

# Adherence and long-term outcomes of therapy in pediatric subjects in Argentina using easypod™ electromechanical device for growth hormone treatment: the Phase IV multicenter Easypod™ Connect Observational Study (ECOS)

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## INTRODUCTION

- According to the World Health Organization approximately 50% of medication prescribed for long term illnesses is not taken as directed;<sup>1</sup> it is reported that poor compliance is one of the most common factors underlying suboptimal growth during growth hormone (GH) therapy.<sup>2</sup>
- The Easypod™ Connect Observational Study (ECOS) assessed real-time adherence in patients from 24 countries who were receiving recombinant human GH (r-hGH; Saizen®) via easypod™, which is an electronic injection device connected to the easypod™ connect platform.<sup>3</sup>
- The connect platform allows uploading of the dose history to a secure online database, subsequently enabling the physician or nurse, using a personal computer, to view and print graphical and schematic data displays.<sup>4</sup>
- Overall, ECOS showed a median adherence rate of ≥80% was maintained by the majority of patients over 3 years of treatment and over each individual treatment period.<sup>3</sup>
- In this study, we assessed the adherence to r-hGH administered via easypod™ in the Argentinian cohort of patients from ECOS (NCT01582334).

## OBJECTIVES

### Primary

- To assess the level of adherence of participants receiving Saizen® via easypod™ and the easypod™ connect platform.

### Secondary

- To describe the impact of adherence on growth outcomes (change in height standard deviation score [SDS] and change in height velocity SDS) for participants
- To identify participant adherence profiling

## METHODS

- Study design: long-term, observational, open-label, Phase IV study.
- Patients were 2–18 years treated with r-hGH administered via easypod™ for ≥6 months and ≤5 years.
- Adherence data were obtained prospectively via the easypod™ connect for all subjects.
- Demographic, auxological, and diagnostic data were obtained from the patients' medical notes.
- Good adherence (proportion of days with injection received/days with injections planned) was defined as ≥80%.
- All analyses were descriptive.
- Spearman's product-moment correlations were calculated for the association between adherence and outcome.

## RESULTS

### Patients

- 68 patients were enrolled in the ECOS study (full analysis set). The demographic data are shown in **Table 1**.
- 63 patients were included in the adherence data analysis set (DAS; patients with adherence data available for a period of ≥3 months after enrolment in the study)
- 33 were growth hormone naïve
- The patients' diagnoses were (**Figure 1**)
  - Growth hormone deficiency (GHD) (N=44)
  - Small for gestational age (SGA) (N=11)
  - Turner syndrome (TS) (N=8)

