Original Article

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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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What is already known on this topic?
Somatropin is the standard treatment for GHD, but daily injections may reduce adherence and quality of life. Somatrogon, once-weekly long-acting GH 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, IGF-1 dynamics, safety to somatropin. Bioimpedance analyses suggested favorable changes in body composition, quality-of-life scores remained stable, supporting somatrogon's potential to reduce treatment burden without compromising efficacy or safety.

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—and were followed for 6 or 12 months. Bioimpedance analysis, as well as a standardised, 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 SDS (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: chilren; growth hormone; growth hormone deficiency; long-acting growth hormone.

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Introduction

Growth hormone deficiency (GHD) is characterized by inadequate production or secretion of growth hormone (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 on 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 Pediatric Endocrinology Clinic of 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 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 somatropin at 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, 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 Insulin-like Growth Factor 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 an experienced single 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 (Immulite 2000 R, Siemens). 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.

Quality of Life and Psychosocial Measures

Turkish versions of the Pediatric Quality of Life Inventory (PedsQL), the Child Behavior Checklist (CBCL), and the Multidimensional Scale of Perceived Social Support (MSPSS) were administered at baseline and after six months, under the supervision of a child and adolescent psychiatrist. 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 5–7 years. For children aged ≥8, PedsQL was collected via both child self-report and parent proxy, while CBCL remained parent-reported. MSPSS was self-reported in children aged ≥8. 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. 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 Approval

The study was approved by the Institutional Ethics Committee of Aydın Adnan Menderes University (approval number: 2025/23) 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 (SPSS) version 27.0 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp).Descriptive statistics were 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 were 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 normality was 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. The mean age and sex distribution were comparable across groups. Mean height, weight, and BMI SDS values were within the expected ranges for children with GHD, with approximately half of the cohort being prepubertal at study entry. Baseline IGF-1 SDS values were lowest in the naïve group and comparable between the switch and somatropin groups. Growth hormone stimulation test results and 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. All routine biochemical and hormonal parameters were within normal limits.The mean starting dose was 0.66 mg/kg/week for somatrogon (naïve and switch groups) and 0.030±0.003 mg/kg/day for somatropin (somatropin group). 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 at baseline, week 6, and months 3, 6, 9, and 12 are illustrated in **Figures 1–3.** Based on these data, 6- and 12-month outcomes were analyzed, with primary comparisons between the 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.

At 6 months, increases in height SDS (0.4±0.3 vs 0.5±0.3; p = 0.25), height velocity (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 groups. At 12 months, Δheight SDS (0.6±0.3 vs 0.7±0.4; p = 0.78), height velocity (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-naïve 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 height velocity 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.

Quality of Life, Emotional–Behavioral, and Social Support

Paired analyses from baseline to 6 month demonstrated no statistically significant change after Holm correction in PedsQL Total or domain scores in either the naïve or switch groups. A borderline, uncorrected 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.

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 required due to 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 height velocity 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 is non-inferior to daily somatropin in efficacy and safety (4,22). Those trials reported comparable improvements in height SDS, height velocity, 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 long-acting GH 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, 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 is consistent with 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 related to repeated injections into the same anatomical region—and resolved fully after rotation of injection sites. Similar cases have been described with both daily rhGH and somatrogon therapy (29,30), underscoring 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. 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 novel parameters such as body composition and QoL assessments, suggesting that somatrogon may provide additional advantages in adherence and treatment convenience without compromising efficacy.
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 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 and Strengths

This study also 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 real-world evaluations 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 quality-of-life 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

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.

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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Table 1. Baseline characteristics of the study groups

Characteristic	Naïve (n=20)	Switch (n=18)	Somatropin (n=20)
Age (years)	11.1±3.0	9.7±3.4	10.5±3.2
Sex (F/M), n (%)	10/10 (50)	5/13 (27.8/72.2)	9/11 (45/55)
Prepubertal/Pubertal, n (%)	9/11 (45/55)	11/7 (61.1/38.9)	9/11 (45/55)
Height SDS	−3.0±0.8	−1.8±0.6	−2.7±0.5
Weight SDS	−2.0±1.0	−1.4±0.8	−1.6±1.3
BMI SDS	−0.4±0.9	−0.6±0.9	−0.2±1.2
Target height SDS	−1.0±0.7	−1.0±0.9	−1.1±1.0
Bone age (years)	9.0±3.3	7.9±3.5	8.2±3.4
Bone age SDS	−2.3±1.0	−1.9±0.8	−2.4±1.0
Height velocity (cm/year)	2.9±1.1	6.9±2.2	2.5±0.8
Height velocity SDS	−2.0±0.8	0.5±1.3	−2.4±1.3
IGF-1 (ng/mL)	105.9±59.5	151.0±89.2	115.7±73.0
IGF-1 SDS	−1.9±0.9	−0.9±0.9	−1.8±0.6
IGFBP-3 (µg/mL)	4.1±1.6	4.3±1.7	NA
Clonidine peak GH (ng/mL)	4.2±2.9	5.5±2.2	4.9±3.1

