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Once-Weekly Somatrogon in Pediatric Growth Hormone Deficiency: Real-World Efficacy, Safety, and Quality-of-Life Findings

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ABSTRACT

Objective: To report real-world 6- and 12-month outcomes in children with growth hormone deficiency (GHD) treated with somatrogon or somatropin, including those who transitioned from somatropin to somatrogon.

Methods: Eligible patients were categorized into three groups [somatrogon-naïve (naïve), somatrogon-switch (switch), and somatropin only] and were followed for 6 or 12 months. Bioimpedance analysis, as well as a standardized, age-appropriate assessment of the Pediatric Quality of Life Inventory (PedsQL), the Child Behavioural Checklist (CBCL) and the Multidimensional Scale of Perceived Social Support (MSPSS), were conducted at baseline and month 6 in the naïve and switch groups. Psychiatric evaluations were also performed according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) criteria.

Results: A total of 58 patients (58.6% male) were included (naïve: n=20; switch: n=18; somatropin: n=20). Mean ages were 11.1±3.0, 9.7±3.4, and 10.5±3.2 years, respectively. After 12 months, mean changes in height standard deviation score (Δheight SDS) were 0.6±0.3, 0.7±0.3, and 0.7±0.4; and height velocities were 10.0±1.9, 9.1±1.7, and 9.8±1.9 cm/year, respectively. Corresponding increases in IGF-1 SDS (ΔIGF-1 SDS) were 2.2±1.2, 0.9±1.2, and 1.3±1.0, respectively. Among the 38 patients receiving somatrogon, 15.8% (n=6; 3 naïve, 3 switch) developed IGF-1 SDS >+2 during follow-up, managed successfully with observation or dose adjustment. No serious adverse events were observed. Bioimpedance analyses demonstrated a favorable but non-significant trend toward improved body composition in somatrogon-naïve children. At six months, PedsQL domains, CBCL scales, and MSPSS scores remained stable (all p>0.05).

Conclusion: Once-weekly somatrogon demonstrated efficacy and safety comparable to daily somatropin with stable quality-of-life and psychosocial outcomes in children with GHD.

Keywords: Children, growth hormone, growth hormone deficiency, long-acting growth hormone

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What is already known on this topic?

Somatropin is the standard treatment for growth hormone deficiency (GHD), but daily injections may reduce adherence and quality-of-life. Somatrogon, a once-weekly long-acting growth hormone analog, has demonstrated non-inferior efficacy and comparable safety to somatropin in clinical trials. Real-world data on somatrogon use in clinical practice, especially in children switching from somatropin, remain limited.

What this study adds?

This real-world study compared somatrogon and somatropin over 6 and 12 months in children with GHD. Somatrogon demonstrated comparable growth outcomes, insulin-like growth factor-1 dynamics, and safety to somatropin. Bioimpedance analyses suggested favorable changes in body composition, quality-of-life scores remained stable, supporting the potential of somatrogon to reduce treatment burden without compromising efficacy or safety.

Introduction

Growth hormone (GH) deficiency (GHD) is characterized by inadequate production or secretion of GH, resulting in decreased height velocity (HV), impaired linear growth, and short stature (1). Beyond its impact on physical development, GHD may adversely affect emotional and social well-being and is associated with metabolic disturbances, including dyslipidemia, insulin resistance, and increased cardiovascular risk (1,2). GH and insulin-like growth factor-1 (IGF-1) also contribute to hematopoiesis, promoting platelet formation and erythropoiesis through stimulation of renal erythropoietin production (3).

Recombinant human GH (rhGH) has been the standard treatment for nearly four decades, effectively improving growth parameters, optimizing adult height, reducing metabolic risk, and enhancing quality-of-life (QoL) (4,5,6). However, conventional rhGH regimens require daily subcutaneous injections, imposing a significant treatment burden (4). A systematic review reported that up to 71% of children demonstrate suboptimal adherence to therapy, potentially compromising treatment outcomes (7). In recent years, long-acting GH (LAGH) preparations have been developed to improve adherence and treatment satisfaction. Several of these formulations have now received regulatory approval (8). Somatrogon, a once-weekly rhGH analog approved for use in children aged three years and older with GHD, has demonstrated efficacy and safety comparable to daily somatropin, with additional benefits in treatment satisfaction and QoL (1,4).

Despite encouraging results from randomized clinical trials, real-world evidence concerning somatrogon use remains limited. Such data are essential to evaluate treatment adherence, effectiveness, and safety in routine clinical settings. Therefore, the primary objective of this study was to present 6- and 12-month real-world outcomes in children with GHD who initiated somatrogon, switched from daily somatropin to somatrogon, or continued somatropin.

