 5, the patient had a physician sanctioned temporary cessation of treatment ≥1 week
  – The patient's height increased but did not rise above the 10th percentile for age during the study (**Figure 2**)
  – Growth velocity was as expected during years 1 and 2, but slowed from the third year of treatment
 – His final height is expected to be close to the target height

Figure 2. Patient Growth (39 006) During Study Compared With Height-for-age Percentiles

10th, 50th and 90th percentiles from Boys – Growth (Stature) – CDC, 2–20 years.
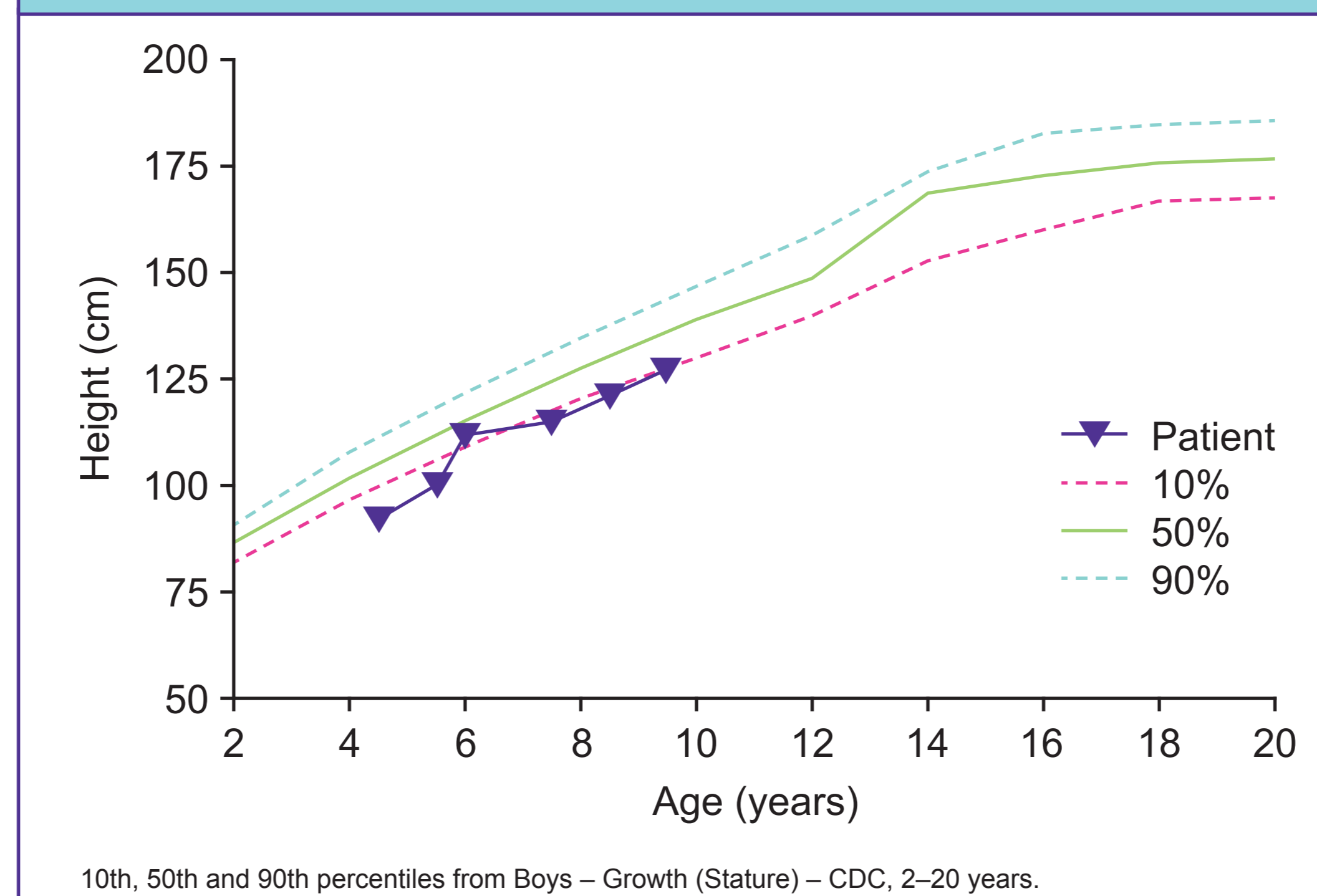
- **Case study 3 (45 003)**
  – Female diagnosed with SGA
  – Age at start of treatment: 7 years 3 months
  – Duration of study treatment: 4 years 2 months
  – Tanner stage 1 up to 3 years of treatment; Tanner stage 2 at 4 years
  – Adherence was >98% throughout the study period
  – The main documented reason for missed doses was forgetting to take the injection
  – The patient's height increased but did not rise above the 10th percentile for age during the study (**Figure 3**)
  – This patient had a moderate response to growth hormone treatment, with acceptable speed of growth in the first year, followed by a fall in the second year, and further increases
  – She presented with rapidly progressive pubertal development between 10.5 and 11.5 years of age
  – Her final height will most probably be close to the target height