L-dopa peak GH (ng/mL)	2.6±2.5	5.0±3.0	3.1±1.9
Pituitary MRI, Normal, n (%) **MRI, Abnormal, n (%)***	17 (85) 3 (15)	13 (72.2) 5 (27.8)	16 (80) 4 (20)
Panhypopituitarism, n (%)	0 (0)	0 (0)	1 (5)
Starting dose	0.66 mg/kg/week	0.66 mg/kg/week	0.030±0.003 mg/kg/day

Abbreviations: 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. **Note:** Values are presented as mean ± SD unless otherwise indicated. *Abnormal findings included empty sella (n=4), ectopic posterior pituitary (n=3), stalk interruption (n=2), pituitary hypoplasia (n=2), and adenoma (n=1).

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

Timepoint	Outcome	Naïve	Somatropin	p	Effect Size Cohen's d
6 month	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 month	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	0.025	0.836
	ΔBA SDS	0.6±0.5	0.6±0.7	0.909	0.108

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

Table 3. Switch Group Outcomes: Somatropin First Year Compared to Somatrogon First Year

Parameter	Somatropin 1st year	Somatrogon 1st year post-switch	p	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

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

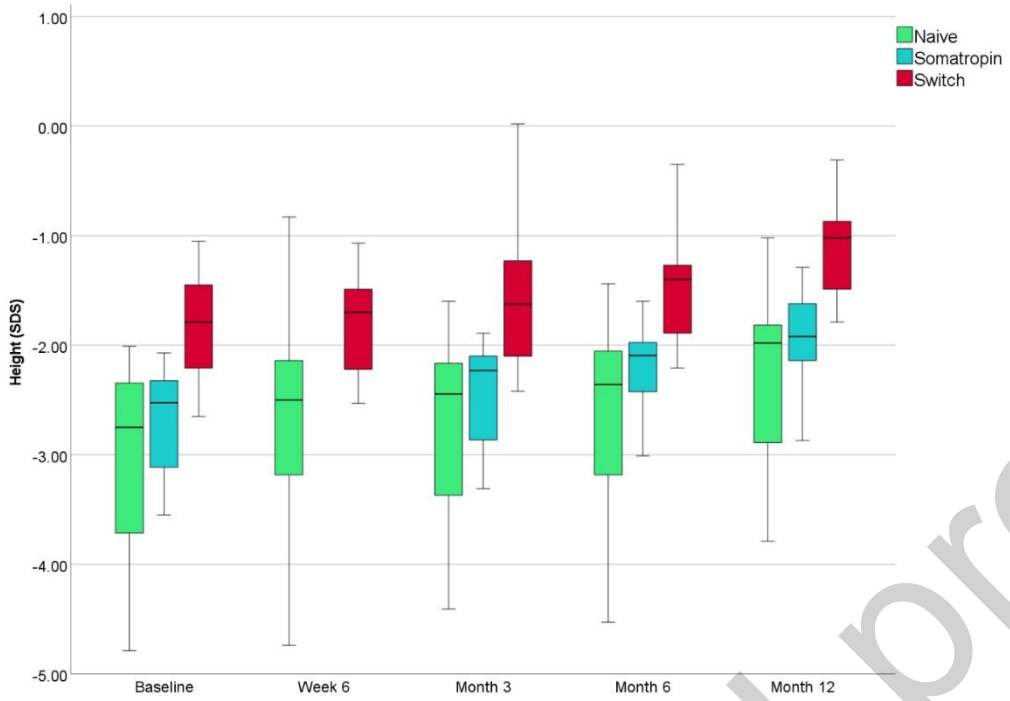

Figure 1: Height SDS at baseline, week 6 and months 3, 6, 9, and 12 in the three study groups. Median values are shown as horizontal lines, and mean values are indicated by diamond symbols. **Abbreviations:** SDS, standard deviation score; naive, treatment-naïve patients who initiated somatrogon; somatropin, patients who continued daily somatropin treatment; switch, patients who transitioned from somatropin to somatrogon.

