

ACHONDROPLASIA.EXPERT CONGRESS REVIEWS ESPE 2023



Welcome to the ESPE 2023 congress review.

The 61st annual meeting of the European Society for Paediatric Endocrinology (ESPE) took place in The Hague, Netherlands, from 21–23 September 2023. The theme for the meeting was *Global Challenges in Paediatric Endocrinology*, which included sessions on growth, as well as bone, growth plate, and mineral metabolism.

We have picked out abstracts with a focus on children with achondroplasia. This includes new clinical data, real-world analyses, and a look at the underlying genetics. Also summarised is a sponsored symposium, looking at integrating clinical and real-world evidence to improve strategies.

We hope this selection of summaries is useful to you, and perhaps shines a light on ways in which we can address global challenges in our own small corner of endocrinology.

The Achondroplasia Team

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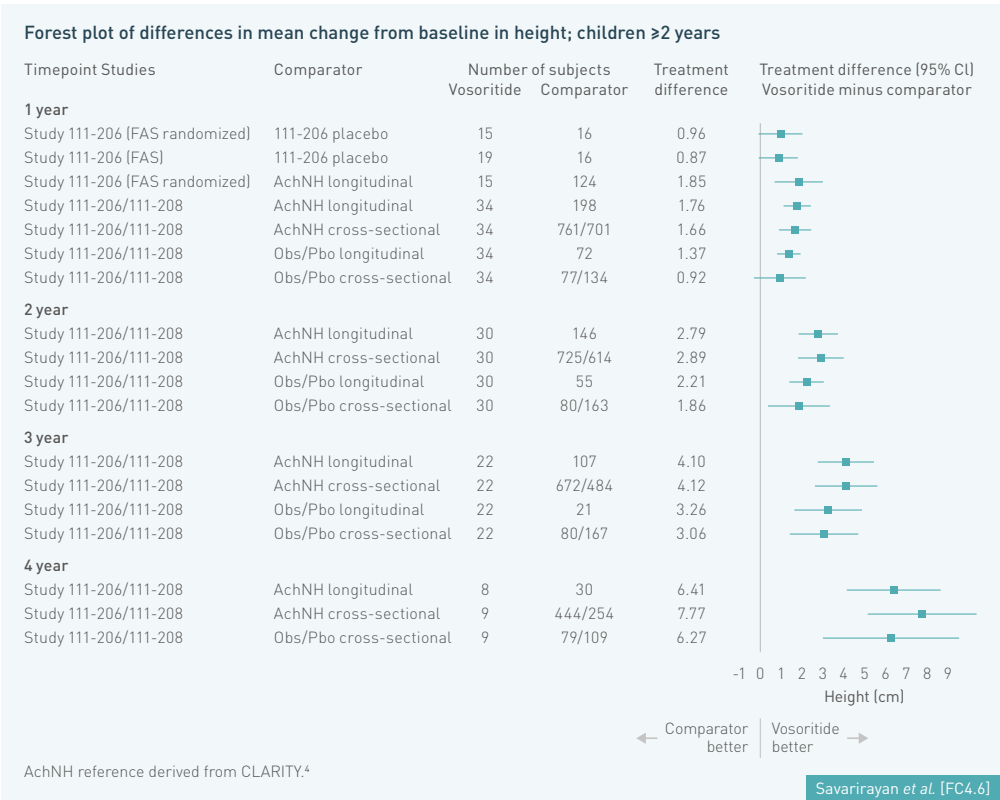
Achondroplasia
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NEW CLINICAL DATA IN ACHONDROPLASIA

Achondroplasia is the most common skeletal dysplasia. Traditionally, there have been no disease-modifying treatments for this condition, but increasing understanding of the role of pathogenic variants in the FGFR3 gene has resulted in novel targeted therapies.

Clinical trial results for vosoritide have previously been published for children aged 5–18 years,¹ and further data shared for younger children aged 3 months to 5 years. In their latest abstract, Savarirayan *et al.* present results from an open-label

