

Free Communications 2: Bone, Growth Plate and Mineral Metabolism

FC2.6

Expansion of the CrescNet Registry Achondroplasia Module: Real-World Demographic Data and Outcomes after up to 2 Years of Vosoritide Treatment

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CrescNet Achondroplasia Study Group
Austria, Belgium, Bulgaria, Czech Republic,
Germany, Greece, Poland, Romania



Disclosure Statement

K. Mohnike

I have the following potential conflicts of interest to report:

Research Contracts & Consulting contracts with BioMarin,
QED, Ascendis, Novo-Nordisk, Zealand, Rezolute



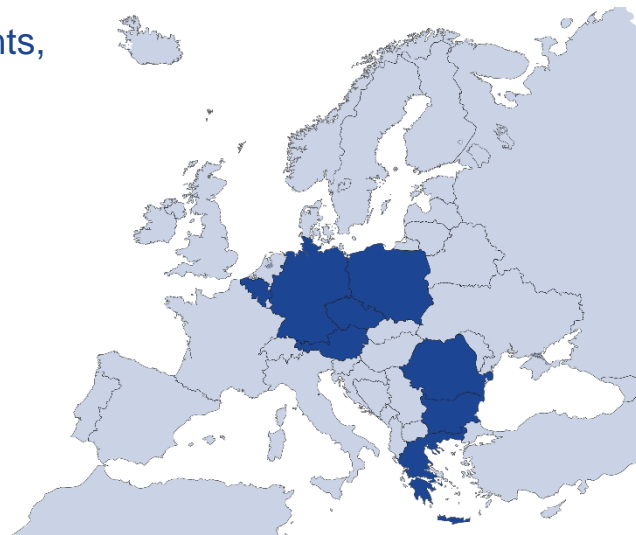
CrescNet (ClinicalTrials.gov ID: NCT03072537)

- Network of primary care physicians and paediatricians (n=445) and specialised treatment centres in paediatrics (n=43)
- Established in Leipzig in 1998 by Prof. E. Keller
- Operated by the Medical Faculty and Children's Hospital of the University of Leipzig, Germany
- Aim is to improve the early detection of growth disorders, epidemiological analyses of growth data
- >1,055,000 children are enrolled (date access: 10/24/2024)