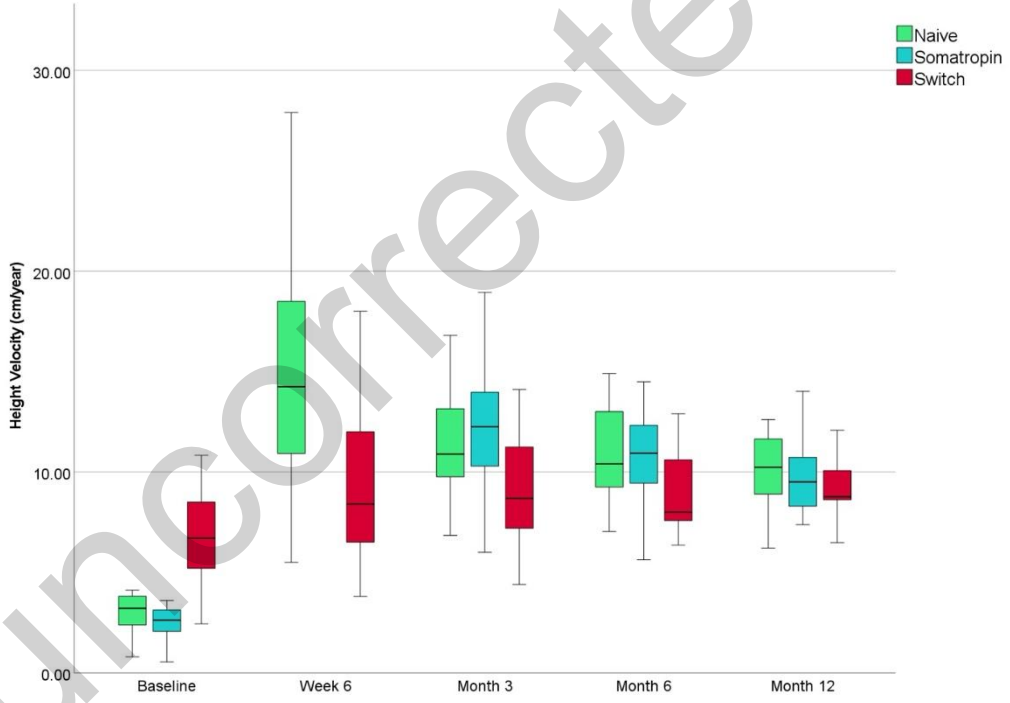

Figure 2: Height velocity (cm/year) at baseline, week 6 and months 3, 6, 9, and 12 in the three study groups. Median values are shown as horizontal lines, and mean values are indicated by diamond symbols. **Abbreviations:** naive, treatment-naïve patients who initiated somatrogon; somatropin, patients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