Methods

Study Design and Population

This single-center study was conducted at the Clinic of Pediatric Endocrinology, Aydın Adnan Menderes University Faculty of Medicine. The analysis was conducted using a retrospective review of prospectively collected data, allowing consistent follow-up and standardized assessments. Between June 1, 2024, and June 1, 2025, children aged 3-18 years with a confirmed diagnosis of GHD who either newly initiated somatrogon therapy, transitioned from somatropin to somatrogon, or continued somatropin treatment were enrolled. Follow-up evaluations were performed at baseline, 6 months, and 12 months.

Inclusion and Exclusion Criteria

Inclusion criteria: Confirmed GHD diagnosis; chronological age ≥3 years; peak GH ≤10 ng/mL in two stimulation tests (clonidine and L-dopa); bone age (BA) delay ≥2 years in prepubertal children at the initiation of GH therapy or BA ≤ chronological age in pubertal children; normal karyotype in females; annual HV standard deviation score (SDS) <-0.7 SDS at the initiation of GH therapy; and IGF-1 SDS ≤-1 at the initiation of GH therapy.

The peak GH ≤10 ng/mL cut-off was based on the diagnostic criteria applied in routine clinical practice during the study period and is consistent with thresholds used in pivotal phase 3 growth hormone trials (4). Although lower thresholds have been suggested in more recent guidelines, this criterion was maintained to ensure methodological consistency across retrospectively and prospectively included patients.

Exclusion criteria: age <3 or >18 years; chromosomal abnormalities or syndromic conditions (e.g., Turner syndrome, Prader-Willi syndrome, Noonan syndrome, Silver-Russell syndrome, SHOX mutations/deletions, ACAN mutations, skeletal dysplasias); chronic illnesses (e.g., chronic kidney disease, celiac disease); malignancy, radiotherapy, or chemotherapy; history of being born small for gestational age; Body mass index (BMI) <-2 SDS; positive anti-rhGH antibodies; or psychosocial dwarfism.

Group Allocation

Participants were categorized into three groups based on treatment status:

Somatrogon-naïve group: Treatment-naïve patients who initiated once-weekly somatrogon therapy.

Somatrogon-switch group: Patients who transitioned from somatropin to once-weekly somatrogon.

Somatropin group: Patients who continued daily somatropin therapy.

Treatment Protocol

Somatrogon was administered at a dose of 0.66 mg/kg/week on a fixed weekly schedule, whereas the somatropin dose was 0.025-0.035 mg/kg/day. Both treatments were delivered using multidose prefilled pens equipped with 31G, 5 mm disposable pen needles. Missed somatrogon doses were administered within three days or omitted if more than three days had elapsed. Doses were adjusted based on body weight and IGF-1 SDS targeting levels between -2 to +2 (ideally near 0). In cases of persistently elevated IGF-1 >+2 SDS, the dose was reduced by 15% and reassessed after 4-8 weeks.

Follow-up and Assessments

At each visit, vital signs, auxological parameters (height, weight, BMI, HV cm/year, HV SDS), pubertal staging according to Tanner criteria (9,10), adverse events, and laboratory results were recorded. Laboratory evaluations included complete blood count, liver and kidney function tests, electrolytes, hemoglobin A1c (HbA1c), fasting glucose, insulin, C-peptide, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, free thyroxine, thyroid-stimulating hormone, cortisol, calcium, phosphate, alkaline phosphatase, 25-hydroxyvitamin D, parathyroid hormone, IGF-1, and IGF binding protein-3 (IGFBP3).

Height was measured using a Harpenden stadiometer (Holtain Ltd., Crymych, UK) and weight with a calibrated digital scale. SDS values for height, weight, BMI, and HV were calculated based on national reference data using the Child Metrics system (www.ceddcozum.com) (11,12).

Bone age was assessed at baseline, 6, and 12 months using the Greulich and Pyle digital atlas (13) by a single experienced pediatric endocrinologist to ensure consistency and minimize interobserver variability, and BA SDS was calculated using the BA software (14).

IGF-1 and IGFBP3 concentrations were measured using a chemiluminescence immunoassay (CLIA) with the IMMULITE 2000 XP Immunoassay System (Siemens Healthineers, Erlangen, Germany; Siemens Healthcare Sağlık A.Ş. İstanbul, Türkiye) IGF-1 SDS values were calculated based on age- and sex-specific reference ranges. In the somatrogon naïve and switch groups, blood sampling for IGF-1 measurement was standardized at 96 hours post-injection. When samples were drawn outside this time window, appropriate time-adjusted corrections were applied during SDS calculation (15).

Bioelectrical impedance analysis (InBody 230, Biospace Co., Seoul, South Korea) was conducted at baseline and at 6 months in the somatrogon naïve and switch groups to assess body composition parameters, including body fat percentage and skeletal muscle mass percentage.