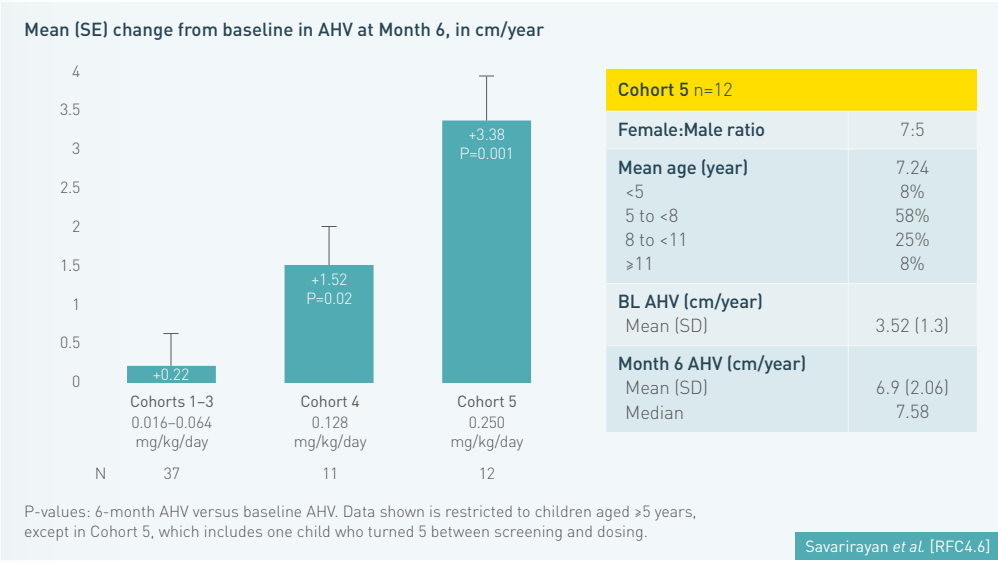
extension study spanning up to 4 years' treatment in 34 children aged 2–5 years at study start, looking at the persistence of growth-promoting effects in these infants and toddlers. Comparative cross-sectional analyses were performed for each year of



follow-up based on two control groups: observational/placebo data from the earlier clinical trials,^{2,3} and an external natural history dataset from CLARITY.⁴ The abstract shared at ESPE 2023 reports that vosoritide remained well-tolerated – with no change in the AE profile, and no discontinuations due to TRAE. After 4 years, treated children demonstrated greater height gain compared with both untreated controls and matched children from CLARITY; LSM change of 6.27 cm and 7.77 cm, respectively. The change in mean height Z-score at Year 4 was +1.10 for treated versus untreated, and +1.42 for treated versus CLARITY. Compared with the observational/placebo control group, those receiving vosoritide also showed an improvement in upper-to-lower body segment ratio after 4 years. The authors conclude that vosoritide was well tolerated, and maintained positive effects on linear growth over time. This treatment effect

on growth in young children who started vosoritide before the age of 5 demonstrates the benefit of early treatment initiation. ▶ [FC4.6]

Savarirayan *et al.* also shared results from an open-label, dose-finding study for ingigratinib – an oral, selective FGFR1-3 tyrosine kinase inhibitor being investigated for children with achondroplasia. PROPEL2 included 72 children aged 3–11 who had already participated for at least 6 months in PROPEL, a non-interventional clinical assessment. The dose-escalation phase included five dose cohorts, ascending from 0.016 to 0.25 mg/kg/day. Results from over 6 months' treatment found that Cohorts 1–3 (n=37) did not have a significant increase in AHV; these doses (0.016, 0.032, 0.064 mg/kg/day) were assessed as non-efficacious. Treatment at the Cohort 4 dose (0.128 mg/kg/day) resulted in an AHV increase from baseline of 1.52 cm/year in



11 children aged 5 or older ($P=0.02$). However, infigratinib at the Cohort 5 dose of 0.25 mg/kg/day ($n=10$) resulted in a significant mean increase from baseline of 3.03 cm/year ($P=0.0022$). Overall, 83% of children in Cohort 5 responded to infigratinib with an increase in AHV of at least 25% compared with baseline. This increase in growth translates to an increase in Z-score of +0.29 SDS compared with achondroplasia growth charts, and +0.25 SDS compared with average height growth charts. In the 6 children in Cohort 5, collagen X marker – a biomarker of endochondrial ossification – also showed a median increase of 28% from baseline at Month 6. Furthermore, infigratinib

was well tolerated, with no serious AEs or AEs leading to discontinuation, and most AEs reported were mild or moderate in severity. At the Cohort 5 dose, there were no Grade 3 AEs or TRAEs reported, no hyperphosphatemia, no ocular AEs, and no accelerated progression of bone age. Based on these findings, the 0.25 mg/kg/day dose will be explored in a Phase 3 study. The authors note that, if the Phase 2 data are confirmed, infigratinib could potentially offer children with achondroplasia the first effective oral therapy to improve growth, enhance functionality, and decrease medical complications.

► [RFC4.6]