Figure 1. Indications for GH treatment

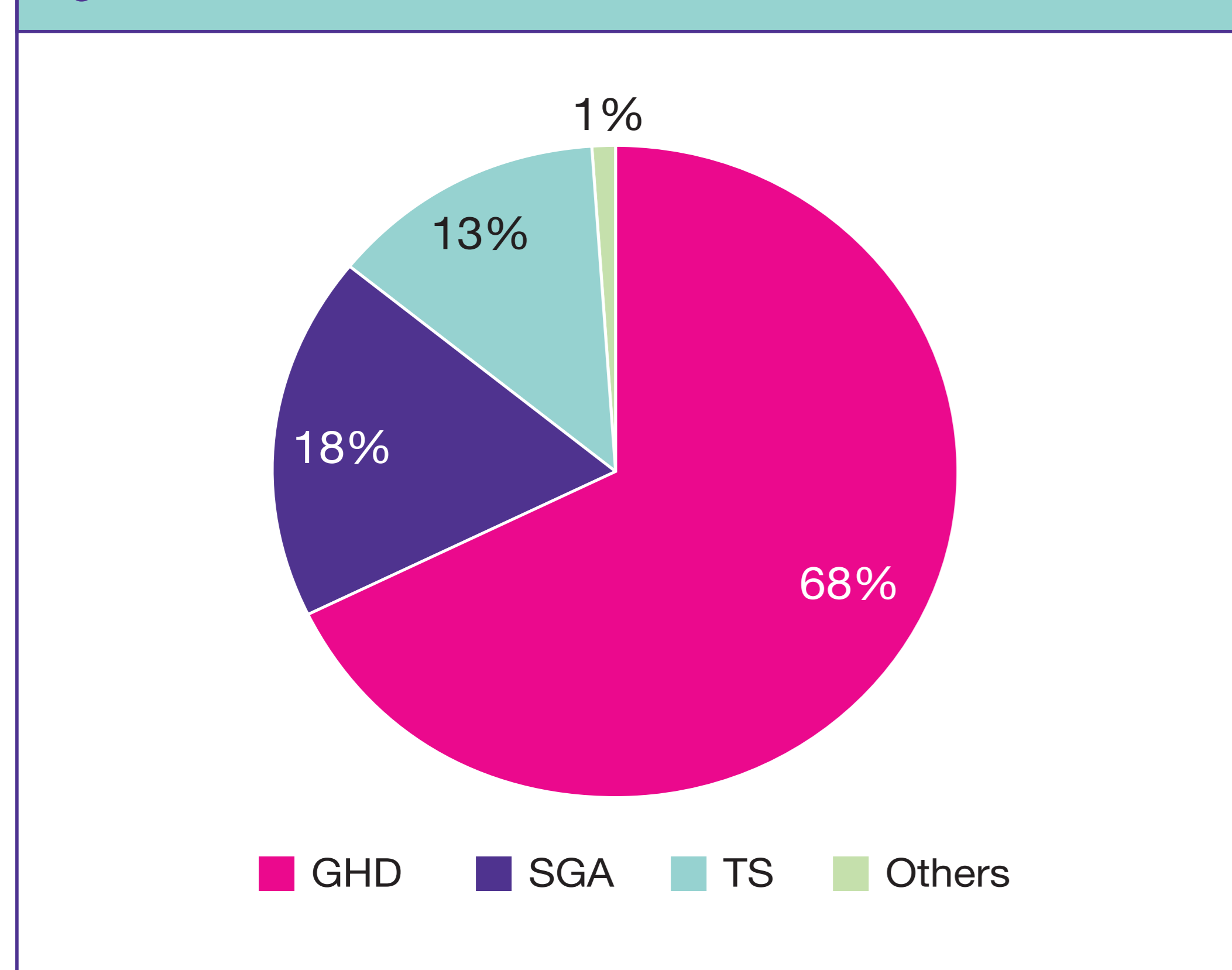


Table 1. Baseline Demographics of Full Analysis Set

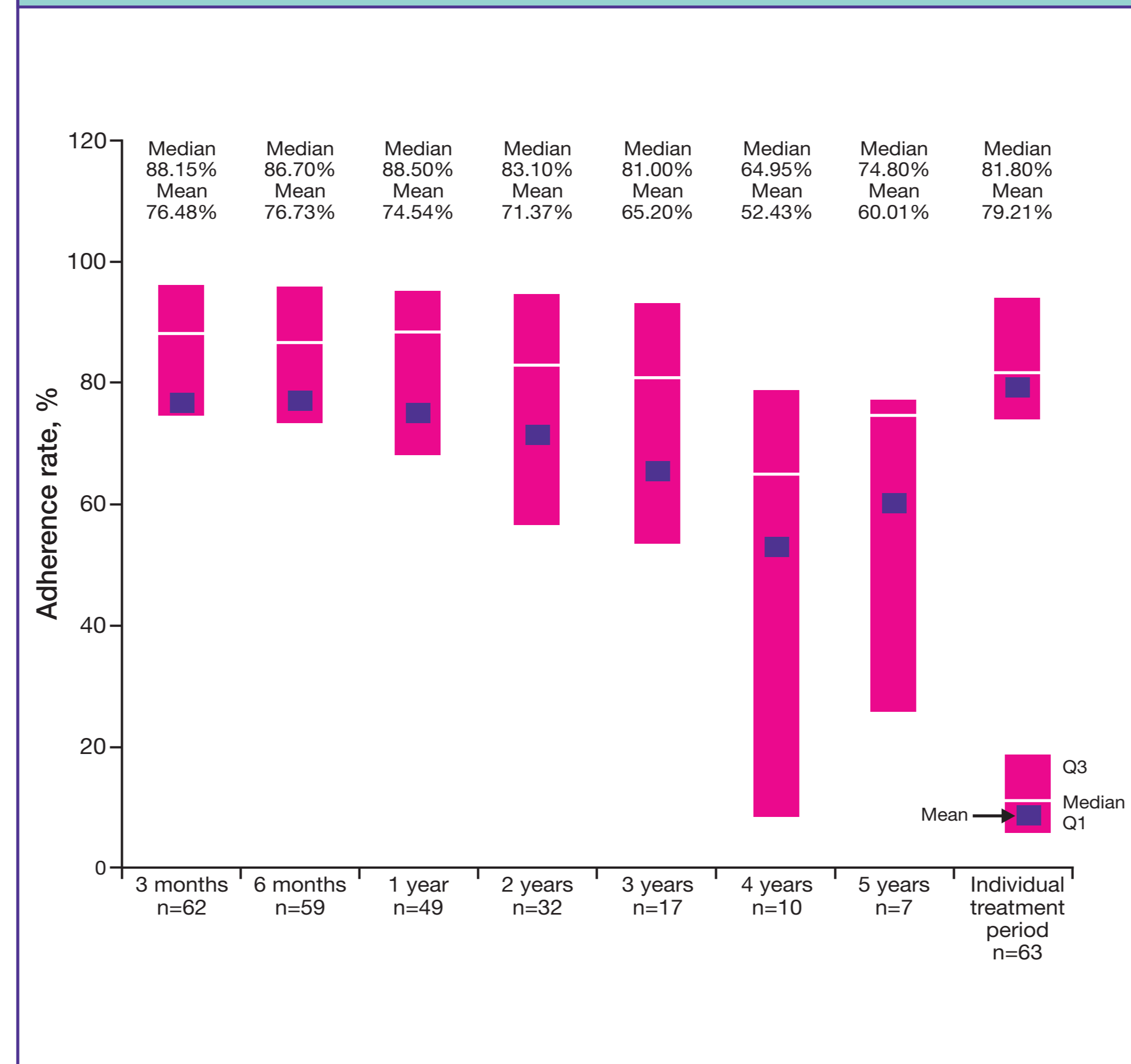
	GHD (n=46)	SGA (n=12)	TS (n=9)	Other/missing (n=1)	Overall N=68
Age, years Mean (SD)	11.50 (4.19)	9.92 (3.06)	9.89 (2.26)	9.00	10.97 (3.81)
Sex, n (%) Female Male	9 (19.6) 37 (80.4)	2 (16.7) 10 (83.3)	9 (100) 0	0 1 (100)	20 (29.4) 48 (70.6)
Ethnicity, n (%) Caucasian Missing	46 (100) 0	12 (100) 0	9 (100) 0	- 1	67 (98.5) 1 (1.5)
Tanner stage (male), n (%) n (missing) Tanner 1 Tanner >1	15 (22) 9 (60.0) 6 (40.0)	2 (8) 1 (50.0) 1 (50.0)	0 (0)	0 (1)	17 (31) 10 (58.8) 7 (41.2)
Tanner stage (female), n (%) n (missing) Tanner 1 Tanner >1	3 (6) 2 (66.7) 1 (33.3)	2 (0) 1 (50.0) 1 (50.0)	2 (7) 2 (100) 0	0 (0)	7 (13) 5 (71.4) 2 (28.6)
Growth velocity at GH treatment start (cm/year)	3.77 (1.47)	4.58 (1.99)	3.63 (1.07)	ND	3.90 (1.54)
Height at GH treatment start (cm) Mean (SD)	119.45 (21.34)	115.46 (18.17)	108.68 (13.27)	ND	117.29 (20.02)

GHD, growth hormone deficiency. ND, not determined. SD, standard deviation. SGA, small for gestational age. TS, Turner syndrome.

### Adherence

- After 1 year of treatment, median (Q1:Q3) adherence in the easypod™ connect DAS was 88.5% (67.9%:95.6% [N=49]) (**Figure 2**).
- Good adherence decreased each year but was maintained to 3 years: 81.0% (53.2%:93.5%) [N=17]) (**Figure 2**).