QoL and Psychosocial Measures

Turkish versions of the Pediatric QoL Inventory (PedsQL), the Child Behavior Checklist (CBCL), and the Multidimensional Scale of Perceived Social Support (MSPSS), each supported by original development studies and Turkish validation studies, were administered at baseline and after six months, under the supervision of a child and adolescent psychiatrist (16,17,18,19,20,21). For children aged 3-7, the PedsQL and CBCL were completed by parents, with the PedsQL additionally administered as a structured interviewer-assisted child form in the 5-7 years age-group. For children aged ≥8 years, PedsQL was collected via both child self-report and parent proxy, while CBCL remained parent-reported. MSPSS was self-reported in children aged ≥8 years. The PedsQL items were reverse-coded and linearly transformed (0/1/2/3/4→100/75/50/25/0), with higher scores indicating better QoL. The PedsQL is a tool designed to assess physical, emotional, social, and school functioning in children and adolescents (16,17). The CBCL utilises a structured assessment approach, evaluating a range of syndrome scales and broad-band composites. These include scales such as Anxiety/Depression, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking, and Aggressive Behaviours. Higher CBCL scores are indicative of a greater number of problematic behaviours (18,19). MSPSS provided Family, Friends, Significant Other, and Total scores (20,21). At 0 and 6 months, child and adolescent psychiatrist performed DSM-5-TR clinical evaluations (e.g., ADHD, ASD, intellectual disability, developmental language disorder). These diagnoses informed pre-specified sensitivity analyses (excluding any psychiatric diagnosis) and descriptive subgroup summaries. The somatropin group consisted of patients whose first-year treatment data were included retrospectively as part of the overall comparative evaluation of growth and safety outcomes. QoL and psychosocial questionnaires were not routinely administered during the earlier somatropin treatment period; therefore, retrospective QoL data were not available

for the somatropin group. QoL analyses were conducted prospectively in the naïve and switch groups using within-group paired comparisons (baseline vs. 6 months), and change scores were compared between these two groups.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Aydın Adnan Menderes University (approval no.: 2025/23, date: 30.01.2025) and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians and assent was obtained from pediatric participants when appropriate, in accordance with age and national regulations. Where applicable, written informed consent for publication was also obtained.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences, version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as frequencies and percentages for categorical variables, and as means with standard deviations for continuous variables with normal distribution. For non-normally distributed continuous variables, data are presented as medians with minimum and maximum values. The normality of continuous variables was assessed using descriptive statistics, Skewness and Kurtosis coefficients, histograms, and the Kolmogorov-Smirnov test. The chi-square test was used to compare categorical variables. For comparisons between two independent groups, the independent samples t-test and Cohen's d were applied when criteria for normality were met, and the Mann-Whitney U test and Cliff's delta were used otherwise. A Type I error rate of 5% was considered acceptable, and $p<0.05$ was regarded as statistically significant.

Results

A total of 58 patients were included: somatrogon-naïve (n=20), somatrogon-switch (n=18), and somatropin (n=20) groups. Age, sex distribution, and pubertal status were comparable among the three groups (Table 1). Significant differences were observed in height SDS, HV, HV SDS, IGF-1 SDS, L-dopa peak GH response, and starting dose. Height SDS, HV, HV SDS, and IGF-1 SDS were

Table 1. Baseline characteristics of the study groups

Characteristic	Somatrogon-naïve (n=20)	Somatrogon-switch (n=18)	Somatropin (n=20)	p value
Age (years)	11.1±3.0	9.7±3.4	10.5±3.2	0.411
Sex (F/M), n (%)	10/10 (50)	5/13 (27.8/72.2)	9/11 (45/55)	0.351
Prepubertal/Pubertal, n (%)	9/11 (45/55)	11/7 (61.1/38.9)	9/11 (45/55)	0.525
Height SDS	-3.0±0.8	-1.8±0.6	-2.7±0.5	<0.001
Weight SDS	-2.0±1.0	-1.4±0.8	-1.6±1.3	0.258
BMI SDS	-0.4±0.9	-0.6±0.9	-0.2±1.2	0.381
Target height SDS	-1.0±0.7	-1.0±0.9	-1.1±1.0	0.952
Bone age (years)	9.0±3.3	7.9±3.5	8.2±3.4	0.606
Bone age SDS	-2.3±1.0	-1.9±0.8	-2.4±1.0	0.214
Height velocity (cm/year)	2.9±1.1	6.9±2.2	2.5±0.8	<0.001
Height velocity SDS	-2.0±0.8	0.5±1.3	-2.4±1.3	<0.001
IGF-1 (ng/mL)	105.9±59.5	151.0±89.2	115.7±73.0	0.159
IGF-1 SDS	-1.9±0.9	-0.9±0.9	-1.8±0.6	<0.001
IGFBP-3 (µg/mL)	4.1±1.6	4.3±1.7	NA	0.845
Clonidine peak GH (ng/mL)	4.2±2.9	5.5±2.2	4.9±3.1	0.380
L-dopa peak GH (ng/mL)	2.6±2.5	5.0±3.0	3.1±1.9	0.010
Pituitary MRI, normal, n (%) MRI, abnormal, n (%)*	17 (85) 3 (15)	13 (72.2) 5 (27.8)	16 (80) 4 (20)	0.661
Panhypopituitarism, n (%)	0 (0)	0 (0)	1 (5)	1.000
Starting dose	0.66 mg/kg/week	0.66 mg/kg/week	0.030±0.003 mg/kg/day	<0.001