REAL-WORLD EXPERIENCE WITH VOSORITIDE

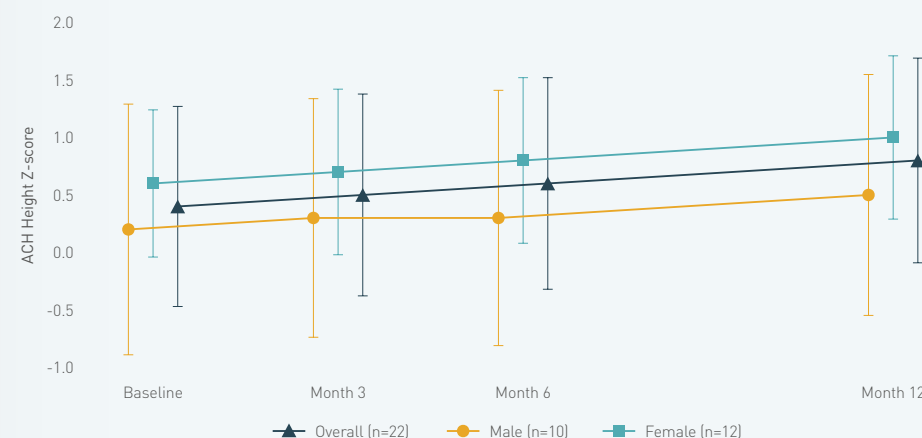
Vosoritide, an analogue of C-type natriuretic peptide, has been developed for the treatment of short stature in children with achondroplasia, and was approved by the EMA in August 2021 for children aged 2 and up.

With the introduction of new targeted drugs, a better knowledge of the natural history of achondroplasia is essential to plan the healthcare resources required by individuals through the lifespan. Kunkel et al. share insights into the real-world experience with vosoritide from CrescNet®, a patient-registry at the University of Leipzig that has been used for 20 years to monitor auxological, laboratory, and treatment data in over 1 million children with various conditions. To date, 270 children with achondroplasia have been entered by 15 centres, and 105 of these have started treatment with vosoritide. The mean age at vosoritide initiation is 7.1 years, and so far the registry has a

documented treatment duration of 1.23 years. Using achondroplasia-specific reference data,⁵ an increase from 0.53 to 1.06 H-SDS has been confirmed, which is consistent with data from clinical trials. These findings suggest that this established registry can be used to evaluate the long-term outcomes of rare diseases such as achondroplasia, and monitor the frequency of multisystemic complications, including AFMS, and the use of healthcare resources. ► [P1-414]

In June 2021, the French health authorities granted early access to vosoritide for children aged 5 years or older with open epiphyses. This programme continued until the agent

Height Z-scores of patients treated for 12 months referenced to untreated achondroplasia population⁴ over time



Cormier-Daire et al. [RFC4.5]

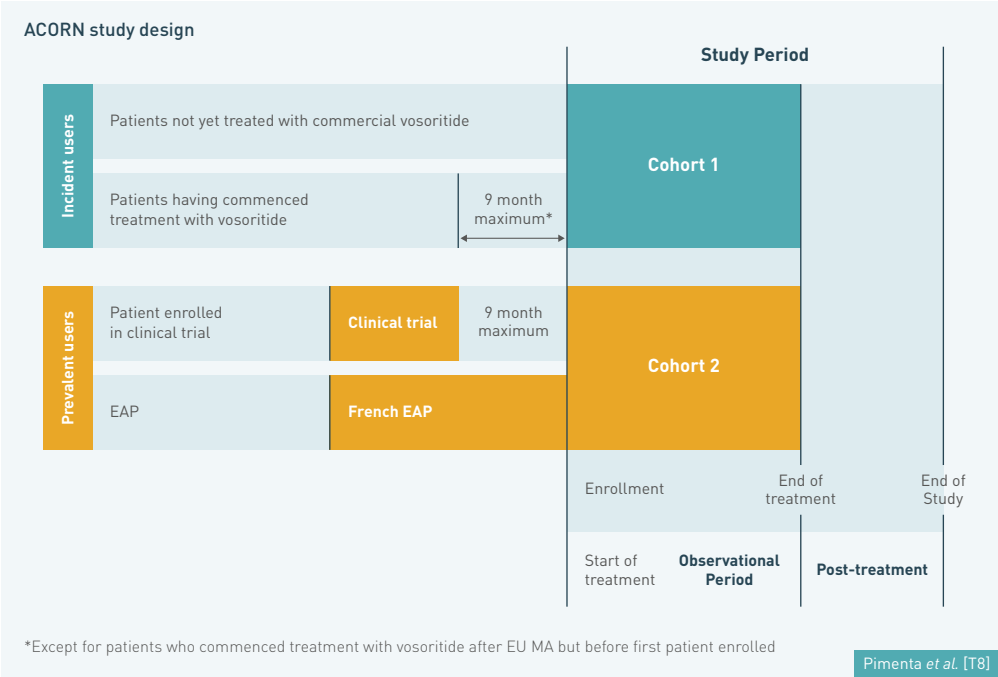
was commercially available in December 2022. In a session on growth and syndromes, Cormier-Daire et al. reported real-world safety and effectiveness findings from 57 patients in the French early-access cohort, with mean treatment exposure of 277 days. The mean age at initiation was 8.6, and 52% of those taking part were male. Among 22 patients (39%) who completed 12 months of treatment, males ($n=10$) showed a mean height increase from baseline of 5.8 cm, with a Z-score improvement of 1.0; females ($n=12$) showed a mean increase of 6.5 cm and Z-score improvement of 1.2. After 6 months' treatment ($n=37$), the mean AGV was 5.8 and 6.3 cm/year in males and females, respectively. In total, 21 AEs were reported during the study period; all were mild, and the majority were injection-site reactions and vomiting. No serious AEs were reported. In all, 43 missed doses were reported by 14 patients, but no patients discontinued vosoritide. The conclusion of the abstract

was that vosoritide under real-world conditions has a safety and effectiveness profile consistent with that seen in the clinical trials. In this early access programme, patients demonstrated good adherence and remained on treatment. Long-term data collection for these patients will continue where possible through the post-authorisation safety study. ► [RFC4.5]

