

Up to 5 Years of Once-Weekly Somatrogen Treatment in Paediatric Patients With Growth Hormone Deficiency: Results From an Open-label Extension of a Global Phase 3 Study

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Objective

- To assess the efficacy and safety of once-weekly somatrogen in children with GHD following up to 5 years of somatrogen treatment in the global phase 3 study (12-month main study followed by 4 years of an open-label extension).



Conclusions

- After up to 5 years of somatrogen administered once weekly, patients with pGHD continued to demonstrate above mean HV for their age range, which further improved height SDS relative to baseline.
 - The change in HV and height SDS over this 5-year period is similar to the catch-up growth routinely observed in children with GHD treated with once-daily somatropin.
- Somatrogen maintained a favourable safety profile throughout the 5-year study period.
- Based on immunogenicity data available to date (up to OLE Y3), the presence of ADAs did not appear to have an effect on the efficacy or safety of somatrogen.

Background

- Somatrogen is a long-acting recombinant human growth hormone (rhGH) composed of the amino acid sequence of hGH and 3 copies of the carboxy-terminal peptide (CTP) of human chorionic gonadotropin.
 - The CTPs extend the half-life of somatrogen compared with rhGH, allowing longer intervals between doses.¹
- Somatrogen is currently approved in several countries as a once-weekly subcutaneous (SC) injection for children with paediatric growth hormone deficiency (pGHD).
- A global phase 3 (NCT02968004)² study demonstrated that over 12 months, once-weekly somatrogen was noninferior to once-daily somatropin with regard to annualized height velocity (HV) in patients with pGHD. Both treatments had similar safety and tolerability profiles.

Methods

- In the 12-month main study, prepubertal paediatric patients were randomized 1:1 to receive somatrogen (0.66 mg/kg/wk administered as a once-weekly SC injection) or somatropin (0.24 mg/kg/wk administered as a once-daily SC injection).²
- Prepubertal children (boys: aged 3–11 years; girls: aged 3–10 years) diagnosed with GHD were eligible for enrolment into the main study if they had impaired HV, defined as annualized HV below the 25th percentile for chronological age (HV <−0.7 standard deviation score [SDS]), baseline insulin-like growth factor-1 (IGF-1) SDS ≤−1, and no prior rhGH therapy.
- Patients who completed the 12-month main study were eligible to enrol into an open-label extension (OLE), during which somatrogen-treated patients continued to receive somatrogen and somatropin-treated patients switched to somatrogen (0.66 mg/kg/wk).
- IGF-1 levels were to be sampled 4 days (−1 day) post dose, but some measurements were recorded outside of this window during the study.
- Data for up to 5 years of somatrogen treatment (1-year main study period + 4-year OLE) are reported; statistical analyses of these data are descriptive, and no formal hypothesis testing was performed.



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Disclosures

LAS: Advisory board: Ascendis Pharma, BioMarin, Endo Pharmaceuticals, Novo Nordisk, Pfizer; consultant: OPKO Health, Pfizer; research investigator: Novo Nordisk. **JS:** Consultant: Azurity Pharmaceuticals, BioMarin; speaker: Pfizer. **JC:** Employee: OPKO Health. **RS:** Research investigator: Ascendis Pharma, OPKO Health; research support: OPKO Health, Pfizer, Sandoz. **CLD:** Advisory board: Ipsen, Levo Therapeutics, Neurocrine Biosciences, Pfizer, Worldwide Clinical Trials; consultant: OPKO Health, Pfizer, Worldwide Clinical Trials; other: ad hoc consultant: Acadia Pharmaceuticals, Inversago Pharma, Ipsen, Levo Therapeutics, Lumos Pharma, Neurocrine Biosciences, Poxel SA, Tolmar, Worldwide Clinical Trials. **MPW, MT, DLT, CTT, RW, JC:** Employee and stock owner: Pfizer. **MP:** Advisory board: AstraZeneca, Dompé, DreaMed Diabetes, Eli Lilly, Insulet, Medtronic, Novo Nordisk, Pfizer, Sanofi; consultant: DreaMed Diabetes, Pfizer, QuLab Medical, RSP Systems; grant recipient (institute headed by MP): AstraZeneca, Dexcom, Dompé, DreaMed Diabetes, Eli Lilly, Insulet, Lexicon Pharmaceuticals, Medtronic, NG Solutions, Novo Nordisk, Nutriteen Professional, OPKO Health, Pfizer, Roche, Sanofi; research investigator: NIH Flair study (via Health Partners); stock owner: DreaMed Diabetes, NG Solutions, Nutriteen Professional.

