

Real-world evidence of vosoritide treatment in children under 2 years of age with achondroplasia in Colombia: a cases series

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Abstract

Introduction: Achondroplasia is the most common skeletal dysplasia and is associated with significant medical complications and impaired linear growth. Vosoritide is the first targeted therapy approved for achondroplasia; however, real-world data in children younger than 2 years of age are scarce, particularly in Latin America.

Objectives: To describe the real-world clinical characteristics, treatment patterns, short-term safety profile, and early growth trajectories of outcomes of Colombian children younger than 2 years of age with genetically confirmed achondroplasia, treated with vosoritide.

Materials and Methods: We conducted a descriptive real-world cohort study including pediatric patients with molecularly confirmed achondroplasia who initiated vosoritide treatment before 24 months of age in Colombia. Clinical, anthropometric, neurodevelopmental, radiologic, respiratory, neurologic, and treatment-related variables were collected from routine clinical practice records. Variables analyzed included age at clinical diagnosis, age at molecular confirmation, age at treatment initiation, time from treatment request to effective drug access, treatment exposure and continuity, growth trajectory, adverse events, disease-related complications, and reasons for treatment interruption. Growth outcomes were interpreted using achondroplasia-specific growth references rather than general population standards.

Results: Five female patients with genetically confirmed achondroplasia caused by the *FGFR3*:c.1138G > A;(p.Gly380Arg) variant were included. Mean age at last evaluation was 25.2 months (range 17–30 months). Diagnosis was confirmed early in life in all patients, with molecular confirmation occurring between 2 and 10 months after birth.

Vosoritide treatment was initiated between infancy and early toddlerhood. Delays between treatment request and effective drug initiation ranged from 90 to 180 days. Most patients demonstrated maintenance of growth within achondroplasia-specific reference ranges during follow-up. Treatment continuity was significantly affected by medication dispensing interruptions in several patients.

No serious adverse events directly attributable to vosoritide were identified. Reported adverse events were mild and mainly occurred during initial administration, including nausea, hirsutism and elevation of alkaline phosphatase. No patient permanently discontinued therapy because of adverse effects.

Several disease-related complications associated with achondroplasia were identified during follow-up, including sleep apnea, cervicomedullary stenosis, myelomalacia, hearing abnormalities, and respiratory infections requiring hospitalization. Neurodevelopmental progression was generally appropriate for age.

Conclusion: This Colombian real-world cohort provides preliminary evidence supporting the feasibility and short-term safety of vosoritide treatment in children younger than 2 years with achondroplasia. The findings also highlight important barriers to timely access and treatment continuity in routine clinical practice. Given the small sample size, limited follow-up, and treatment interruptions, conclusions regarding growth efficacy should be interpreted with caution. Larger longitudinal studies are needed to

evaluate long-term growth outcomes, body proportionality, neurologic impact, respiratory morbidity, functional outcomes, and the potential clinical benefits of early vosoritide initiation.

INTRODUCTION

Achondroplasia is the most common skeletal dysplasia, approximately 1 in 25,000–30,000 individuals worldwide, corresponding to an estimated 250,000 affected people. It is caused by pathogenic variants in the fibroblast growth factor receptor 3 (FGFR3) (1). Excessive FGFR3 signaling impairs endochondral ossification and negatively regulates longitudinal bone growth.

This condition presents multiple challenges in both clinical management and quality of life (1, 2). It is associated with complications including foramen magnum stenosis, genu varum, kyphosis, lordosis, scoliosis, recurrent otitis media, sleep apnea, spinal stenosis, joint pain. Short stature and limb disproportion can affect the performance of activities of daily living, impacting quality of life. Therefore, improving physical function is a key treatment goal for people with achondroplasia (3).

Vosoritide, a C-type natriuretic peptide analog, represents the first targeted pharmacologic therapy approved for achondroplasia. By antagonizing the downstream effects of FGFR3 overactivation, vosoritide promotes endochondral bone growth and improves growth velocity (3). It was initially approved by the Food and Drug Administration (FDA) in 2021 to increase linear growth in patients with achondroplasia aged 5 years and older with open epiphyses. However, the FDA updated the indication, removing the minimum age limit, under an accelerated approval process based on the improvement in annualized growth velocity (AGV) (4). More recently, regulatory approval has expanded to younger pediatric populations, including infants. However, real-world evidence in children under 2 years remains limited, particularly in Latin America.