Figure 3. Patient Growth (45 003) During Study Compared With Height-for-age Percentiles
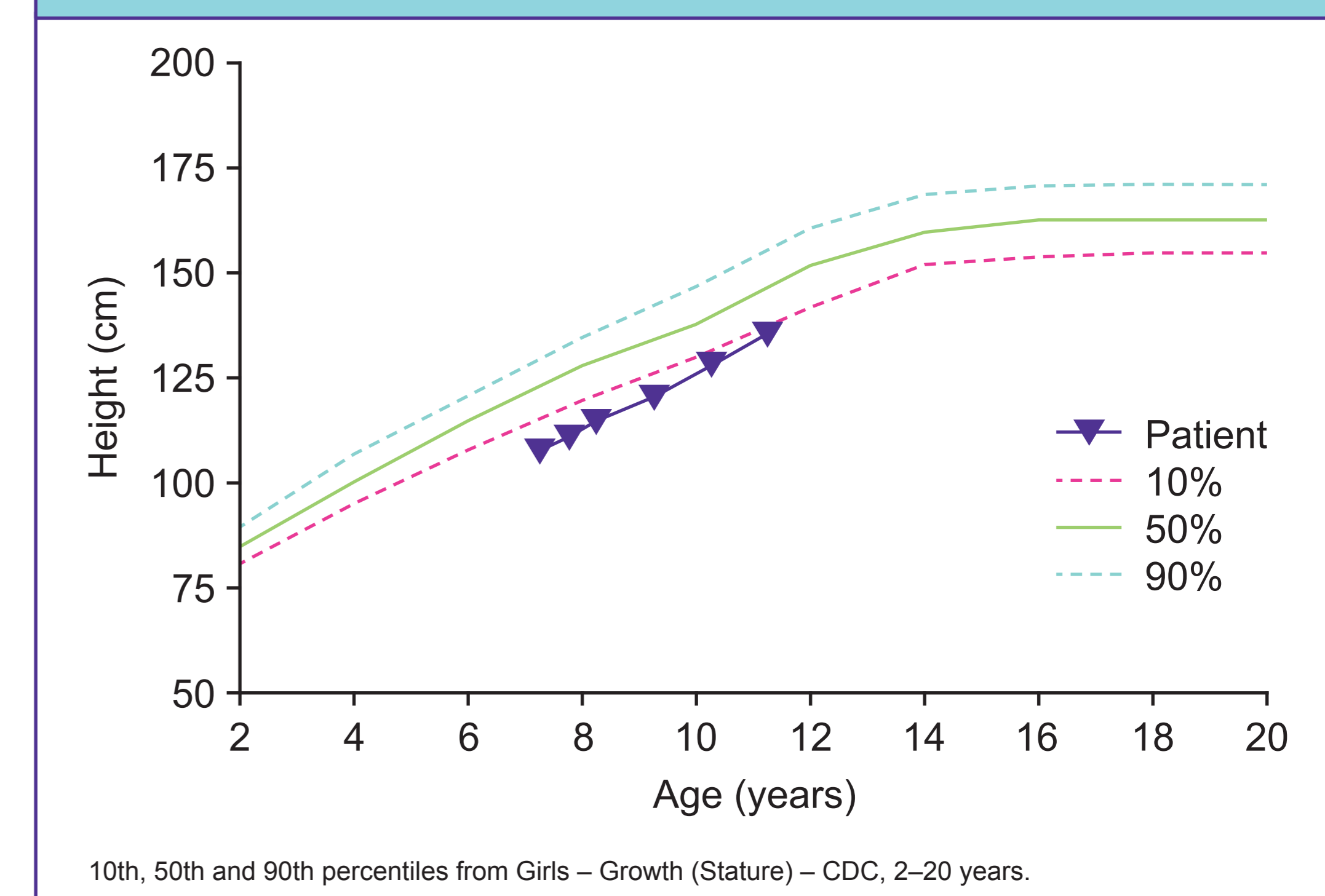
10th, 50th and 90th percentiles from Girls – Growth (Stature) – CDC, 2–20 years.

CONCLUSIONS

- Overall, the majority of children adhered extremely well to their treatment regimen using the easypod™ device
- The majority of caregivers responsible for administering injections were married or cohabiting and were in employment, and similar proportions had either a primary or a university standard of education
- Individual cases showed distinctive patterns of growth outcomes

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DISCLOSURES

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