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Results

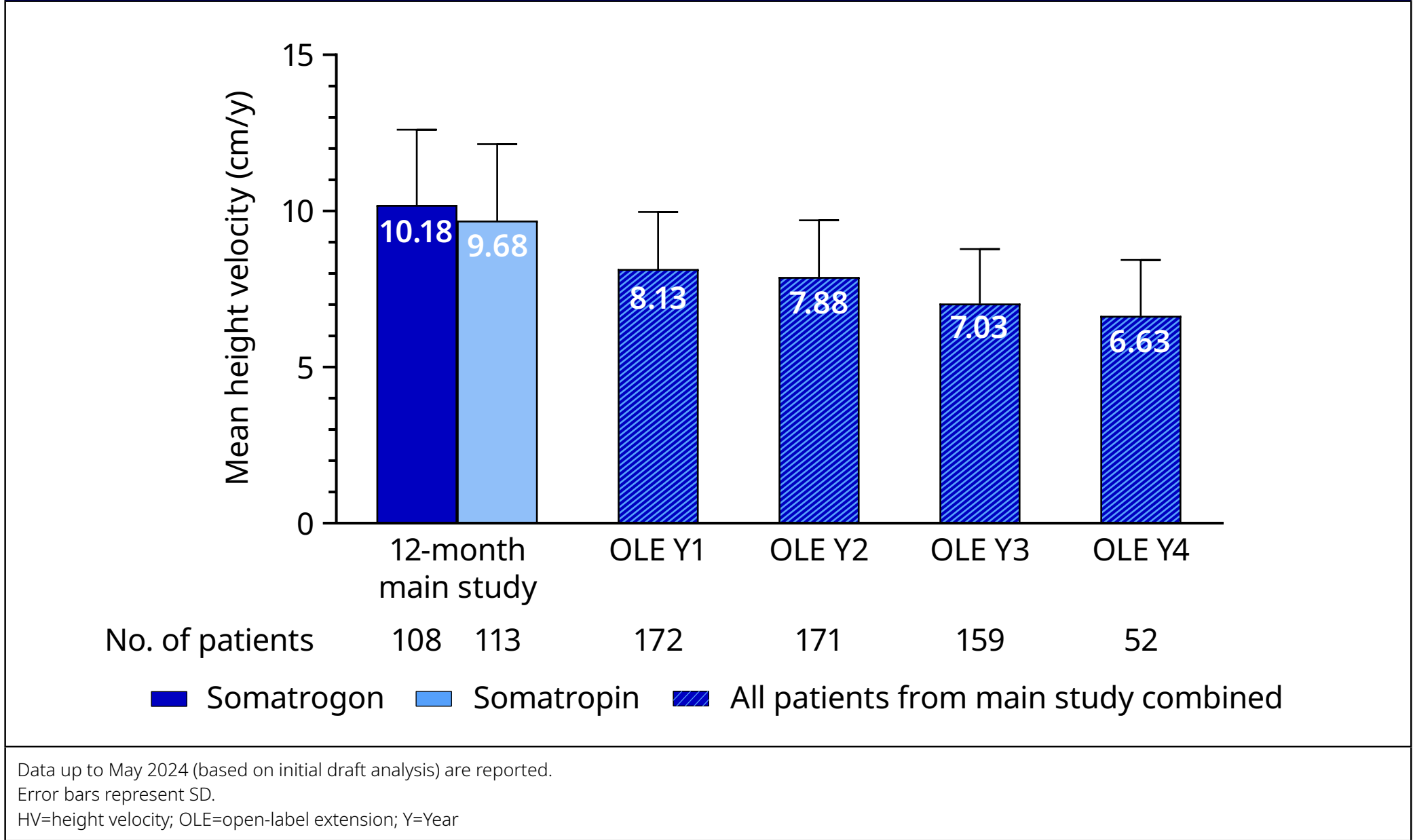
PATIENTS

- A total of 224 patients (somatrogen=109, somatropin=115) received ≥1 dose of study treatment in the 12-month main study.
- Of the 222 patients (somatrogen=108, somatropin=114) who completed the 12-month main study, 212 (somatrogen=104; somatropin=108) entered the OLE and received somatrogen.

