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THE AMERICAN JOURNAL OF MANAGED CARE

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This publication was sponsored by Pfizer.

Adherence to Somatropin Therapy in the United States: Highlights of a Real-world Study of Patients With Pediatric Growth Hormone Deficiency

This AJMC® Clinical Brief provides key information regarding a study by Loftus et al, which was published in *Current Medical Research and Opinion* (doi:10.1080/03007995.2021.1982682). Please consult the full publication for complete study information and author affiliations.¹

INTRODUCTION

Pediatric growth hormone deficiency (pGHD), which occurs in about 1 in 4000 to 1 in 10,000 children, is treated with daily subcutaneous injections of somatropin, a recombinant human growth hormone (r-hGH).²⁻⁵ Adherence to somatropin treatment has been demonstrated to be suboptimal over time. Lack of adherence to daily somatropin therapy has been associated with impaired growth in patients with pGHD.⁶⁻⁸

Evidence is lacking regarding long-term adherence to and discontinuation of somatropin treatment in large US populations using validated, objective, quantitative measures. Previous studies have not limited their analyses to pediatric patients with GHD.^{6,9-12} Also, many studies were conducted outside the United States, and/or they involved small sample sizes.⁶⁻¹² To address this gap in evidence, a retrospective cohort study was conducted to analyze adherence to somatropin therapy and discontinuation of therapy in patients who had been diagnosed with pGHD and who were newly treated with somatropin. The results of this study are presented herein.¹

SUBOPTIMAL ADHERENCE TO SOMATROPIN: A US REAL-WORLD STUDY

The objectives of the study by Loftus et al were to determine rates of adherence to somatropin treatment and discontinuation of somatropin treatment over 4 years among patients with pGHD using data from a US commercial claims database; to identify demographic and clinical characteristics of patients with good versus suboptimal adherence; and to determine risk factors for suboptimal adherence and discontinuation.¹

METHODS

This retrospective cohort study was conducted using data from the Optum Clinformatics Data Mart database. Eligible patients were 3 years or older but younger than 16 years, and they had at least 2 prescription claims for somatropin between July 1, 2002, and September 30, 2019; the first prescription was considered the "index prescription." Additional eligibility criteria included the receipt of a diagnosis of pGHD in the baseline period (≤ 6 months prior to index date) and coverage by commercial insurance with continuous medical and pharmacy coverage from baseline through the follow-up period. Patients with claims for somatropin at baseline and psychosocial dwarfism and other causes of short height were excluded from the study. Based upon available follow-up time after the index date, 5 nonexclusive cohorts were created (3, 12, 24, 36, and 48 months of postindex continuous enrollment). For the adherence analysis, nonexclusive cohorts were comprised of patients followed for up to 48 months postindex date: > 12 months, > 24 months, > 36 months, and > 48 months. For the discontinuation analysis, all patients with 3 or more months of follow-up were included.¹

Medication adherence was defined by medication possession ratio (MPR); good adherence was defined as an MPR of 80% or higher or less than 1 missed injection weekly, on average; suboptimal adherence was defined as an MPR of less than 80%. To evaluate whether baseline characteristics were

significantly associated with good adherence, logistic regression models were used. For each of the characteristics, odds ratios and 95% CIs were calculated.¹

Discontinuation was defined as a gap of more than 60 days between prescription fills. Demographic characteristics were also evaluated, and descriptive analyses were performed for all study variables. To evaluate whether baseline characteristics were associated with time to discontinuation of somatropin, Cox regression models were used. For each of the characteristics, hazard ratios and 95% CIs were calculated.¹

RESULTS

Demographics

The final study analysis included 3969 patients in the 3-month follow-up cohort, 3091 patients in the 12-month follow-up cohort, 2231 patients in the 24-month follow-up cohort, 1604 patients in the 36-month follow-up cohort, and 1193 patients in the 48-month follow-up cohort. The mean (SD) age for patients across all cohorts was 11.3 (2.9) years. Most of the patients were male (eg, 75.9% in the 12-month cohort), and the majority were non-Hispanic White (eg, 74.4% in the 48-month cohort). Demographic characteristics were similar across cohorts. Less than 2% of the study cohort was classified as obese.¹

Adherence

Mean adherence was reduced over time. The MPR (95% CI) was 0.89 (0.88–0.89), 0.85 (0.84–0.85), 0.83 (0.82–0.84), and 0.82 (0.81–0.83) for those with 12, 24, 36, and 48 months of follow-up time after the index date, respectively.¹ Similarly, suboptimal adherence increased with time (Figure).¹ Overall, in the 12, 24, 36, and 48 month follow-up cohorts, 19.6%, 29.8%, 34.2%, and 35.9% of patients had suboptimal adherence. Adherence was not associated with age. Suboptimal adherence was most prevalent in Black and Hispanic patients, and the prevalence of suboptimal adherence increased with time.¹

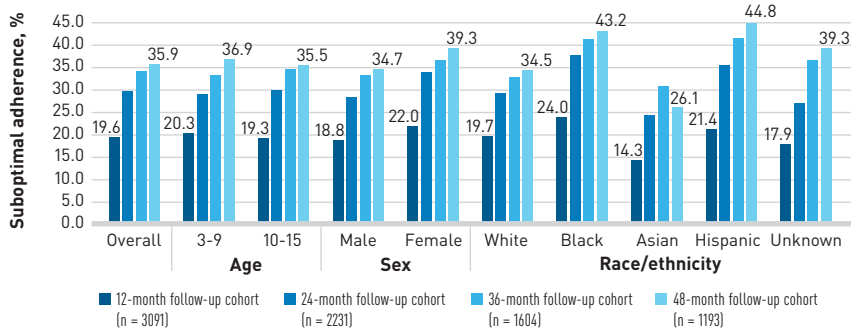
Discontinuation

Among all patients followed for at least 3 months (n = 3969), 42.2% discontinued somatropin therapy. The mean time to discontinuation was 524.4 days (SD 374.6, median 442.0). Based on Cox regression models, discontinuation occurred more frequently in patients 10 years or older, females, Black or Hispanic patients (compared with White patients), and those with obesity.¹

LIMITATIONS

This research is subject to several limitations. Claims data may not accurately capture all clinical diagnoses or relevant variables, and they do not capture causes of medication cessation or suboptimal adherence. Also, this study used a commercially insured population;

Figure. Suboptimal Somatropin Adherence Over 4 Years Among Children Diagnosed With pGHD¹



pGHD, pediatric growth hormone deficiency.

The version of scholarly record of this article is published in *Current Medical Research and Opinion* 2021, available online at: <http://www.tandfonline.com/doi:10.1080/03007995.2021.1982682>

its findings may not be generalizable to other populations. Another possible limitation of this study is the use of MPR rather than proportion of days covered to evaluate adherence.¹

CONCLUSIONS

The results of this study showed that suboptimal adherence to somatropin increased over time in children with pGHD, with more than 1 in 3 children exhibiting suboptimal adherence by 48 months following the initiation of somatropin therapy. About 4 in 10 children with pGHD treated with somatropin in the current study discontinued treatment following therapy initiation, with an average time to discontinuation of about 1.4 years. The risk of discontinuation was higher in older patients, females, Black or Hispanic patients, and those with obesity.¹ •

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