Figure 2. Treatment Adherence Rates Over Time in the easypod™ Adherence Data Analysis Set



### Growth Outcomes

- After 1 year, the median (Q1:Q3) change in height SDS was 0.43 (0.21;0.64), change in height velocity was 7.61 cm/year (6.44;8.47) and the change in height velocity SDS was 2.02 (0.33;4.30) (**Table 2**).
- In the r-hGH treatment-naïve patients, the 1-year growth outcomes showed variable outcomes based on the origin of GHD.
- The sub-analysis of adherence and growth outcomes at 1 year in patients with no missing data and no gaps in treatment >1 week produced similar results: change in height SDS was 0.45 (0.21;0.64) and change in height velocity SDS was 2.15 (0.61;4.30) (N=22).

### Correlation of Growth Outcomes with Adherence at 1 Year

- The Spearman's product-moment correlation for adherence rate and change in height SDS was 0.458 for all indications and 0.536 for the GHD patients.
- There was a positive correlation between adherence rate and growth response (change in height SDS) in the GHD patients ( $P=0.048$ ) (N=44).

### Patients adherence profiling

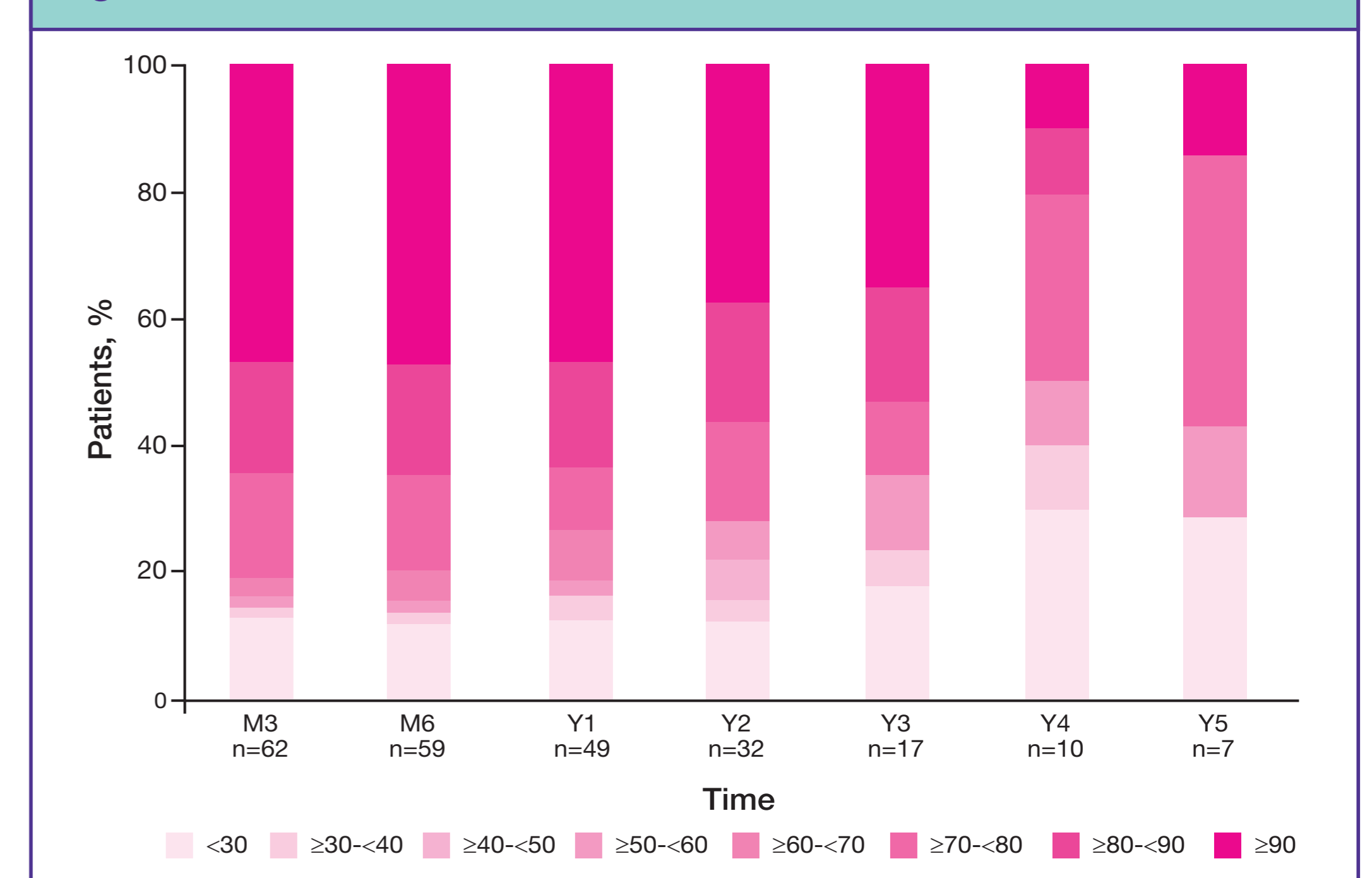
- The adherence profile over time (**Figure 3**) demonstrates the variation in the proportion of patients from higher to mid-lower adherence rates during the follow up. This suggests that adherence rates decrease during the course of prolonged treatment.