EFFICACY

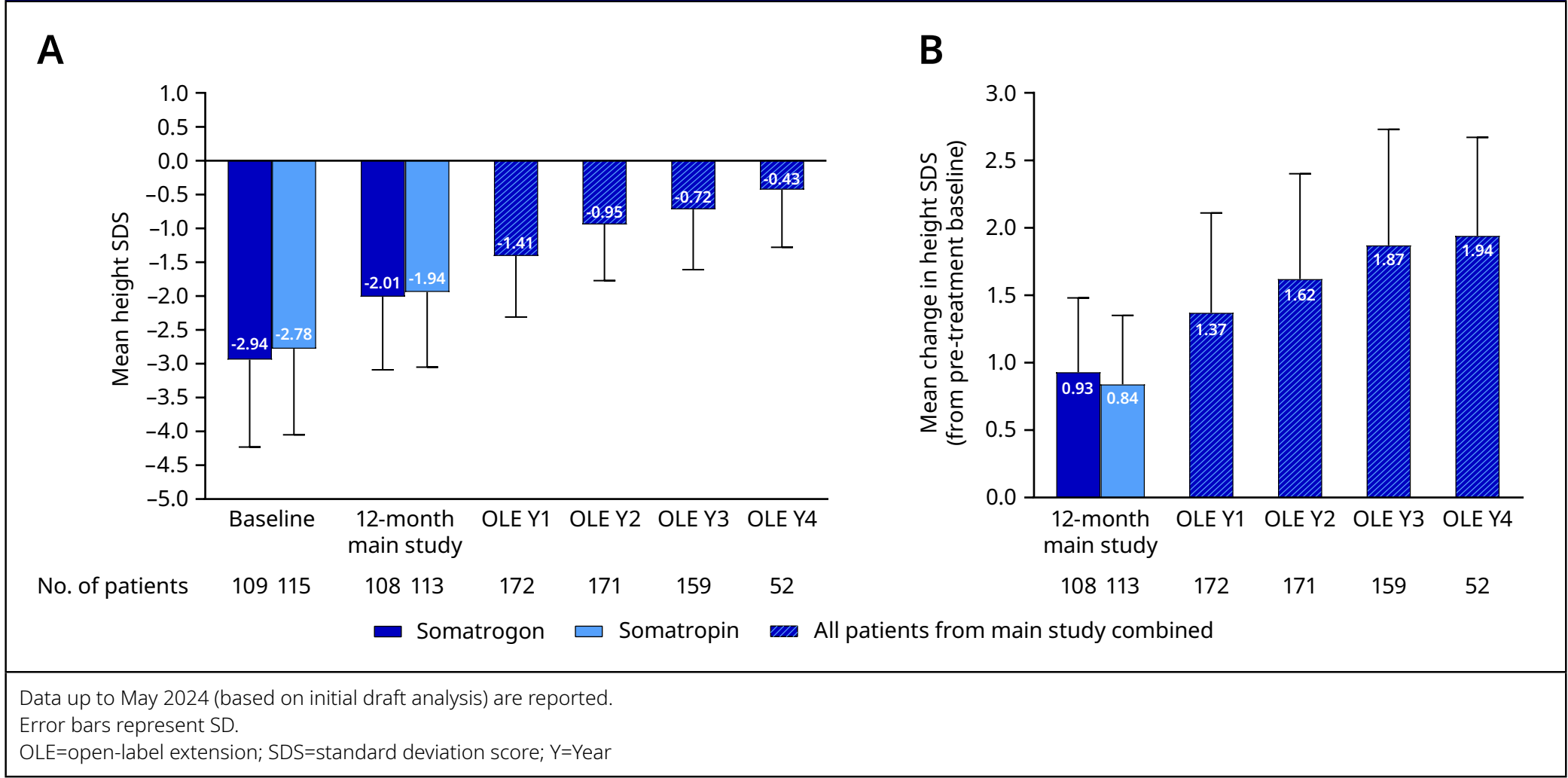
- At the end of the main study, somatrogen- and somatropin-treated patients had similar mean annualized HV and height SDS (**Figure 1** and **Figure 2**).

