The Easypod™ Connect Observational Study (ECOS): comparison of results from interim analyses

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Introduction

- The easypod™ electronic auto-injector device is designed to make daily administration of recombinant human growth hormone (r-hGH) easier, more comfortable and convenient for the patient.[1]
- The device enables accurate, real-world digital records of patients' adherence to r-hGH to be collected for evaluation.
- The easypod™ connect observational study (ECOS) is a long-term, open-label study, started in 2010 in 24 countries, which follows children with Growth Hormone deficiency (GHD), Small for Gestational Age (SGA) and Turner Syndrome (TS) and other conditions, such as chronic renal failure, receiving r-hGH therapy for up to 5 years, with annual interim analyses.
- Global ECOS study data showed that adherence rates with the easypod™ device were high and maintained over time.[2]
- Data from interim analyses carried out on patients from Canada, France and the participating Nordic countries (Sweden and Finland) are presented here.

Objectives

- The primary objective of this analysis is to evaluate real-world adherence data of the use of easypod™ in paediatric patients in Canada, France, Sweden and Finland, and to compare with the high adherence levels seen in the ECOS global study.
- Secondary objectives include assessment of the impact of adherence on changes in height standard deviation score (SDS).

Methods

- The ECOS study is an observational, open-label Phase IV study utilizing the easypod™ device to provide objective evidence of levels of adherence to r-hGH therapy. Pediatric patients are recruited according to the indications applicable in the countries involved. The study combines retrospective and prospective data over the planned 5-year duration.
- Demographic, auxological and diagnostic data are obtained from medical notes, with adherence data obtained directly from the patients' easypod™.
- Adherence is defined as days with injections received, divided by days with injections planned, expressed as a percentage.
- An interim global analysis was completed in 2014. Interim analyses have since been completed for the Nordic countries (Sweden, Finland), France and Canada. The real-world use of easypod™ (routine visits/year, local easypod™ data upload methodology) in these analyses was compared to assess any country-specific differences.
- Exposure to study treatment (treatment duration, drug dose at start and number of dose adjustments) and treatment experience (reasons for changes in prescribed dose, reasons for missed injections and person who performed the majority of injections) were assessed in the ECOS global study and for the individual countries; these data are not shown in these interim results.
- Interim data presented here are for patients naïve to the easypod™ device (naïve patients).

Results

Patients

- At the time of the analysis, 1,972 patients had been enrolled globally with 220, 204 and 150 patients from France, Canada and the Nordic countries respectively (**Table 1**).

Table 1. Patient enrolment and diagnosis for ECOS global study and by country (France, Canada and Nordic countries)

	GHD	SGA	TS	All indications*
ECOS	1295**	295	152	1972
France	107	68	19	220
Canada	149	4	28	204
Sweden	95	30	10	140
Finland	9	0	0	10

GHD, Growth Hormone Deficiency; SGA, Small for Gestational Age; TS, Turner Syndrome; *Includes other/missing indications.
**GHD group included patients with both congenital and acquired origins of GHD.

- Patient baseline demographics and auxological characteristics were well balanced between countries (**Tables 2 and 3**).