Although evidence remains limited, phase 2 studies (BMN 111–206 and BMN 111–208) involving 75 children younger than 60 months of age across 16 centers in Australia, Japan, the United Kingdom, and the United States evaluated the safety, tolerability, and growth outcomes of vosoritide. These studies demonstrated an acceptable safety profile and suggested potential benefits on growth in infants and young children with achondroplasia.

Colombia faces additional healthcare challenges related to access, treatment authorization, multidisciplinary monitoring, and continuity of care for patients with rare diseases despite having a robust legislative framework aimed at protecting and guaranteeing comprehensive care for individuals with orphan diseases. Real-world data from this setting may provide valuable information regarding treatment implementation and early outcomes outside controlled clinical trial environments.

The objective of this study was to describe the clinical characteristics, safety profile, treatment adherence, and early growth outcomes of Colombian children younger than 2 years of age with achondroplasia treated with vosoritide in routine clinical practice.

MATERIALS AND METHODS

A retrospective descriptive cohort study was conducted using real-world clinical data from pediatric patients with achondroplasia treated with vosoritide in Colombia. Patients were eligible if they: had genetically confirmed achondroplasia, initiated vosoritide before 2 years of age, and had available clinical follow-up information. Clinical information was collected from routine medical follow-up records and caregiver-reported data.

The following variables were collected from routine clinical records and caregiver-reported information when available: age at clinical diagnosis, age at molecular confirmation, age at treatment initiation, time from treatment request to effective drug access, treatment duration, treatment interruptions, adverse events, anthropometric measurements, growth trajectory, neurodevelopmental milestones, neurologic findings, respiratory complications, radiologic abnormalities, and disease-related comorbidities. Particular attention was given to complications commonly associated with achondroplasia, including sleep apnea, cervicomedullary stenosis, myelomalacia, hearing abnormalities, recurrent respiratory infections, and hospitalizations. Growth outcomes were assessed using achondroplasia-specific growth references rather than general population growth standards.

Statistical analysis: Given the small sample size, data are presented descriptively using frequencies, percentages, ranges, and mean values when applicable.

The study was conducted in accordance with the Declaration of Helsinki and approved by the each institutional ethics committee (Salud Comfamiliar Risaralda, Fundación Cardiovascular de Colombia, Fundación Centro Colombiano de Epilepsia y Enfermedades Neurológicas, FIRE, and Fundación Santa fe de Bogotá, Bogotá). Informed consent for data collection and publication was obtained from parents or legal guardians.

Clinical trial number: not applicable.

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RESULTS

Five female pediatric patients with genetically confirmed achondroplasia were included. Patients originated from different geographic regions of Colombia, including Santander, Risaralda, Atlántico, Bolívar and Bogotá, with one patient receiving partial care coordination from the United States. All patients had contributive health insurance (in Colombia is the mechanism of the General Social Security System in Health (SGSSS) for people with the ability to pay. It is financed through monthly contributions guaranteeing comprehensive medical coverage for the contributor and their family).

Prenatal suspicion of skeletal dysplasia was documented in some patients; however, definitive diagnosis occurred after birth following clinical and molecular evaluation. The FGFR3:c.1138G > A;(p.Gly380Arg) pathogenic variant was identified in all patients. The age at molecular confirmation ranged from 3 to 10 months.

All patients demonstrated classic phenotypic manifestations of achondroplasia, including: frontal bossing, midface hypoplasia, depressed nasal bridge, rhizomelic limb shortening, trident hand configuration, macrocephaly or relative macrocephaly.

Neuroimaging findings demonstrated varying degrees of craniocervical junction abnormalities. One patient demonstrated severe craniocervical stenosis with bulbomedullary signal changes compatible with myelomalacia. Another patient showed narrowing of the foramen magnum without clinical compression. Polysomnography findings included moderate obstructive sleep apnea in one patient, while another patient demonstrated normal sleep architecture. Most patients had normal auditory evaluations, although one patient developed mild bilateral hearing loss.

Developmental progression was generally appropriate for age considering the underlying skeletal dysplasia. Reported milestones included: head control between 2 and 4 months, sitting between 7 and 10 months, crawling between 7 and 11 months, independent ambulation between 14 and 19 months. Language acquisition was variable but overall compatible with expected development.