Table 2. Change in Growth Outcome Parameters After 1 Year in the DAS

	GHD (n=44)	SGA (n=11)	TS (n=8)	Other/missing (n=0)	Overall N=63
Height (cm) at baseline n (missing) Mean (SD) Median Q1:Q3	25 (19) 124.61 (19.56) 127.00 114.60;133.40	3 (8) 125.17 (26.84) 115.50 104.50;155.50	1 (7) 125.00 125.00 125.00;125.00	0 (0) - - -	29 (34) 124.68 (19.48) 125.00 114.60;133.40
Change in height (cm) n (missing) Mean (SD) Median Q1:Q3	19 (25) 7.07 (1.76) 7.40 5.90;8.40	3 (8) 6.37 (1.31) 6.50 5.00;7.60	1 (7) 5.70 5.70 5.70;5.70	0 (0) - - -	23 (40) 6.92 (1.68) 7.30 5.70;8.10
Height SDS at baseline n (missing) Mean (SD) Median Q1:Q3	25 (19) -2.40 (0.85) -2.39 -2.82;-1.75	3 (8) -2.56 (0.79) -2.15 -3.47;-2.05	1 (7) -1.38 -1.38 -1.38;-1.38	0 (0) - - -	29 (34) -2.38 (0.84) -2.21 -2.82;-1.75
Change in height SDS n (missing) Mean (SD) Median Q1:Q3	19 (25) 0.44 (0.26) 0.43 0.23;0.67	3 (8) 0.42 (0.20) 0.46 0.21;0.61	1 (7) -0.09 -0.09 -0.09;-0.09	0 (0) - - -	23 (40) 0.41 (0.26) 0.43 0.21;0.64
Height velocity (cm per year) n (missing) Mean (SD) Median Q1:Q3	19 (25) 7.80 (1.73) 7.48 6.59;8.47	3 (8) 7.09 (1.44) 7.07 5.67;8.54	1 (7) 5.41 5.41 5.41;5.41	0 (0) - - -	23 (40) 7.61 (1.71) 7.47 6.44;8.47
Height velocity SDS n (missing) Mean (SD) Median Q1:Q3	18 (26) 2.70 (2.70) 2.16 0.61;4.30	3 (8) 2.50 (2.68) 1.67 0.33;5.50	1 (7) -0.61 -0.61 -0.61;-0.61	0 (0) - - -	22 (41) 2.52 (2.66) 2.02 0.33;4.30

DAS, adherence data analysis set. GHD, growth hormone deficiency. ND, not determined. SD, standard deviation. SDS, standard deviation score. SGA, small for gestational age. TS, Turner syndrome.

Figure 3. Adherence Profile Over Time



## CONCLUSIONS

- In agreement with the results from the global analyses of ECOS, treatment with r-hGH administered via easypod™ led to high adherence rates in this representative population from Argentina
- Overall, 1-year growth outcomes were clinically meaningful
- Adherence rates trend to decrease over time in patients taking prolonged treatment
- Real-world data provide a unique opportunity to understand patients' adherence to treatment
- Continuous monitoring of adherence via the easypod™ connect database is a valuable tool to appreciate adherence profiles and perform an intensified individualized follow-up

## DISCLOSURES

The ECOS study was sponsored by Merck Healthcare KGaA, Darmstadt, Germany.

## REFERENCES

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