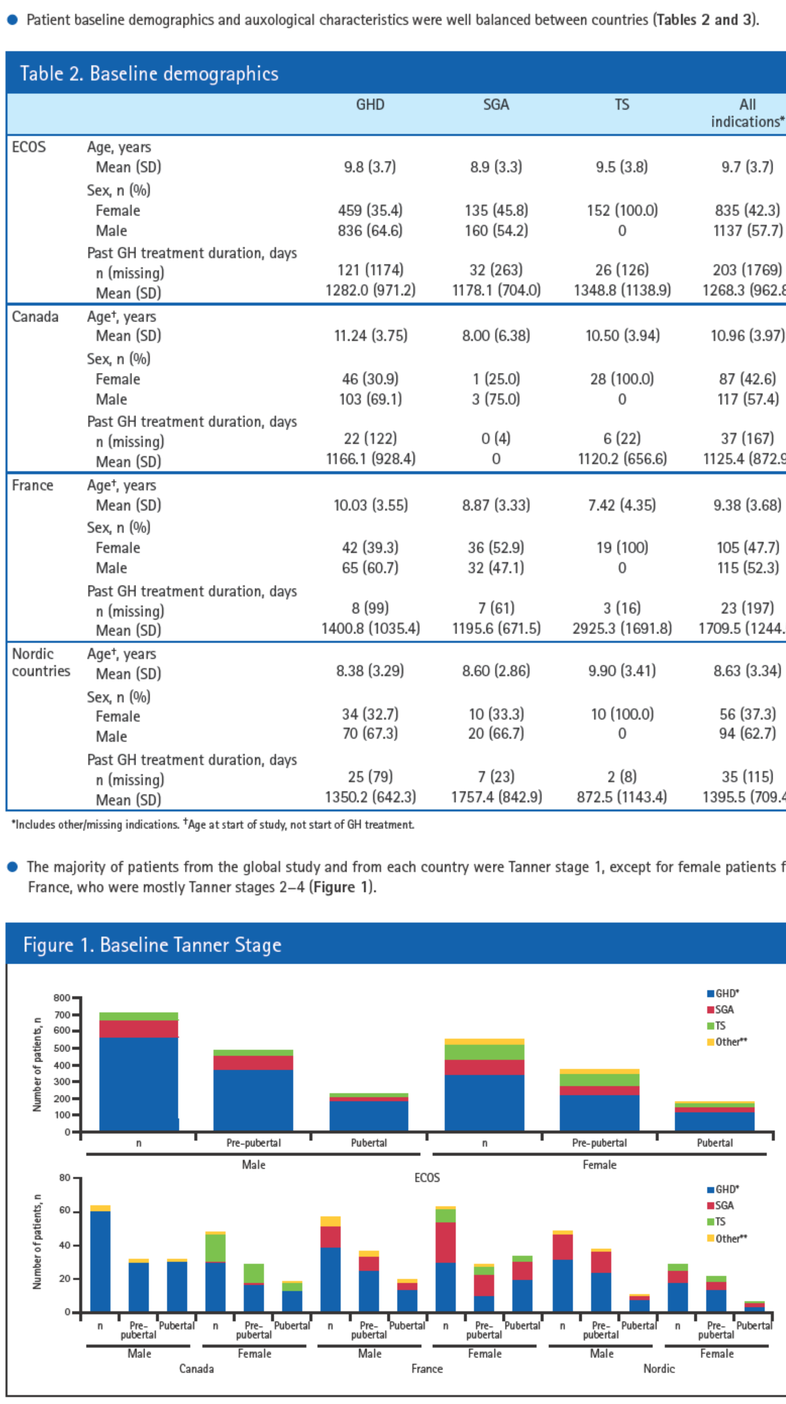
Table 2. Baseline demographics

		GHD	SGA	TS	All indications*
ECOS	Age, years				
	Mean (SD)	9.8 (3.7)	8.9 (3.3)	9.5 (3.8)	9.7 (3.7)
	Sex, n (%)				
	Female	459 (35.4)	135 (45.8)	152 (100.0)	835 (42.3)
	Male	836 (64.6)	160 (54.2)	0	1137 (57.7)
	Past GH treatment duration, days				
	n (missing)	121 (1174)	32 (263)	26 (126)	203 (1769)
	Mean (SD)	1282.0 (971.2)	1178.1 (704.0)	1348.8 (1138.9)	1268.3 (962.8)
Canada	Age†, years				
	Mean (SD)	11.24 (3.75)	8.00 (6.38)	10.50 (3.94)	10.96 (3.97)
	Sex, n (%)				
	Female	46 (30.9)	1 (25.0)	28 (100.0)	87 (42.6)
	Male	103 (69.1)	3 (75.0)	0	117 (57.4)
	Past GH treatment duration, days				
	n (missing)	22 (122)	0 (4)	6 (22)	37 (167)
	Mean (SD)	1166.1 (928.4)	0	1120.2 (656.6)	1125.4 (872.9)
France	Age†, years				
	Mean (SD)	10.03 (3.55)	8.87 (3.33)	7.42 (4.35)	9.38 (3.68)
	Sex, n (%)				
	Female	42 (39.3)	36 (52.9)	19 (100)	105 (47.7)
	Male	65 (60.7)	32 (47.1)	0	115 (52.3)
	Past GH treatment duration, days				
	n (missing)	8 (99)	7 (61)	3 (16)	23 (197)
	Mean (SD)	1400.8 (1035.4)	1195.6 (671.5)	2925.3 (1691.8)	1709.5 (1244.5)
Nordic countries	Age†, years				
	Mean (SD)	8.38 (3.29)	8.60 (2.86)	9.90 (3.41)	8.63 (3.34)
	Sex, n (%)				
	Female	34 (32.7)	10 (33.3)	10 (100.0)	56 (37.3)
	Male	70 (67.3)	20 (66.7)	0	94 (62.7)
	Past GH treatment duration, days				
	n (missing)	25 (79)	7 (23)	2 (8)	35 (115)
	Mean (SD)	1350.2 (642.3)	1757.4 (842.9)	872.5 (1143.4)	1395.5 (709.4)