ACORN is a multicentre, non-interventional post-authorisation safety study for vosoritide that was requested by the EMA as part of the risk management plan. During ESPE, Pimenta et al. presented the study's design and objectives, including its aim to recruit approximately 330 patients into two cohorts. The first will be ~300 incident users aged ≥ 2 to ≤ 8 years, defined as those who either recently started, or plan to start treatment with vosoritide. The second cohort will be ~30 prevalent users aged ≥ 2 years who initiated treatment as part of the French

expanded access programme or vosoritide open-label clinical trial. Patients will be recruited from around 30 sites in 8–10 countries. The primary objective is to evaluate the long-term impact of vosoritide on bone-related safety events, such as fractures and slipped capital femoral epiphyses. Secondary objectives include the long-term impact on safety and disease-related outcomes, including achondroplasia-related complications, surgeries, and changes in height and weight. The study

period is 10 years from the first patient enrolment in April 2023. In addition, patients who complete (reach final adult height) or discontinue during the study, will be followed up 2 years later. Almost all vosoritide-treated patients aged ≥2 to ≤8 years will be eligible for the study, leading to a more representative population of achondroplasia patients than that seen in clinical trials. The authors hope that the observational data collected in ACORN will reflect standard clinical practice and real-life management. ▶ [T8]



EXPLORING COMMON COMPLICATIONS

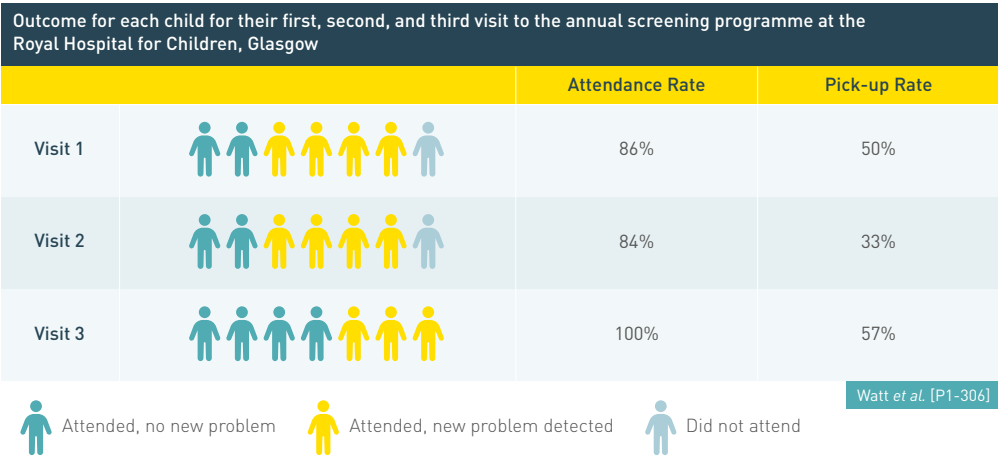
Achondroplasia is associated with a number of medical complications throughout the lifespan. Here, we focus on findings from two groups looking at insulin resistance, and hearing loss in real-world populations.

Acanthosis nigricans is common in conditions associated with reduced insulin sensitivity, and has been reported in skeletal dysplasias due to *FGFR3* mutations. Balci *et al.* set out to explore obesity and insulin resistance in patients with achondroplasia – specifically those carrying the *FGFR3* variant c.1138G>A (p.Gly380Arg). Physical examination, anthropometric measurements, and puberty examination were carried out, as well as measures of fasting plasma glucose, insulin, HbA1c, and an oral glucose tolerance test. A total insulin level of 300 U/mL was accepted as a cutoff for decreased insulin sensitivity. The study included 28 patients with a mean age of 13.1 years. All had a fasting plasma glucose in normal range, and the oral glucose tolerance was normal in 75%. Insulin resistance was identified in 6 patients (21.4%), and a further 2 (7.1%) had impaired glucose tolerance at 120 minutes. Of note, all patients with insulin resistance or impaired glucose tolerance were obese or overweight. HOMA-IR was >2.5 in 80% of patients with insulin resistance. Additionally, 50% of all patients (n=14) had acanthosis nigricans. When looking at oral glucose tolerance in the acanthosis nigricans subset, 21.4% had insulin resistance and 7.1% had impaired glucose tolerance; the remainder were normal. Only one patient with impaired glucose tolerance and one with insulin resistance did not have

acanthosis nigricans. Although the frequency of acanthosis nigricans was high in this group of young people with achondroplasia, it was not possible to demonstrate a significant relationship with insulin resistance. Analyses revealed no significant correlation between insulin resistance and age, H-SDS, or HbA1c level; however, a significant positive correlation was found between BMI and HOMA-IR (P=0.003). The authors conclude that the frequency of obesity and insulin resistance is high in children with achondroplasia. Monitoring is important, but HOMA-IR alone is not sufficient. They recommend an oral glucose tolerance test as a safe and practical method to check for glucose metabolism. Furthermore, efforts to prevent obesity may avert the decrease in insulin sensitivity. ▶ [P1-413]