Treatment initiation and access barriers

The mean age at vosoritide initiation was 16.5 ± 4 months (range 12–18 months). All treated patients received daily subcutaneous vosoritide at the approved weight-based dose, the interval between treatment request and drug initiation ranged from approximately 90 to 180 days, reflecting substantial administrative and access-related barriers; one of the cases to date has not received approval and could not start treatment before 2 years of age. The mean duration of vosoritide treatment was determined as 18 months (range 8–36 months) in treated patients. See Baseline characteristics in Table 1.

Among the four patients who initiated vosoritide treatment, annualized growth velocity ranged from 6.0 to 9.67 cm/year, with a mean of 8.03 cm/year. Three patients with the greatest treatment continuity demonstrated upward shifts in height SDS relative to achondroplasia-specific growth references, reaching values near or above + 1 SD from their baseline trajectories. In contrast, treatment interruptions due to medication dispensing delays were common and may have influenced individual growth outcomes. Patients with more consistent treatment exposure appeared to demonstrate more stable anthropometric progression. See growth curves in Fig. 1. Although specific segment measurements were not performed, parents reported perceived improvements in mobility and agility; however, objective measurements of body proportionality were not performed.

Treatment interruptions secondary to delayed medication dispensing by healthcare providers or insurance systems were frequent. Only one patient maintained uninterrupted therapy during the

evaluated period (case 5).

Patient number	Height at birth (cm)	Baseline height SDS*	Age at the start of treatment (mo)	Duration of vosoritide treatment (mo)	Calculated mean annual growth velocity (cm/yr)	Height SDS at last visit
1	49	+ 1 DS	18	16	9,4	+ 1.73 SD
2	48	0 DS	17	8	6	- 1.88 SD
3	46	- 1 DS	-	0	-	-
4	47,5	0 DS	12	Current	8,7	+ 1.067 SD
5	46,5	- 1 DS	18	Current	9,67	+ 1.32 SD
*Based on achondroplasia growth curves						

Table 1. Baseline characteristics of patients with Achondroplasia included in the cohort

No serious treatment-related adverse events were identified. The most commonly reported adverse effects occurred during early administrations and included: nausea, hirsutism, elevation of alkaline-phosphatase. All reported adverse events were transient and self-limited. No clinically significant hepatic abnormalities were observed during follow-up.

DISCUSSION

This case series presents one of the first real-world descriptions of vosoritide use in children younger than 2 years of age with achondroplasia in Colombia and Latin America. The cohort reflects the growing implementation of precision therapies for skeletal dysplasias in routine clinical practice. All patients carried the classic *FGFR3*: c.1138G > A pathogenic variant and demonstrated phenotypic findings consistent with achondroplasia.

An important finding of this study was the presence of substantial healthcare access barriers. Delays of several months between treatment authorization and actual initiation were common. Furthermore, repeated interruptions in medication dispensing affected treatment continuity in most patients. These findings differ from controlled clinical trial environments and highlight real-world challenges specific to middle-income healthcare systems. The burden of complications observed in our cohort is consistent with previous reports from Latin America. A systematic review by Fano et al. highlighted the substantial clinical burden of achondroplasia in Latin American populations and emphasized the need for higher-quality regional evidence and greater public health engagement.

According to published reference data from untreated children with achondroplasia, mean height SDS is – 2.5 in girls aged <1 year (9). It decreases to – 5.3 SDS in girls by the age of 5 years. Despite inconsistent and short treatment exposure, early clinical observations suggest an association between vosoritide treatment and improved growth parameters, including height SDS and AGV, deviating from the usual behavior of achondroplasia curves while maintaining an acceptable safety and tolerability profile. Patients with uninterrupted therapy appeared to demonstrate more favorable growth progression. Parental reports of improved mobility and agility may suggest functional benefits associated with treatment; however, body proportionality was not formally assessed. Earlier intervention may theoretically influence skeletal growth during periods of maximal developmental plasticity and potentially modify disease burden over time. Ongoing international studies are evaluating these hypotheses (10, 11).