*Includes other/missing indications. †Age at start of study, not start of GH treatment.

- The majority of patients from the global study and from each country were Tanner stage 1, except for female patients from France, who were mostly Tanner stages 2–4 (**Figure 1**).

Figure 1. Baseline Tanner Stage



Pre-pubertal includes patients at Tanner stage 1; pubertal includes patients at Tanner stages 2–5.
*GHD group included patients with both congenital and acquired origins of GHD; **Other/missing indications.

Table 3. Baseline auxological characteristics

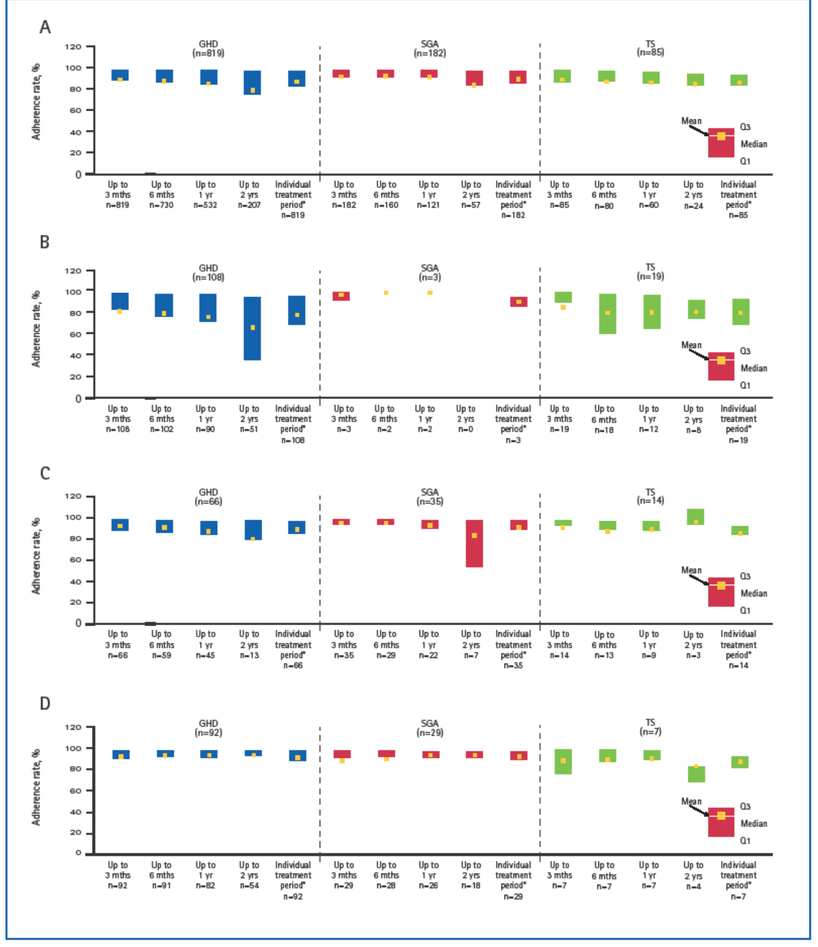
		GHD	SGA	TS	All indications*
ECOS	Growth velocity at treatment start‡, cm/year				
	n (missing)	1072 (223)	257 (38)	114 (38)	1548 (424)
	Mean (SD)	4.49 (2.59)	4.71 (1.79)	6.34 (12.10)	4.65 (4.06)
	Height at GH treatment start, cm				
	n (missing	1270 (25)	287 (8)	149 (3)	1841 (131)
	Mean (SD)	118.66 (20.91)	113.35 (18.10)	109.66 (19.67)	116.98 (20.70)
Canada	Growth velocity at treatment start‡, cm/year				
	n (missing)	69 (80)	3 (1)	10 (18)	90 (114)
	Mean (SD)	5.33 (5.59)	7.27 (3.81)	4.31 (2.26)	5.32 (5.15)
	Height at GH treatment start, cm				
	n (missing	144 (5)	4 (0)	27 (1)	187 (17)
	Mean (SD)	119.49 (24.01)	102.03 (31.49)	112.26 (18.07)	117.16 (23.89)
France	Growth velocity at treatment start‡, cm/year				
	n (missing)	105 (2)	63 (5)	19 (0)	198 (22)
	Mean (SD)	4.95 (2.33)	4.95 (1.78)	7.89 (11.09)	5.25 (4.05)
	Height at GH treatment start, cm				
	n (missing	107 (0)	66 (2)	19 (0)	211 (9)
	Mean (SD)	123.71 (20.30)	114.97 (19.08)	100.71 (23.46)	117.72 (22.03)
Nordic countries	Growth velocity at treatment start‡, cm/year				
	n (missing)	101 (3)	29 (1)	10 (0)	144 (6)
	Mean (SD)	5.56 (2.25)	5.37 (1.05)	4.30 (1.90)	5.43 (2.04)
	Height at GH treatment start, cm				
	n (missing	103 (1)	30 (0)	10 (0)	148 (2)
	Mean (SD)	108.46 (20.62)	106.62 (11.55)	116.59 (18.34)	108.45 (19.73)