Hearing loss and ENT problems are frequent in children with achondroplasia. Current international consensus guidelines recommend audiological assessment before the age of 1 year, and thereafter for children with speech delay, hearing difficulties, or features of middle ear effusion.⁶ In January 2019, an annual screening programme was initiated for children with achondroplasia who attend the Complex Bone Clinic at the Royal Hospital for Children in Glasgow, Scotland. At ESPE, Watt *et al.* presented a poster assessing whether the screening programme

is an effective use of resources, and has a good detection rate for new ontological problems. A retrospective analysis was performed to collect data on age, ear and hearing symptoms, audiometric test results, and subsequent outcomes for the first 4 years of the screening programme. Overall, 10 children were identified, and 7 participated in the annual hearing screening programme at some point, with a median age of 10.8. Most children had experienced an episode of hearing loss at some point over the 4-year period, with prevalence in individual years ranging from 25–80%; only 1 child had normal hearing throughout. A new episode of hearing loss was detected by screening in 3 children, who were then referred to ENT surgeons. These findings highlight the fluctuating nature of hearing loss in children with achondroplasia, and the need for continued and regular screening. Results at this stage suggest there is a worthwhile pick-up rate for new ontological problems in the annual screening programme. The authors point out that the continued detection beyond Year 1 highlights that annual screening is likely beneficial for this cohort, although larger case numbers are required. Annual screening will allow for prompt identification and treatment of hearing loss, and help to prevent the speech and language delays that affect children with achondroplasia. ▶ [P1-306]



BONE AND SURGERY

People with achondroplasia have impaired endochondral ossification, resulting in short stature and altered bone microarchitecture. This may also result in a need for surgery.

Although fractures and reduced bone mineralisation are not comorbidities frequently reported in achondroplasia, bone density data are lacking. Angelelli *et al.* set out to address this by looking at DXA bone parameters in children with achondroplasia. The results were shared in a poster in the *Bone, Growth Plate and Mineral Metabolism* category. Overall, 57 patients were evaluated, with a mean age of 11.1 years. DXA was used to measure BMD at the lumbar spine and TBLH. Lumbar BMAD and Z-score were calculated, and height, weight, and BMI recorded and expressed as SDS according to Merkel *et al.* reference standards.⁵

Mean LS-BMD: 0.673±0.030 g/cm² and -1.41±0.18 Z-score

Mean TBLH-BMD: -2.18±0.13 Z-score

Mean BMAD: 0.247±0.010 g/cm³ and -0.99±0.28 Z-score

Males and females differed for BMI SDS (P=0.04), LS-BMD (P=0.09), and LS-BMAD (P=0.04), while pre- and post-pubertal children differed for age (P<0.0001), LS-BMD (P<0.0001), and LS-BMAD (P=0.04). A significant delta between LS-BMD Z-score and LS-BMAD Z-score was found in the post-pubertal group (P=0.03). Furthermore, H-SDS was lower (P=0.01) and BMI-SDS higher (P=0.0175) in patients who had

undergone FMS, but there were no differences found in DXA bone parameters when comparing those who had undergone FMS versus those who had not. In multivariable analyses, TBLH-BMD Z-score was predicted by BMI SDS, and by FMS after adjustment for age, gender, and pubertal status. LS-BMD Z-score and BMAD Z-score were predicted only by BMI SDS. H-SDS was not a predictor of DXA bone parameters. These preliminary data show that children and adolescents with achondroplasia display low BMD values for age and sex at the TBLH, low normal values at the lumbar spine, and normal LS-BMAD Z-score values based on references for the general paediatric population. The poster states that, although specific normative data for achondroplasia are warranted, the use of BMAD is suggested. ▶ [P1-17]

FMS is a life-threatening complication in children with achondroplasia, which may require cervicomedullary decompression. But there is no evidence as to whether FMS and decompression affect growth in children with achondroplasia. Fava *et al.* set out to address this, looking at data from 65 patients – with a mean age at evaluation of 5.2 years. Of these, 39 had undergone decompression within the first year of life, and a further 18 after the age of 1 year. H-SDS, W-SDS and BMI-SDS were calculated according to Merker *et al.* reference standards.⁵

Results showed that the H-SDS was significantly lower for patients with versus without decompression (-0.55 ± 0.99 versus 0.85 ± 1.24 ; $P=0.01$), and even lower when the decompression surgery occurred after 1 year of age (-0.81 ± 0.95 versus 0.07 ± 1.04 ; $P=0.006$). Furthermore, H-SDS was more affected in males than females ($P=0.01$). There were no significant differences in BMI-SDS, but in patients without FMS the W-SDS was significantly higher than in those who had undergone compression surgery after 1 year of age (-0.07 ± 1.22 versus -0.86 ± 0.97 ; $P=0.03$).