Values are presented as mean ± SD unless otherwise indicated. In the somatrogon-switch group, auxological and IGF-1 data represent values recorded at the time of switching from daily somatropin to once-weekly somatrogon. Growth hormone stimulation test results, including clonidine and L-dopa peak GH responses, represent diagnostic values obtained before initiation of any growth hormone treatment. Starting doses are presented according to the dosing schedule of each treatment: mg/kg/week for somatrogon and mg/kg/day for somatropin.

*Abnormal findings included empty sella (n=4), ectopic posterior pituitary (n=3), stalk interruption (n=2), pituitary hypoplasia (n=2), and adenoma (n=1).

F, female; M, male; n (%), number (percentage); SDS, standard deviation score; BMI, body mass index; IGF-1, insulin-like growth factor-1; ng/mL, nanogram per milliliter; IGFBP-3, Insulin-like growth factor binding protein-3; µg/mL, microgram per milliliter; NA, not available; GH, growth hormone; MRI, magnetic resonance imaging

higher in the somatrogon-switch group, which consisted of patients who had previously received daily somatropin treatment before switching to once-weekly somatrogon. Therefore, baseline auxological and IGF-1 data in the somatrogon-switch group refer to the time of somatrogon initiation rather than treatment-naïve status. Growth hormone stimulation test results, including clonidine and L-dopa peak GH responses, represent diagnostic values obtained before the initiation of any growth hormone treatment. Mean weight and BMI SDS values were within the expected ranges for children with GHD. Pituitary MRI findings are detailed in Table 1. Most patients (79.3%) had normal pituitary MRI scans, while isolated structural abnormalities, including empty sella, ectopic posterior pituitary, stalk interruption, and pituitary hypoplasia, were observed in a minority of cases. The mean starting dose was 0.66 mg/kg/week for somatrogon in both the naïve and switch groups and 0.030±0.003 mg/kg/day for somatropin in the somatropin group. The difference in starting dose reflects the distinct dosing schedules of once-weekly somatrogon and daily somatropin. Baseline demographic, auxological, biochemical, and radiological characteristics of the study groups are presented in Table 1.

Treatment Outcomes at 6 and 12 Months

Changes in height SDS, HV (cm/year) and IGF-1 SDS for all three study groups (somatrogon-naïve, somatrogon-switch, and somatropin) at baseline, week 6, and months 3, 6, 9, and 12 are illustrated in Figures 1, 2, and 3. Based on these data, 6- and 12-month outcomes were analyzed; the primary comparison was performed between the somatrogon-naïve and somatropin groups. As summarized in Table 2, both the somatrogon-naïve and somatropin groups demonstrated comparable improvements in growth parameters at 6 and 12 months. Accordingly, in the paired values presented below, the first value refers to the somatrogon-naïve group and the second value refers to the somatropin group. At 6 months, increases in height SDS (0.4±0.3 vs 0.5±0.3; p=0.25), HV (10.8±2.5 vs 11.3±3.0 cm/year; p=0.61), and IGF-1 SDS (1.9±1.3 vs 1.4±0.9; p=0.16) were similar between

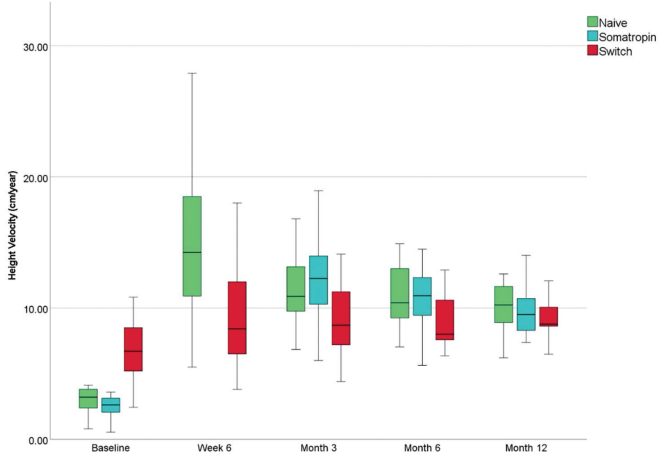

Figure 2. Height velocity (cm/year) at baseline, week 6 and months 3, 6, 9, and 12 in the three study groups. Median values are shown as horizontal lines, and mean values are indicated by diamond symbols naive, treatment-naïve patients who initiated somatrogon; somatropin, patients who continued daily somatropin treatment; switch, patients who transitioned from somatropin to somatrogon