Figure 1: Mean annualized HV in each year (main study and OLE)



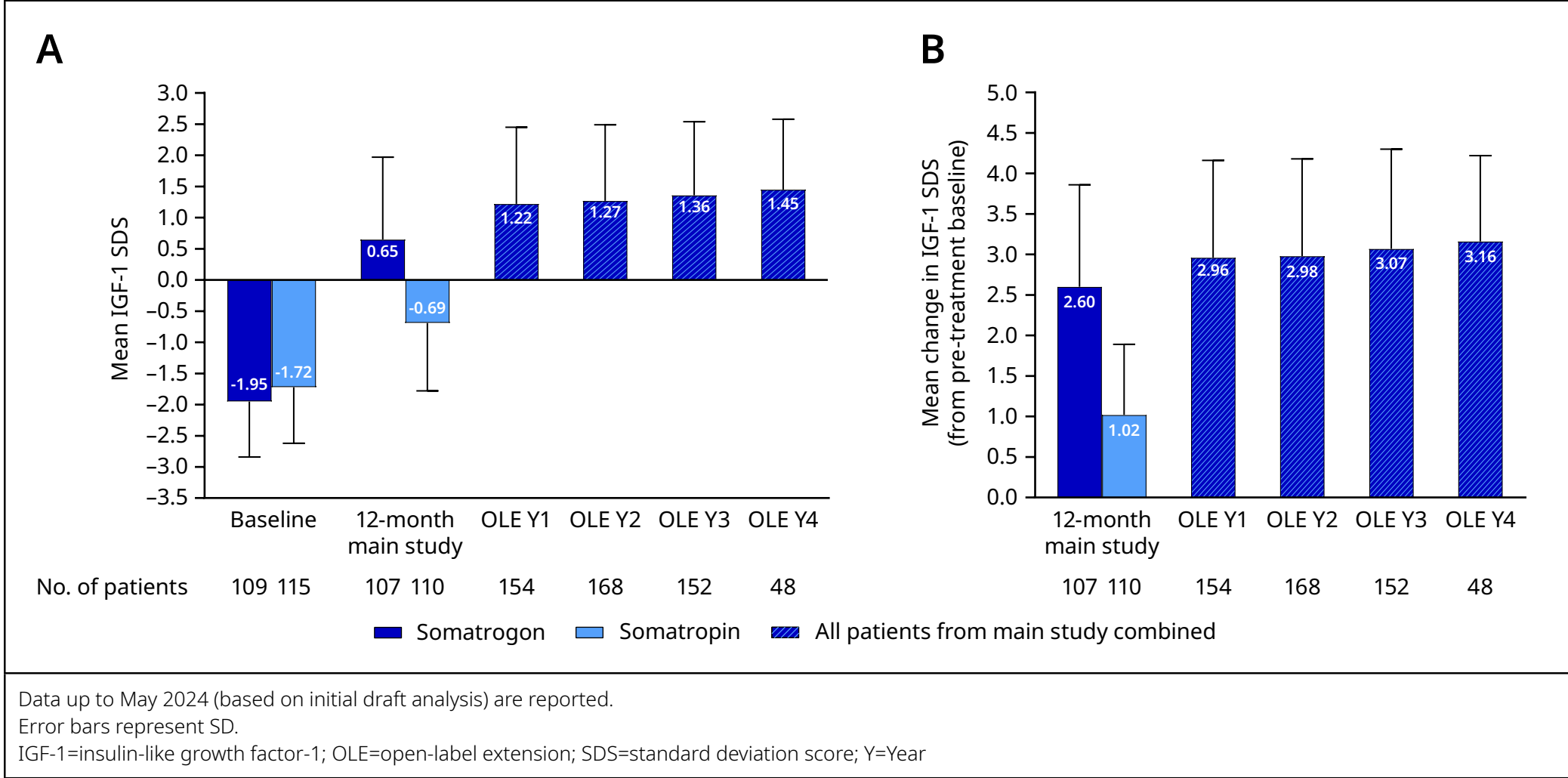
- During the OLE, mean annualized HV was 8.13, 7.88, 7.03, and 6.63 cm/y in Y1, Y2, Y3, and Y4, respectively (**Figure 1**); height SDS continued to increase in the OLE (**Figure 2**).
- The decrease in mean annualized HV during the OLE is consistent with patients approaching adult height.