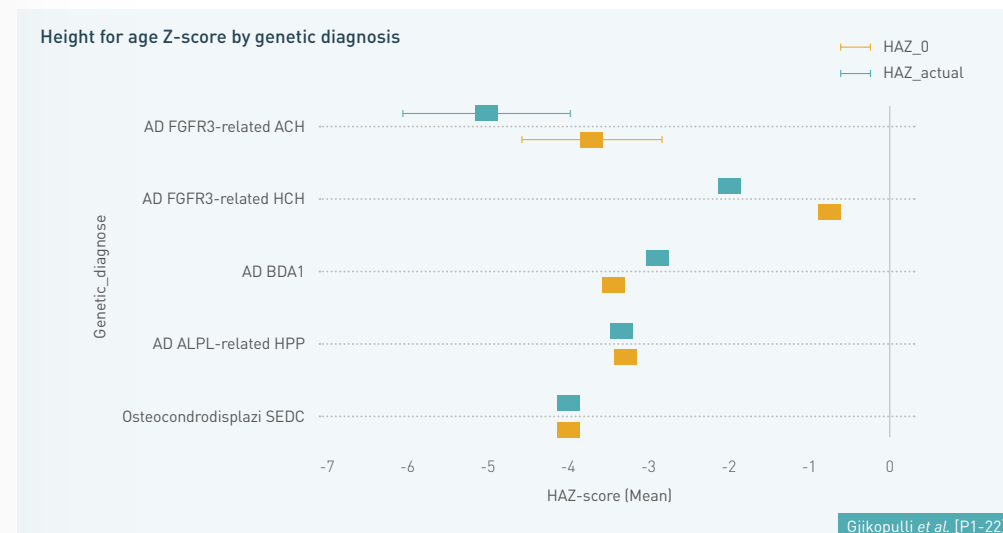
Based on these findings, the authors conclude that H-SDS evaluated at the age of 5 years is more affected in children with achondroplasia who have undergone decompression surgery versus those who have not. Furthermore, height and weight appear to be influenced by the patient's age at the time of surgery. These data suggest that FMS and/or cervicomedullary decompression may have a negative impact on growth in children with achondroplasia, and that early initiation of medical therapy is desirable. ▶ [P1-520]

GENETICS

Achondroplasia is not the only condition caused by *FGFR3* mutations. Genetic testing is important to establish the correct diagnosis.

Gjikopulli *et al.* shared a poster looking at *FGFR3* mutations in 17 children with clinically suspected hypochondroplasia or achondroplasia. Both are autosomal dominant conditions characterised by a rhizomelic shortening of the limbs, genu varum, trident hands, large head with frontal bossing and hypoplasia of the mid-face. Both are also caused by missense mutation in the *FGFR3* gene. To emphasise the importance of genetic diagnosis, clinical data and test results from 17 children with suspected achondroplasia or hypochondroplasia were analysed. The genetic results were interpreted in the context of clinical findings, family history, and other laboratory data. In total, 11 children (64.7%) were clinically diagnosed with achondroplasia, and 6 (35.3%) with hypochondroplasia. After genetic testing, this changed to

FGFR3-related achondroplasia in 13 (76.4%), and *FGFR3*-related hypochondroplasia in 1 child (5.9%). Diagnoses for the remaining 3 children were one each of: autosomal dominant hypophosphatasia related to *ALPL* mutation; autosomal dominant brachydactyly type A1 related to *IHH* gene mutation; spondyloepiphyseal dysplasia congenital related to *COL2A1* gene mutation. According to the height SDS, the micromelic short stature was present in all conditions, but was more severe in those with achondroplasia. After regrouping the patients according to their genetic diagnoses, short stature was more profound in the group of children with achondroplasia, followed by those with hypochondroplasia. In this study, genetic tests identified a diagnosis discrepancy of 17.6% by detecting different pathologies than those originally suspected. This highlights