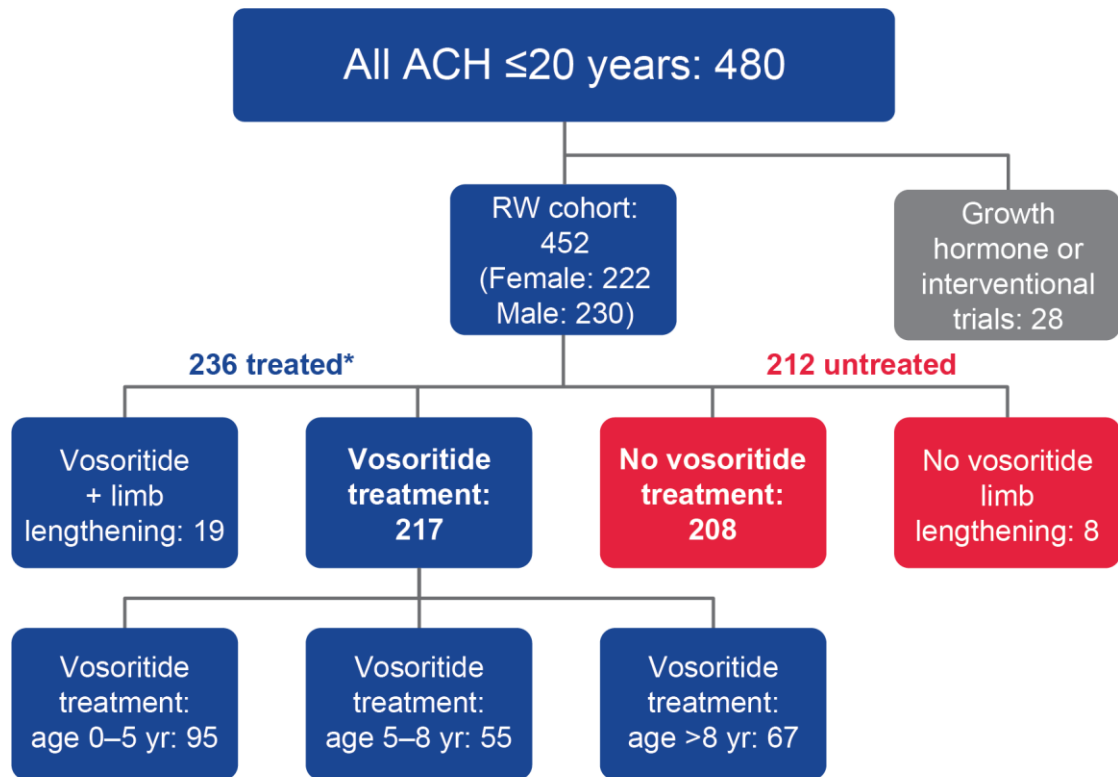
Achondroplasia Module

- Was set up in 2021 for this specific growth disorder as a sub study within the CrescNet registry in order to:
 - Describe natural course of genetically confirmed individuals
 - Document related complications, using HPO terms
 - Survey for HR-QoL, developmental milestones by patients, parents, caregivers (QR-code configured)
 - Monitor for growth data, pubertal stage, bone age
- 30 specialised treatment centres in 8 countries*

*24 Oct. 2024: Austria (1), Belgium (1), Bulgaria (1), Czech Republic (2), Germany (21), Greece (1), Poland (1), Romania (2)



Patient Numbers Within the Achondroplasia Module



*Mean age (SD) at treatment start: 6.12 (3.67)

Standardised Documentation During Patient Visits: CrescNet® Case Reports

Date of birth*

GA: 39 wk 1 d

Sex: ☒ male ☐ female

Indications

Mother:

177.3 cm

Weight

kg

Father:

195.7 cm

Weight

kg

* Mandatory fields, where either an initial or a first name must be given.

Save Master data

Diagnoses a. Consils

Q77.4 – Achondroplasia

Magnetic Resonance Imaging
Neurologic Examination
Otorhinolaryngologic Surgical Procedures
Neurosurgical Procedures

Phenotype a. Mutations

Cervical cord compression
Central sleep apnea Comment REM-Schlepp-besitzene Atmungsregulationsstörung mit leichten SuO2-Abfällen

FGFR3 cDNA code: c.1138C>A, Protein code: p.Gly380Arg

Birth values

Length: 42.0cm SGA (5.39cm below lower limit)
Weight: 2820g NBW (184g above lower limit, 1553g below upper limit)

For medical letter

Visit at 07/26/2022 (age: 5.6 years):
Height: 90.9cm (SDS: 0.34 / P_{63.3}), Weight: 17.50kg (SDS: 0.54 / P_{70.2}), BMI: 21.18kg/m² (SDS: 0.33 / P_{63.3}), Head girth: 58.0cm (SDS: 0.76 / P_{77.7}), Sitting height: 62.2cm (SDS: 0.40 / P_{63.3}),
Sitting height/Height: 0.684 (SDS: 0.05 / P_{5.13}), Arm span: 80.0cm, Arm span/Height: 0.88