The early initiation of vosoritide in infants and toddlers raises important clinical considerations beyond linear growth. In achondroplasia, the first years of life represent a critical period for skeletal development, neurodevelopmental acquisition, respiratory surveillance, and detection of craniocervical complications. Therefore, treatment outcomes in this age group should not be interpreted exclusively through height or annualized growth velocity, but also through longitudinal assessment of body proportionality, motor development, sleep-disordered breathing, foramen magnum stenosis, hearing status, functional performance, and caregiver-reported outcomes. In this cohort, the identification of sleep apnea, craniocervical stenosis, myelomalacia, hearing abnormalities, and respiratory infections, underscores the need for structured multidisciplinary follow-up, regardless of pharmacological treatment. These findings support the concept that vosoritide should be integrated into a comprehensive care model for achondroplasia, rather than considered an isolated growth-promoting intervention.

The burden of complications observed in our cohort is consistent with previous reports from Latin America. A systematic review by Fano et al. (12) highlighted the substantial clinical burden of achondroplasia in Latin American populations and emphasized the need for higher-quality regional evidence and greater public health engagement.

From a health-system perspective, this case series highlights the gap between regulatory approval, clinical indication, and effective treatment access in real-world practice. Delays in authorization, medication dispensing interruptions, and variability in follow-up may reduce treatment exposure and complicate the interpretation of effectiveness outcomes. These barriers are particularly relevant in rare diseases, where early therapeutic windows may be narrow and continuity of care is essential. Real-world evidence from Latin America is therefore important not only to describe safety and growth outcomes, but also to identify modifiable health-system factors that influence the implementation and sustainability of precision therapies for skeletal dysplasias.

This study has several limitations. The retrospective design, small sample size, heterogeneous follow-up, incomplete anthropometric datasets, and treatment interruptions limit interpretation of efficacy

outcomes. In addition, standardized annualized growth velocity calculations were not consistently available.

Nevertheless, the study provides valuable insight into real-world implementation of vosoritide therapy in Colombia and highlights important considerations regarding access, continuity of care, and multidisciplinary monitoring in infants and toddlers with the diagnosis.

Achondroplasia is associated with a substantial burden of clinical complications in Latin American populations. The interpretation of available evidence is limited by potential residual confounding, inadequate reporting, and considerable heterogeneity among studies. As highlighted by Fano et al., there is a pressing need for robust, well-designed clinical research in achondroplasia and greater engagement of public health authorities.

This study has several limitations that should be acknowledged. First, the small sample size and the inclusion of patients from a single country limit the generalizability of the findings. Second, the descriptive observational design and the absence of an untreated comparison group preclude definitive conclusions regarding the efficacy of vosoritide on growth outcomes or disease-related complications. Third, the relatively short follow-up period does not allow assessment of long-term effects on growth, body proportionality, neurologic outcomes, respiratory morbidity, functional status, or quality of life. In addition, treatment interruptions related to medication access and dispensing challenges may have influenced individual growth trajectories and treatment outcomes. Despite these limitations, this study provides valuable real-world evidence on the early use of vosoritide in children younger than 2 years of age with genetically confirmed achondroplasia in a Latin American setting.

CONCLUSION

This Colombian real-world case series provides early evidence on the implementation of vosoritide treatment in children younger than 2 years of age with genetically confirmed achondroplasia, representing one of the first reports from Latin America in this age group. In this cohort, vosoritide was generally well tolerated, with only mild and transient adverse events and no serious treatment-related safety concerns identified during follow-up.

Although the small sample size, retrospective design, heterogeneous follow-up, and treatment interruptions preclude definitive conclusions regarding efficacy, the observed maintenance or upward shift of growth trajectories on achondroplasia-specific growth curves, together with annualized growth velocities comparable to those reported in treated populations, suggest a favorable early growth response among patients with more consistent treatment exposure.

Importantly, this study highlights that real-world outcomes are influenced not only by pharmacological response but also by timely access to treatment, authorization processes, medication availability, and continuity of multidisciplinary care. Delays in treatment initiation and repeated interruptions in drug

dispensing represented major barriers that may reduce treatment exposure and potentially limit the benefits of early therapy.

Further prospective, multicenter, longitudinal studies in Latin American populations are needed to confirm the long-term safety and effectiveness of vosoritide and to evaluate its impact on growth, body proportionality, craniocervical and respiratory outcomes, neurodevelopment, functional performance, quality of life, and health-system factors associated with sustained treatment in infants and toddlers with achondroplasia.