*Includes other/missing indications.
‡Growth velocity at baseline as recorded in CRFs. This value was not calculated.

Efficacy

- Overall adherence rates in patients naïve to easypod™ remained consistently high over time for Canada, France and the Nordic countries despite a slight reduction in adherence in GHD patients in the Canadian sub-analysis (**Figure 2a–d**). The variation in minimum values was due to limitations of the analysis. Also, variations of adherence rates in other groups (e.g. SGA in France) are likely to be explained by small numbers of patients and short follow-up period for SGA.

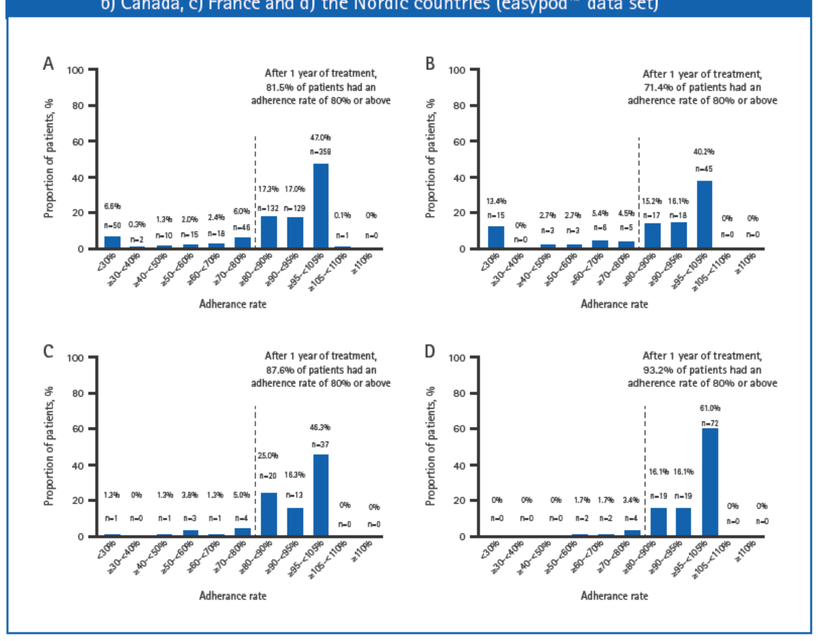
Figure 2. Continuous summary of treatment adherence rate (%) for a) ECOS global study, b) Canada, c) France and d) the Nordic countries (easypod™ data set)