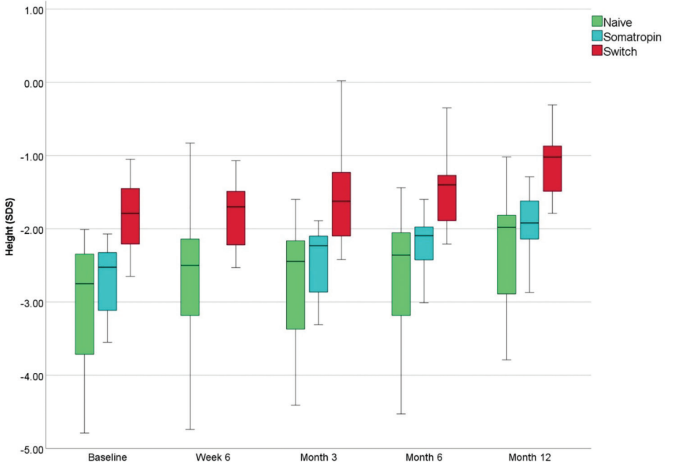

Figure 1. Height SDS at baseline, week 6 and months 3, 6, 9, and 12 in the three study groups. Median values are shown as horizontal lines, and mean values are indicated by diamond symbols

SDS, standard deviation score; naive, treatment-naïve patients who initiated somatrogon; somatropin, patients who continued daily somatropin treatment; switch, patients who transitioned from somatropin to somatrogon

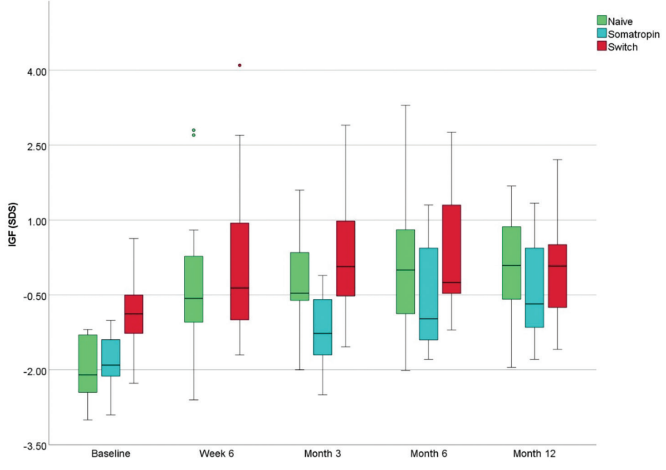

Figure 3. IGF-1 SDS at baseline, week 6 and months 3, 6, 9, and 12 in the three study groups. Median values are shown as horizontal lines, and mean values are indicated by diamond symbols

IGF-1, insulin-like growth factor-1; SDS, standard deviation score; naive, treatment-naïve patients who initiated somatrogon; somatropin, patients who continued daily somatropin treatment; switch, patients who transitioned from somatropin to somatrogon

groups. At 12 months, Δheight SDS (0.6±0.3 vs 0.7±0.4; p=0.78), HV (10.0±1.9 vs 9.8±1.9 cm/year; p=0.73), and ΔBA SDS (0.6±0.5 vs 0.6±0.7; p=0.91) remained comparable, whereas the increase in IGF-1 SDS was significantly greater in the somatrogon-naive group (2.2±1.2 vs 1.3±1.0; p=0.03).

No significant differences were observed between groups regarding BMI SDS, BA SDS, pubertal progression, or safety outcomes. A sensitivity analysis was performed excluding the naïve patient with an IGF-1 SDS value >+2 at year 1. After exclusion, the between-group difference was attenuated and no longer reached conventional statistical significance (p=0.051). However, the mean ΔIGF-1 SDS in the naïve group remained 2.1±1.0, and the effect size remained moderate-to-large (Cohen's d=0.733).

Switch Group Outcomes

In the switch group, treatment outcomes during the first year on daily somatropin were compared with those from the first year after transitioning to once-weekly somatrogon (Table 3). Growth and biochemical responses were comparable across both treatment periods. Mean HV remained unchanged (9.1±2.1 vs 9.1±1.7 cm/year; p=0.45), as did HV SDS (2.0±1.6 vs 2.0±0.9; p=1.00). Changes in height SDS (0.8±0.7 vs 0.6±0.3; p=0.99), IGF-1 SDS (0.9±1.0 vs 0.9±1.2; p=0.53), and BA SDS (0.6±1.5 vs 0.2±0.5; p=0.45) were also similar between phases.