Declarations

Author Contribution

M, P and MC wrote the main manuscript text and figure, and GL and N prepared table 1. All authors reviewed the manuscript.

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Figures

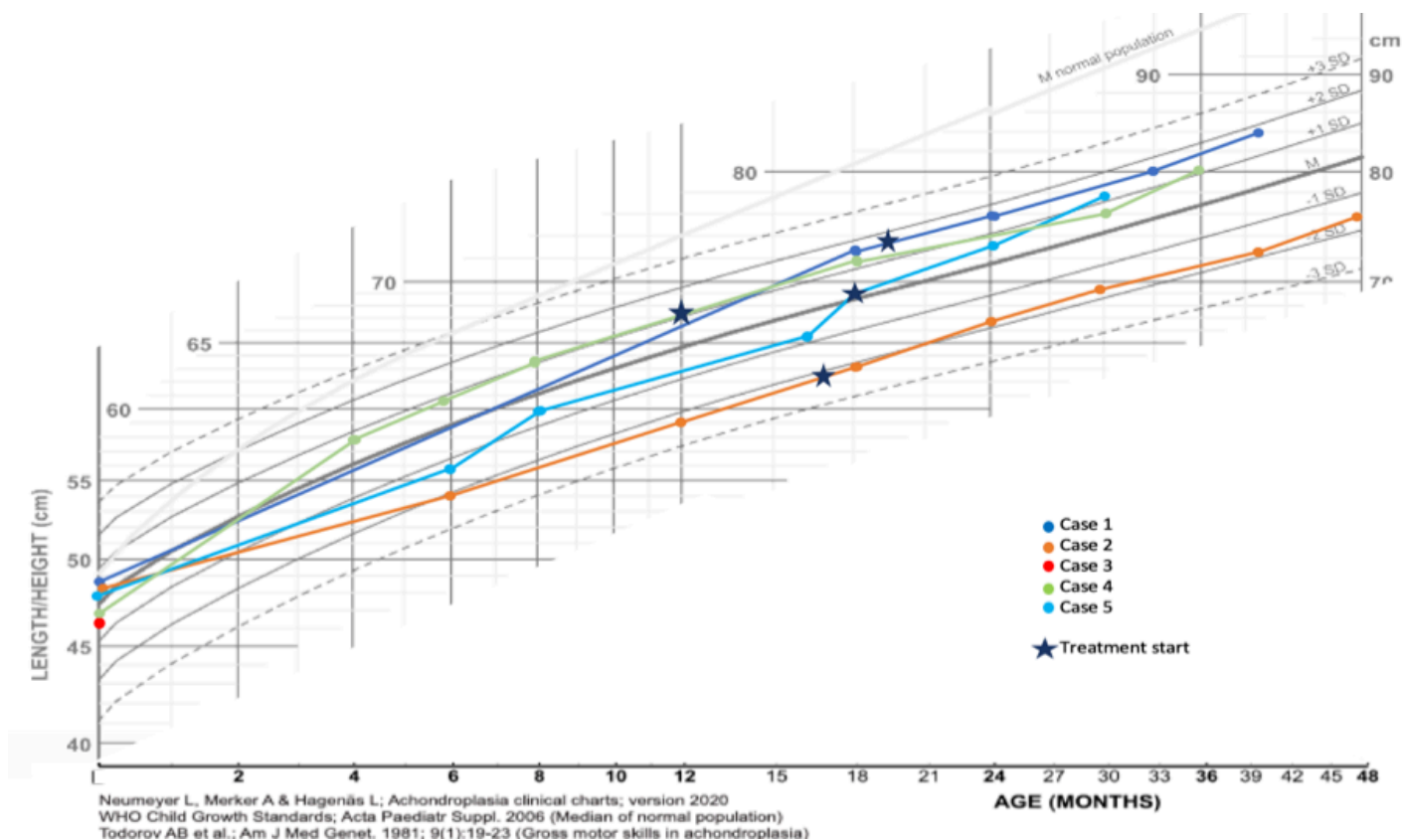


Figure 1

Growth Trajectories of a Colombian Cohort of Patients with Achondroplasia During Vosoritide Treatment (adapted from Merker, A., Neumeyer, L., et al. *Am J Med Genet – Part A*. 2018 (176): 1723-1734. doi: 10.1002/ajmg.a.38853)