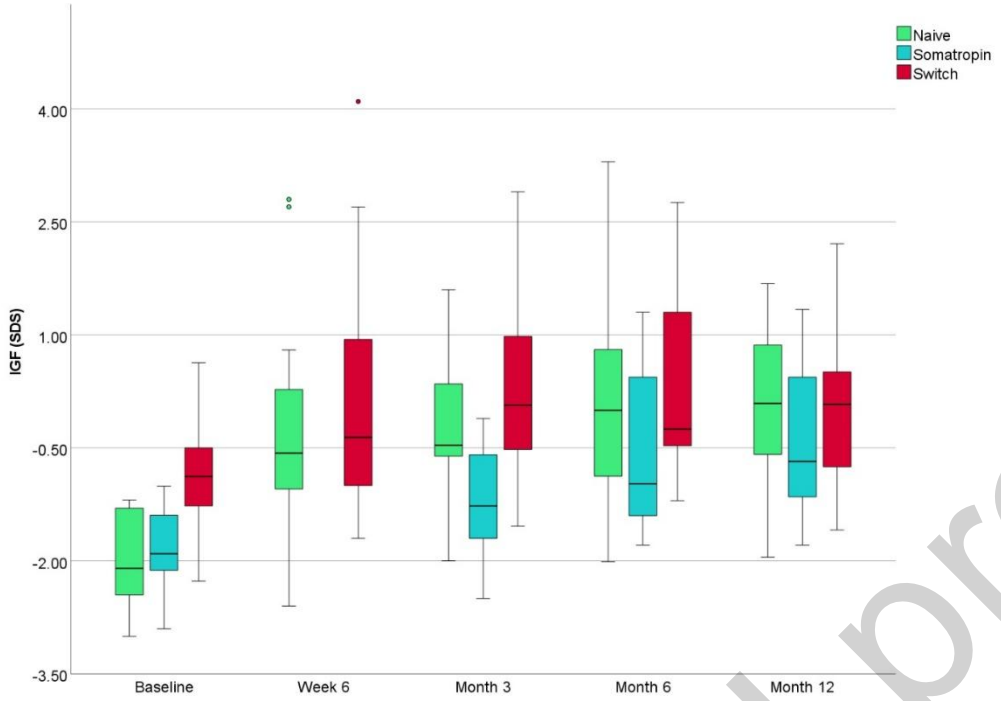

Figure 3: IGF-1 SDS at baseline, week 6 and months 3, 6, 9, and 12 in the three study groups. Median values are shown as horizontal lines, and mean values are indicated by diamond symbols. **Abbreviations:** IGF-1, insulin-like growth factor-1; SDS, standard deviation score; naive, treatment-naïve patients who initiated somatrogon; somatropin, patients who continued daily somatropin treatment; switch, patients who transitioned from somatropin to somatrogon.

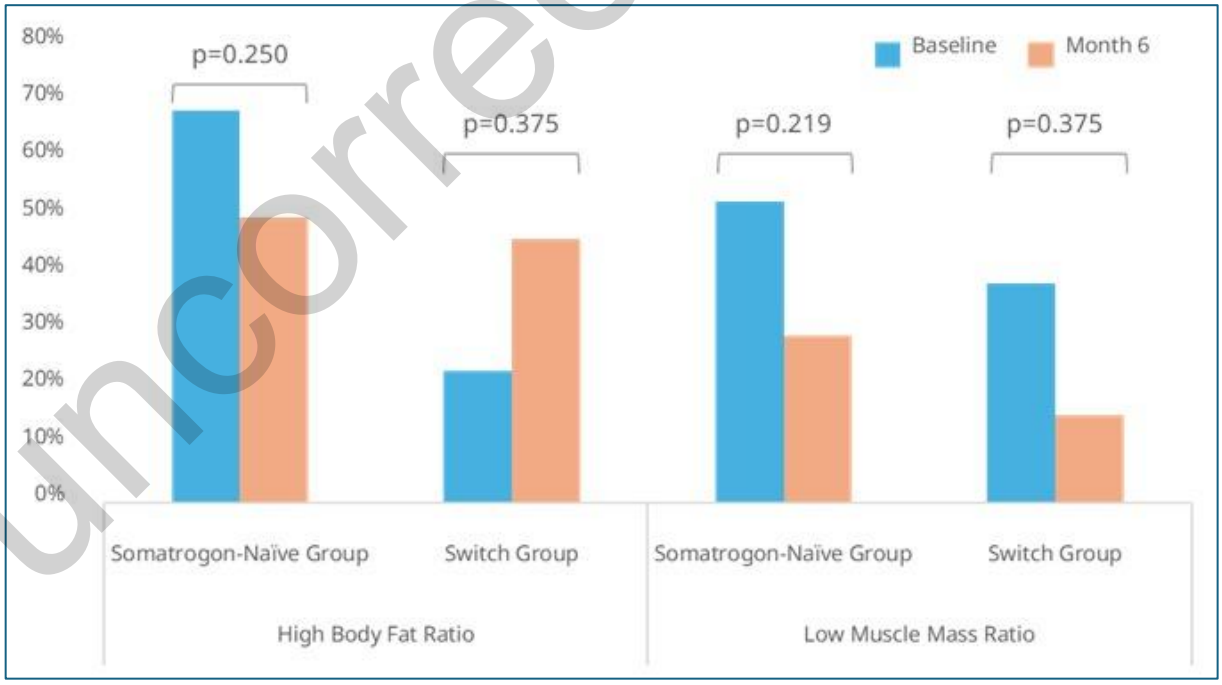

Figure 4: Body composition changes at baseline and month 6 in the somatrogon-naïve and switch groups (p-values shown above bars). $p < 0.05$ was considered statistically significant. **Abbreviations:** somatrogon-naïve, treatment-naïve patients who initiated somatrogon; switch, patients who transitioned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