QoL, Emotional-Behavioral, and Social Support

Paired analyses from baseline to 6 months demonstrated no significant change after Holm correction in PedsQL Total or domain scores in either the naïve or switch groups. A trend towards improvement was observed for the PedsQL Psychosocial Health Summary in the naïve subgroup (Δ≈+6.2 points; *p*=0.058), which did not survive multiplicity. The CBCL syndrome scales (anxiety/depression, social withdrawal, somatic, social problems, thought problems, attention, rule-breaking, aggression), and broad-band internalizing/externalizing totals demonstrated no significant change (p>0.05). The MSPSS scores for family/friends/significant other and total also did not change materially from the baseline (p>0.05). Sensitivity analyses that excluded children with any psychiatric diagnosis yielded similar point estimates and inferences, indicating that stable QoL/CBCL/MSPSS findings were not driven by comorbidity. In the naïve group, 85.0% (17/20) had no psychiatric diagnosis; 10.0% (2/20) had ADHD; and 5.0% (1/20) had moderate intellectual disability. Within the switch group, 88.9% (16/18) had not received a diagnosis; 5.6% (1/18) had been diagnosed with ADHD; and 5.6% (1/18) had been diagnosed with developmental language disorder. No significant differences in change scores from baseline to 6 months were observed between the naïve and switch groups.

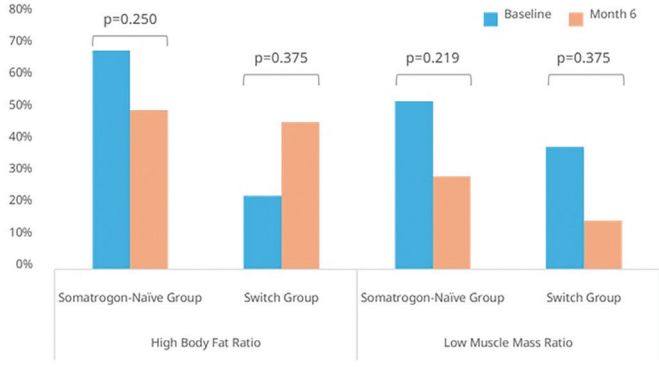

Figure 4. Body composition changes at baseline and month 6 in the somatrogon-naïve and switch groups (p values shown above bars). p<0.05 was considered statistically significant. Somatrogon-naïve, treatment-naïve patients who initiated somatrogon; switch, patients who transitioned from somatropin to somatrogon

Table 2. Comparison of treatment outcomes at 6 and 12 months in the naïve and somatropin groups

Timepoint	Outcome	Naïve	Somatropin	p value	Effect size Cohen's d
6 months	ΔHeight SDS	0.4±0.3 (n=20)	0.5±0.3 (n=20)	0.253	0.367
	HV (cm/year)	10.8±2.5	11.3±3.0	0.614	0.161
	HV SDS	2.8±1.8	2.9±2.3	0.799	0.050*
	ΔIGF-1 SDS	1.9±1.3	1.4±0.9	0.155	0.472
	ΔBA SDS	0.2±0.3	0.2±0.3	0.620	0.092*
12 months	ΔHeight SDS	0.6±0.3 (n=16)	0.7±0.4 (n=19)	0.783	0.094
	HV (cm/year)	10.0±1.9	9.8±1.9	0.728	0.116
	HV SDS	2.4±1.4	2.2±1.5	0.589	0.098*
	ΔIGF-1 SDS	2.2±1.2	1.3±1.0	0.025	0.836
	ΔBA SDS	0.6±0.5	0.6±0.7	0.909	0.108

Values are presented as mean±SD. Δ Indicates change from baseline. p<0.05 was considered statistically significant. *Cliff's delta
n, number; SDS, standard deviation score; HV, height velocity; IGF-1, insulin-like growth factor-1; BA, bone age

Table 3. Switch group outcomes: somatropin first year compared to somatrogon first year

Parameter	Somatropin 1st year	Somatrogon 1st year post-switch	p value	Effect size
HV (cm/year)	9.1±2.1	9.1±1.7	0.453	0.311
HV SDS	2.0±1.6	2.0±0.9	0.995	0.003
ΔHeight SDS	0.8±0.7	0.6±0.3	0.989	0.006
ΔIGF-1 SDS	0.9±1.0	0.9±1.2	0.530	0.043
ΔBA SDS	0.6±1.5	0.2±0.5	0.445	0.317

Values are presented as mean±SD. Δ indicates change from baseline. $p<0.05$ was considered statistically significant
HV, height velocity; SDS, standard deviation score; IGF-1, insulin-like growth factor-1; BA, bone age

Body Composition Outcomes

In the somatrogon-naïve group, bioimpedance analyses demonstrated a favorable but non-significant trend toward improved body composition: the proportion of patients with high body fat decreased from 68.8% to 50% (p=0.25), while those with low muscle mass declined from 52.9% to 29.4% (p=0.22). In the switch group, high body fat was observed in 23.1% of patients at baseline, increasing to 46.2% at month 6 (p=0.38), whereas low muscle mass decreased from 38.5% to 15.4% (p=0.38) (Figure 4).