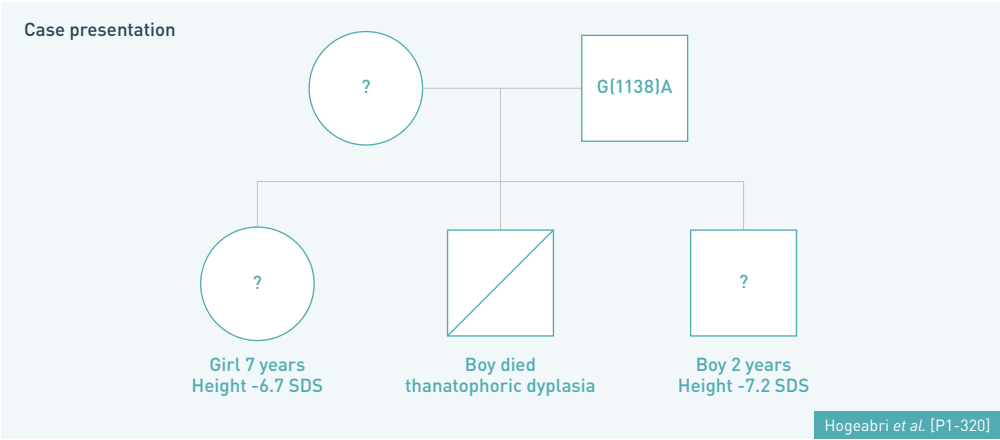


the role of genetic testing in establishing the correct diagnosis, especially in the era of *FGFR3*-directed therapies.

It is essential to sequence mutation hotspots in *FGFR3* first; in cases where common mutations are not found, a whole exome analysis can be performed. ▶ [P1-22]

Hogeabri *et al.* also shared a poster on distinguishing achondroplasia and hypochondroplasia, using a case study from a family with two affected parents, and two children with achondroplasia. The second-born child, a boy with thanatophoric dysplasia, had died. Both surviving children, a 7-year-old girl and a 2-year-old boy, were of short stature, with H-SDS scores of -6.7 and -7.2 , respectively; the girl also exhibited typical signs of achondroplasia on X-ray. Trio exome sequencing of the four family members identified a new *de novo* intronic variant

(c.1075 + 95C>G) in the mother and the two surviving children with achondroplasia-like features. The father was found to have the classic c.1138G>A variant. This new intronic variant alters mRNA splicing by causing retention of a 90-nucleotide segment of intron 8 in the mRNA, resulting in a 30-amino-acid insertion in the extracellular domain of the protein. This is the first known family with demonstrated inheritance of this newly described splice variant identified in the *FGFR3* gene, and suggests that the novel intronic variant is likely pathogenic from a human genetics perspective. The authors say their genetic studies confirm previously reported results strongly suggesting that c.1075 + 95C>G is a recurrent mutation, and should be included in genetic testing for *FGFR3* mutations, especially in patients with unclear clinical findings and no identifiable exonic variant. They conclude that genetic testing for achondroplasia requires intronic sequence analysis of exome data. ▶ [P1-320]



ADVANCING CARE

A BioMarin-sponsored symposium Chaired by Moira Cheung looked at Advancing the standard of care for achondroplasia: Integrating clinical and real-world evidence to improve strategies.

The first section of the symposium focused on long-term efficacy of vosoritide in children of different ages. Yasemin Alanay opened with a presentation on long-term growth-promoting effects, starting with an overview of the vosoritide clinical trial programme in the context of growth patterns of children with achondroplasia as compared with that of average stature children. Key findings from Phase 2 and 3 studies in children aged 5 years and older highlight an overall mild AE profile, plus a significant increase in AGV versus placebo after 1 year.^{1,2,7} In Phase 3, the 3.5-year safety data revealed no new safety concerns: injection-site reactions remain the most common AE, the majority of which are Grade 1 and self-limiting.⁸ Out to 7 years in Phase 2, vosoritide

continued to be well-tolerated, with no treatment-related SAEs over a total treatment exposure of 186 person-years.⁹ In children with achondroplasia who received vosoritide for 3.5 years in the Phase 3 trial, growth velocity was higher than in untreated⁴ patients across ages in both genders, but a growth spurt was not observed.⁸ Growth velocity remains slightly below that of children with average stature up to age 13, but treated patients appear to continue growing until a later age than children with average stature, although patient numbers are low for these age groups.⁸ Seven-year data from the Phase 2 study show similar results, with a greater growth velocity in treated versus untreated⁴ patients across ages, but absence of a growth spurt.⁹

Summary of efficacy findings in children ≥5 years		
Change vs age-matched untreated children	Phase 2 [111-202/205] 7-year findings ⁹	Phase 3 [111-301/302] 3.5-year findings ⁸
Sustained increase in AGV	✓	✓
Sustained increase in height Z-score	✓	✓
Sustained decrease in upper-to-lower body segment ratio	✓	✓

► [RFCF4.5]

Melita Irving shared safety and efficacy findings in children under 5 years of age. As for the older age group, there was an acceptable safety profile, with most AEs mild and self-limiting,¹⁰ and no new safety issues in children receiving vosoritide for up to 4 years.¹¹ Of the 75 participants in 111-206/208, 34 started vosoritide treatment between the ages 2 and <5 years.¹¹ These data have been used for both cross-sectional and longitudinal analyses, and compared against two independent external controls (FC4.6). The results show a sustained treatment effect with mean height Z-score gain >1 SDS after 4 years, plus consistent improvement in upper-to-lower body segment ratio over time in treated children.¹¹ Effects on growth were seen regardless of comparator group and statistical methodology. Overall, in clinical trials in patients aged 2 years and older, there has been a sustained positive impact on AGV, height Z-score, and upper-to-lower body segment ratio, with acceptable safety result for the duration of the studies so far.