Figure 2: (A) Mean height SDS and (B) mean change from baseline in height SDS at Month 12 of each year (main study and OLE)



- At the end of the main study period, mean IGF-1 SDS was 0.65 and −0.69 for somatrogen- and somatropin-treated patients, respectively (**Figure 3**).
 - At all time points in the OLE, mean IGF-1 SDS remained >1, and mean change in IGF-1 SDS was between 2.96 and 3.16 (**Figure 3**).

Figure 3: IGF-1 at Month 12 of each year (main study and OLE)



SAFETY

- During the main study, the incidence of adverse events (AEs) was 87.2% and 84.3% in somatrogen- and somatropin-treated patients, respectively.
 - The incidence of AEs in the first 3 years of the OLE was 71.2–72.2%; the incidence in OLE Y4 was substantially lower (54.3%) (**Table**).
- Across all 5 years, most AEs were mild to moderate in intensity, and the incidence of severe AEs in each year was <10% (**Table**).
- The most commonly reported AEs (≥10% of patients) were injection site pain, nasopharyngitis, headache, and pyrexia in the main study, and injection site pain in the OLE.
- Across 5 years, the most common AE was injection site pain, with an incidence of 39.4% (somatrogen) and 25.2% (somatropin) in the main study period and 27.8%, 16.5%, 14.7%, and 11.7% in OLE Y1, Y2, Y3, and Y4, respectively.
- The percentage of patients requiring dose reductions due to IGF-1 SDS >2 was 10.1% in the main study, 23.1% in OLE Y1, 19.3% in OLE Y2, and 17.6% in OLE Y3 (based on available data up to March 2022).

IMMUNOGENICITY

- Based on data available to date (up to OLE Y3), the percentage of patients testing positive for antidrug antibodies (ADAs) to somatrogen in each year was 77.1% (n=84/109) in the main study period, and 65.1% (n=138/212), 56.3% (n=99/176), and 55.9% (n=95/170) in OLE Y1, Y2, and Y3, respectively.
- The data available to date (up to OLE Y3) indicate that the presence of ADAs did not appear to have any effect on the efficacy or safety of somatrogen.

Table: Summary of all-causality TEAEs (main study and OLE)

n (%)	Main Study			OLE			
	Somatrogen n=109	Somatropin n=115	Total N=224	Y1 N=212	Y2 N=176	Y3 N=170	Y4 N=162
Number of AEs	868	570	1438	1078	499	516	437
Patients with AEs	95 (87.2)	97 (84.3)	192 (85.7)	153 (72.2)	127 (72.2)	121 (71.2)	88 (54.3)
Patients with serious AEs	3 (2.8)	2 (1.7)	5 (2.2)	10 (4.7)	1 (0.6)	1 (0.6)	3 (1.9)
Patients with severe AEs	9 (8.3)	6 (5.2)	15 (6.7)	12 (5.7)	5 (2.8)	2 (1.2)	0
Patients discontinued from the study due to AEs ^a	1 (0.9)	0	1 (0.4)	7 (3.3)	2 (1.1)	0	0
Patients discontinued study drug due to AE and continued study ^b	0	0	0	0	0	0	0
Patients with dose reduced or temporary discontinuation due to AE	3 (2.8)	2 (1.7)	5 (2.2)	8 (3.8)	2 (1.1)	4 (2.4)	4 (2.5)

Data up to May 2024 (based on initial draft analysis) are reported.
^aPatients with an AE record that indicates that the AE caused the patient to discontinue from the study.
^bPatients who have an AE record that indicates that action taken with study treatment was "drug withdrawn" but AE did not cause patient to be discontinued from the study.
AE=adverse event; OLE=open-label extension; TEAE=treatment-emergent adverse event; Y=Year

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