Safety and Tolerability

Among 38 patients receiving somatrogon, 15.8% (n=6; 3 naïve, 3 switch) developed IGF-1 SDS values >+2 during follow-up. Four cases were detected at week 6; two normalized spontaneously by month 3, while two required sequential 15% dose reductions, achieving normalization by month 12. In two cases, elevated levels were detected at month 12, with spontaneous normalization observed six weeks later. No deaths occurred during the study, and overall treatment adherence was high. One patient in the naïve group discontinued treatment at month 6 due to personal choice. No treatment-related adverse events were reported in the somatropin group (n=20). Among patients treated with somatrogon, treatment-related adverse events were observed in 50% (n=19), most commonly injection-site pain (n=10), followed by lipoatrophy (n=3), injection-site pruritus (n=2), minor bleeding (n=2), localized swelling (n=2), myalgia (n=1), and headache (n=1). All events were mild and transient. Lipoatrophy developed in patients who consistently injected into the same anatomical region, particularly the upper arm. Discontinuing injections at the affected site and rotating to alternative regions (thighs, abdomen, or buttocks) resulted in complete resolution within 3 months. No treatment interruptions or discontinuations were necessary because of adverse events.

Discussion

This single-center study provides real-world evidence on the use of once-weekly somatrogon in children with GHD. Somatrogon demonstrated efficacy comparable to that of daily somatropin, as reflected by similar gains in height SDS and HV at both 6 and 12 months. Biochemical outcomes, including ΔIGF-1 SDS and ΔBA SDS, also showed parallel trends between treatment groups.

Our findings align closely with phase 3 randomized controlled trials demonstrating that once-weekly somatrogon was non-inferior to daily somatropin in efficacy and safety (4,22). Those trials reported comparable improvements in height SDS, HV, ΔIGF-1 SDS, and ΔBA SDS after 12 months, findings mirrored in our real-world cohort. Long-term extension studies have further confirmed the sustained efficacy and safety of somatrogon over five years, supporting its role as a durable therapeutic option (23). Furthermore, in the switch group, growth and biochemical responses observed during the first year of somatrogon therapy were comparable to those achieved in the preceding year of somatropin treatment, highlighting the feasibility, safety, and clinical stability of transitioning patients from daily to once-weekly dosing.

Beyond clinical trials, systematic reviews and meta-analyses have shown that LAGH analogs achieve comparable growth outcomes to daily GH while improving adherence and treatment satisfaction (24,25). Economic modeling from Spain further suggested potential cost-effectiveness through improved compliance and reduced treatment burden (26). Likewise, global surveys of physicians participating in phase 3 trials highlighted high satisfaction with once-weekly somatrogon, particularly due to convenience and reduced injection frequency (27). In our cohort, adherence and satisfaction were uniformly high, with only one patient electing to discontinue therapy at month 6.

Clinical trial data have emphasized the importance of IGF-1 surveillance during somatrogon treatment. Phase II and III studies reported dose-dependent increases in IGF-1 SDS, occasionally exceeding +2 SDS and necessitating dose adjustment, particularly in the Japanese phase III trial, while such elevations were not observed with somatropin (4,22,28). Transient IGF-1 elevations (IGF-1 SDS >+2) were observed in 15.8% (6/38) of patients treated with somatrogon in the present study, most frequently during the initial weeks of therapy. In four patients, levels normalized spontaneously or following minor dose adjustment, whereas two additional cases identified

at 12 months were scheduled for reassessment. These findings indicate that short-term IGF-1 fluctuations are not uncommon but can be effectively managed through routine biochemical monitoring and timely titration. In addition, although a greater increase in IGF-1 SDS was observed in the naïve group, sensitivity analysis excluding a single elevated value attenuated statistical significance while preserving a moderate-to-large effect size, suggesting that the overall trend was not solely driven by an outlier. However, the long-term clinical significance of these transient elevations remains uncertain, underscoring the need for continued surveillance to clarify their potential impact on metabolic outcomes and overall treatment safety. Of note, one patient in our cohort maintained low IGF-1 SDS despite adequate growth velocity. Although neutralizing antibody testing was unavailable, prior long-term studies suggest that non-neutralizing antibodies do not compromise clinical efficacy (23).