Summary of efficacy findings in children 2 to <5 years	
Change vs age-matched untreated children	Phase 2 [111-206/208] 4-year findings ¹¹
Sustained increase in height Z-score	✓
Sustained height gain	✓
No worsening in body proportions	✓

► [RFCF4.6]

The second section of the symposium turned to consider real-world experience with vosoritide. Geneviève Baujat presented results from the early-access programme in France (RFC4.5). Vosoritide under real-world conditions appears to have a safety profile and effectiveness findings consistent

with vosoritide clinical trials. Further evidence comes from semi-structured telephone interviews with 15 parents of children with achondroplasia being treated with vosoritide in France and Germany for 1.5 to 13 months.¹² Family experiences were documented across four themes: awareness of vosoritide treatment, treatment understanding and decision-making, training and initiation, and managing treatment at home.¹² Parents typically became aware of vosoritide either through their own online research, patient advocacy groups, or their physician or hospital.¹² Child involvement in treatment decision-making typically depends on their age, and parental certainty.¹² Treatment drivers for children with achondroplasia are linked to increased height and the ability to participate in valued activities; concerns revolve around needle phobia and losing their identity within the achondroplasia community.¹² For parents, key factors influencing treatment

decisions are reductions in complications, particularly the need for surgery, and the lack of serious AEs.¹² Results from the interviews showed that hospital initiation and training sessions varied considerably both across and within countries, with different centres using different approaches. Sessions varied per country and hospital in terms of duration, tests, format, and first injection administration.¹² The majority occurred alongside other parents and children, and the first injection was often in a group, which may cause distress for parents and children.¹² In France, parents received at-home nurse support for up to 30 days to help adjust to injections, but in Germany at-home support was available only through a pharmaceutical-sponsored programme.¹² Additionally, there are many challenges faced by parents,

including maintaining a consistent treatment schedule, particularly during holidays or activities.¹² Keeping the treatment reliably cool while travelling away from home was also raised as a problem.¹² However, despite these challenges, parents reported consistently administering the injection daily.¹² Parents are willing to experience short-term difficulties if they lead to long-term quality of life benefits for their child, but there are opportunities for greater support.¹²

At the end of the symposium, there was a dialogue around three patient cases, with comment from Moira Cheung, Tilman Rohrer, and Yasemin Alanay. The clinical scenarios discussed highlighted that careful diagnostic workup and comprehensive counselling of parents or caregivers are crucial.

LIST OF ABBREVIATIONS

AE – adverse event	BMI-SDS – body mass index standard deviation score	H-SDS – height standard deviation score
AFMS – achondroplasia foramen magnum score	DXA – Dual-X-ray-Absorptiometry	LS – lumbar spine
AHV – annualised height velocity	ENT – ear, nose, and throat	LSM – least squares mean
AGV – annualised growth velocity	EMA – European Medicines Agency	TBLH – total body less head
BMAD – bone mineral apparent density	FGFR – fibroblast growth factor receptor	TRAE – treatment-related adverse event
BMD – bone mineral density	HOMA-IR – homeostatic model assessment of insulin resistance	W-SDS – weight standard deviation score
BMI – body mass index		

REFERENCES

1. Savarirayan R, et al. Genet Med 2021;23(12):2443–7.

2. Savarirayan R, et al. Genet Med 2022;24(12):2444–52.

3. Savarirayan R, et al. Lancet 2020;396(10252):684–92.

4. Hoover-Fong J, et al. Orphanet J Rare Dis 2021;16(1):522.

5. Merker A, et al. Am J Med Genet A 2018;176(9):1819–29.

6. Savarirayan R, et al. Nat Rev Endocrinol 2022;18(3):173–89.

7. Savarirayan R, et al. N Engl J Med 2019;381:25–35.

8. Hoover-Fong J, et al. Poster presented at ACMG 2023 [P193], March 14–18, Salt Lake City, UT, USA.

9. Hoover-Fong J, et al. Poster presented at ACMG 2023 [P194], March 14–18, Salt Lake City, UT, USA.

10. Savarirayan R, et al. Poster presented at ENDO 2022, June 11–14, Atlanta, GA, USA.

11. Irving M, et al. Oral presentation (FC4.6) at ESPE 2023; September 21, The Hague, Netherlands.

12. NiMhurchadha S, et al. Adv Ther 2023;40:2457–70.