*Defined as the period from patient's Day 1 of Week 1 until the last complete week with adherence data available.

- Overall, after one year of easypod™ treatment, 71.4%, 87.6% and 93.2% of patients from Canada, France and the Nordic countries, respectively had an adherence rate of ≥80% (**Figure 3b–d**).
- In comparison, for the ECOS global dataset, 81.5% of patients had an adherence rate of ≥80% after 1-year of treatment (**Figure 3a**).

Figure 3. Categorical treatment adherence rate at Year 1 for the overall population of a) ECOS, b) Canada, c) France and d) the Nordic countries (easypod™ data set)



- After one year, the mean change in height SDS for patients naïve to easypod™ was 0.41 in the ECOS global study. Mean change in height SDS was similar for the three countries (0.38, 0.48 and 0.43 for Canada, France and the Nordic countries, respectively) (**Table 4**).
- Mean change in height velocity SDS was 1.34 for Canada, 2.01 for France and 2.10 for the Nordic countries and 2.03 in the global study (**Table 4**).

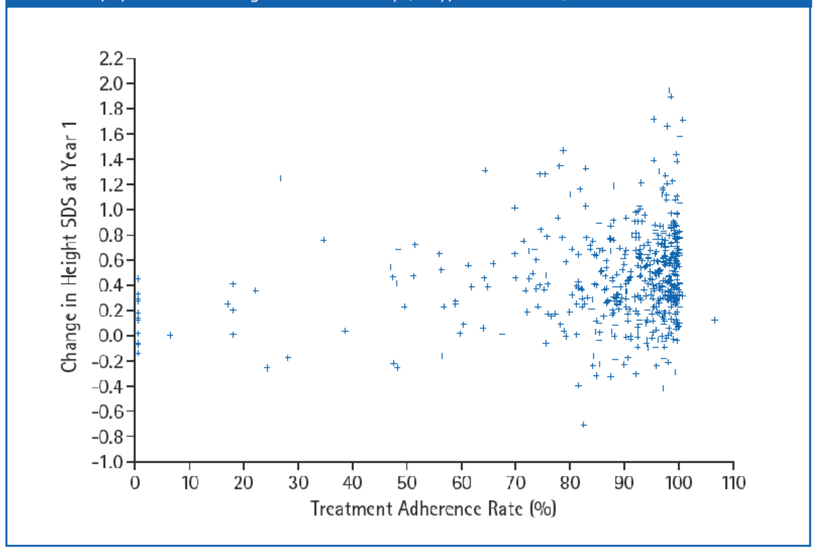
Table 4. Growth outcomes after one year (easypod™ data set)