The overall safety profile in this study was consistent with the existing literature with all adverse events being mild and transient (4,22,23,28). Injection-site pain was the most frequently reported complaint, while lipoatrophy was observed in three somatrogon-treated patients, all instances of which were related to repeated injections into the same anatomical region, and these resolved fully after rotation of injection sites. Similar cases have been described with both daily rhGH and somatrogon therapy (29,30), reiterating the importance of patient education on injection technique and site rotation. No treatment interruptions or discontinuations were required.

Recent research has also focused on the broader dimensions of GH therapy, including psychosocial and metabolic well-being (1,31). In this context, our bioimpedance analysis provides additional insight into body composition changes in somatrogon-treated naïve children and revealed favorable trends. The concomitant increase in both muscle and fat mass in the switch group may be related to the short follow-up duration and the small sample size. Evaluating the long-term effects in a larger population would help clarify this finding. Although QoL measures remained stable, longer follow-up may be needed to capture potential benefits of reduced injection burden on emotional and social functioning, not only for children themselves but also for their parents/caregivers and possibly other family members. Collectively, evidence from randomized trials, systematic reviews, and real-world data, including the present study, supports somatrogon as a safe, effective, and well-tolerated alternative to daily GH therapy. Our findings extend existing evidence by incorporating exploratory parameters, such as body composition and QoL assessments in children receiving somatrogon treatment, including both somatrogon-naïve and somatrogon-switch patients. Although body composition changes did not reach statistical significance, these data provide preliminary insight into the broader effects of somatrogon treatment and should be interpreted cautiously and confirmed in larger studies with longer follow-up.

In this cohort, once-weekly somatrogon was found to maintain QoL and psychosocial stability over a period of six months, as determined by the administration of age-appropriate, validated instruments under the supervision of a psychiatrist. The absence of deterioration on PedsQL and CBCL is consistent with reports that LAGH can reduce treatment burden without adversely affecting psychosocial functioning (1,8,31). Standardized psychiatric evaluations and sensitivity analyses mitigate the concern that unmeasured comorbidity may obscure true change. The near-significant trend in PedsQL Psychosocial domain scores among naïve patients may be indicative of a patient-perceived benefit that warrants testing in larger, longer studies with 12-month QoL endpoints.

Study Limitations

This study has several limitations. It was conducted in a single center with a relatively small sample size, limiting generalizability. The follow-up duration was short, and longer-term data are required to confirm durability of efficacy and safety. Neutralizing antibody testing was unavailable, precluding assessment of potential immunogenicity. Finally, QoL and body composition analyses were exploratory, warranting confirmation in larger and longer studies. However, the study has several strengths. It represents a real-world evaluation of once-weekly somatrogon in pediatric GHD, including both treatment-naïve and switch populations. The inclusion of standardized follow-up visits, bioimpedance analysis, and validated QoL assessments provided a comprehensive evaluation of treatment effects beyond traditional growth parameters. Furthermore, all patients were managed in a single tertiary center by the same multidisciplinary team, ensuring consistency in clinical practice.

Conclusion

In this real-world study, once-weekly somatrogon demonstrated growth outcomes comparable to daily somatropin over 6 and 12 months. Within the limitations of this single-center study with a relatively small sample size and limited follow-up duration, short-term safety findings were comparable between treatments. Transient IGF-1 elevations were managed through observation or dose adjustment, and no serious adverse events were observed during the study period. Bioimpedance analyses suggested favorable changes in body composition, while QoL outcomes remained stable. These findings suggest that somatrogon may represent a clinically effective and well-tolerated alternative to daily GH therapy in pediatric GHD. However, larger multicenter studies with longer follow-up are required to confirm long-term efficacy and safety.

Ethics

Ethics Committee Approval: The study was approved by the Institutional Ethics Committee of Aydın Adnan Menderes University (approval number: 2025/23, date: 30.01.2025).

Informed Consent: Written informed consent was obtained from parents or legal guardians and assent was obtained from pediatric participants when appropriate, in accordance with age and national regulations. Where applicable, written informed consent for publication was also obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Kübra Şen Küçük, Ahmet Anık, Concept: Kübra Şen Küçük, Ahmet Anık, Design: Ahmet Anık, Data Collection or Processing: Kübra Şen Küçük, Sebla Güneş, Mustafa Dinçer, Tolga Ünüvar, Ahmet Anık, Analysis or Interpretation: Kübra Şen Küçük, Mustafa Dinçer, Sercan Öztürk, Ahmet Anık, Literature Search: Kübra Şen Küçük, Mustafa Dinçer, Ahmet Anık, Writing: Kübra Şen Küçük, Mustafa Dinçer, Sercan Öztürk, Ahmet Anık.

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