	Change in height SDS	GHD*	SGA	TS	All indications**
ECOS	n (missing)	509 (310)	115 (67)	54 (31)	709 (489)
	Mean (SD)	0.45 (0.37)	0.44 (0.32)	0.37 (0.35)	0.44 (0.36)
	Median	0.41	0.46	0.42	0.41
	Q1; Q3	0.21; 0.68	0.20; 0.64	0.09; 0.63	0.21; 0.66
Canada	n (missing)	76 (32)	2 (1)	11 (8)	95 (51)
	Mean (SD)	0.36 (0.39)	0.86 (0.75)	0.29 (0.33)	0.38 (0.41)
	Median	0.32	0.86	0.28	0.32
	Q1; Q3	0.12; 0.55	0.33; 1.39	0.09; 0.56	0.13; 0.56
France	n (missing)	53 (13)	26 (9)	10 (4)	92 (37)
	Mean (SD)	0.45 (0.38)	0.54 (0.33)	0.52 (0.40)	0.48 (0.36)
	Median	0.40	0.57	0.62	0.47
	Q1; Q3	0.23; 0.67	0.33; 0.71	0.17; 0.65	0.24; 0.67
Nordic countries	n (missing)	45 (47)	15 (14)	3 (4)	65 (68)
	Mean (SD)	0.46 (0.36)	0.26 (0.28)	0.61 (0.23)	0.43 (0.35)
	Median	0.46	0.20	0.54	0.38
	Q1; Q3	0.27; 0.66	0.00; 0.32	0.44; 0.87	0.20; 0.62
	Height velocity SDS	**GHD***	**SGA**	**TS**	**All indications****
ECOS	n (missing)	489 (330)	114 (68)	47 (38)	680 (518)
	Mean (SD)	2.13 (2.76)	1.81 (2.17)	1.51 (2.92)	2.03 (2.66)
	Median	2.01	1.88	1.43	1.86
	Q1; Q3	0.35; 3.63	0.36; 3.19	−0.08; 2.16	0.31; 3.44
Canada	n (missing)	69 (39)	2 (1)	10 (9)	87 (59)
	Mean (SD)	1.26 (2.37)	1.15 (1.67)	1.17 (2.86)	1.34 (2.51)
	Median	1.23	1.15	1.23	1.23
	Q1; Q3	−0.29; 2.51	−0.03; 2.33	−0.11; 1.84	−0.16; 2.55
France	n (missing)	50 (16)	26 (9)	8 (6)	86 (43)
	Mean (SD)	2.03 (3.43)	2.09 (2.49)	1.72 (1.65)	2.01 (2.97)
	Median	1.68	2.07	1.59	1.75
	Q1; Q3	−0.25; 3.55	1.19; 3.10	1.03; 2.92	0.11; 3.10
Nordic countries	n (missing)	44 (48)	15 (14)	3 (4)	64 (69)
	Mean (SD)	2.39 (2.43)	1.09 (1.79)	1.64 (0.21)	2.10 (2.28)
	Median	1.96	0.83	1.64	1.84
	Q1; Q3	0.68; 3.78	0.35; 2.69	1.43; 1.86	0.59; 3.29

*GHD group included patients with both congenital and acquired origins of GHD.
**Includes other/missing indications.

- Spearman's product-moment correlation for adherence rate and change in height SDS at Year 1 in the ECOS global study was only weakly positive (**Figure 4**).
- As a result of the smaller data sets, correlation for the three countries (not shown) was similar to the global results.

Figure 4. Correlation of adherence rate and change in height SDS at one year in the overall population of the global ECOS study (easypod™ data set)



Data missing for Patient 6.

Discussion

- Local growth outcomes and adherence rates at one year in naïve patients (first time easypod™ users) were similar to the results obtained from the ECOS global study.
- The slightly lower adherence rate seen in the Canadian data may be due to a group of patients with very low adherence (being checked as part of queries/data management review).
- No clinically significant correlation between adherence and change in height SDS was observed.
- Limitations of this interim analysis include: pilot analysis from only one region (Nordic) and two countries presented; a heterogenous GHD population was included which might contribute to a lower response to GH therapy; naïve patients were only naïve to the easypod™ device and not to GH therapy; patients at differing stages of pubertal development complicate interpretation of growth outcomes.

Conclusions

- Individual country analyses show that adherence rates with the easypod™ device are high and maintained over time and are consistent with the results from the ECOS global study.
- Different age range at baseline and possible differences in clinical practice between countries did not appear to have any major impact on adherence rates with easypod™.

References

1. Bozzola M, et al. BMC Endocrine Dis 2011;11:4.
2. The Easypod™ Connect Observational Study (ECOS): Results from the 2014 Interim Analysis. Presented at ENDO 2015, San Diego, CA, USA. Abstract THR-160

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