Reference values: Achondroplasia

Save Visits + New Visit Reload

15 1 Select Standard vis

Date Age	Height cm SDS	Weight kg SDS ff	BMI kg/m ² SDS	Head girth cm SDS	Arm span cm BMI-adjusted	Sitting height cm SDS	Bone age a prop. final height	Puberty stage	Growth velo. cm/y SDS	Vosortide mg/d mg/mass
07/26/2022 5.6	90.9 0.34	17.50 0.54	21.18 0.33	58.0 0.76	80.0 0.88	62.2 0.40		P1	9.11 2.89	0.26 0.015
04/21/2022 5.3	88.5 -0.04	17.20 0.61	21.96 0.74	59.4 1.50	78.2 0.88	61.2 0.17		P1		0.26 0.015
01/21/2022 5.1	86.5 -0.32	17.00 0.74	22.72 1.14	59.0 1.33	75.5 0.87	60.5 0.09		P1		0.26 0.015
12/06/2021 4.9	85.8 -0.37	17.10 0.92	23.23 1.46	59.0 1.35	77.5 0.90	59.0 -0.54		P1	5.10 -2.92	
12/13/2017 1.0	65.5 -0.04	7.400 -0.81	17.25 -0.97	53.5 2.23					14.42 -3.78	
07/03/2017 0.6				52.0 3.81						
03/22/2017 0.2	55.0 0.17	5.510 0.47	18.21 0.95	45.5 1.82						
12/27/2016 0.0	42.0 -2.97	2.820 -1.21	15.99 0.54	38.0 0.89						

Milestones in the development of achondroplasia

English

Please indicate in the following fields from which month your child was capable of the respective action. If your child does not yet possess an ability, please leave the corresponding field empty.

Possible answers could be, for example:

- '4' for "with finished 4th month"
- '7.5' für "approx. in the middle of the 8th month"

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Gross Motor

	Month of life	Ireland ADRF		
		p90	Median	min-max
Lift head when lying		7.0	4.5	0.5-15.5
Roll over		9.9	5.3	1.0-15.5
Snow plough		21.0	12.0	8.0-36.0
Reverse snow plough		13.8	8.0	3.0-16.0
Commando crawl		14.2	9.0	5.75-18.0
Bear walking		18.0	12.0	6.0-21.0
Traditional crawling		18.3	12.0	6.0-24.0
Into sitting from lying		18.5	14.3	9.0-32.0
Into sitting from standing		22.8	15.0	8.0-32.0
Into standing from sitting		20.0	15.0	8.5-32.0

white = entry; highlighted in color = calculation; evaluation can be expanded by clicking on the required measurement variables

Standardised Documentation During Patient Visits: Online Documentation in CrescNet®

Natural History (HPO) & Mutations (HGNC)

Recording of Phenotypes and Mutations

Phenotypes (2 recorded so far)

09/02/2022 Select Phenotype... Select Severity... Comment

Date	Phenotype	Severity	Comment
06/12/2019	Central sleep apnea	REM- Schlaf- bezogene Atmungsregulationsstörung mit leichten SaO ₂ - Abfällen	
07/03/2017	Cervical cord compression		

Date: All Phenotype: All Severity: All

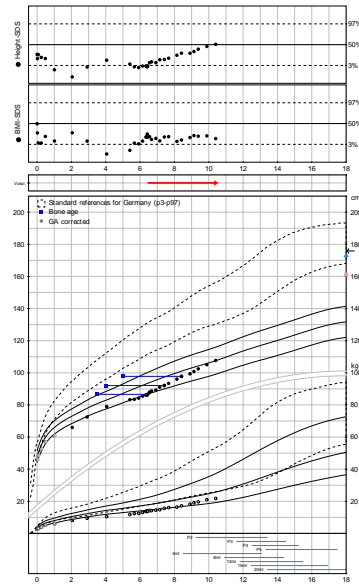
Mutations (1 recorded so far)

09/02/2022 Select Gene... cDNA code Protein code Heterozygous

Date	Gene	cDNA code	Protein code	Zygosity
11/24/2017	FGFR3	c.1138G>A	p.Gly380Arg	Heterozygous

Date: All Gene: All Zygosity: All

Auxology, Treatment, Pubertal Signs



H Z-score (Merker et al.)

BMI Z-score (Merker et al.)
treatment

Normal height

Achondroplasia
reference (Merker et al.)

Weight (normal)

Weight (Merker et al.)

Pubertal stage

Height and ACH Z-score* Improved With Vosoritide Treatment

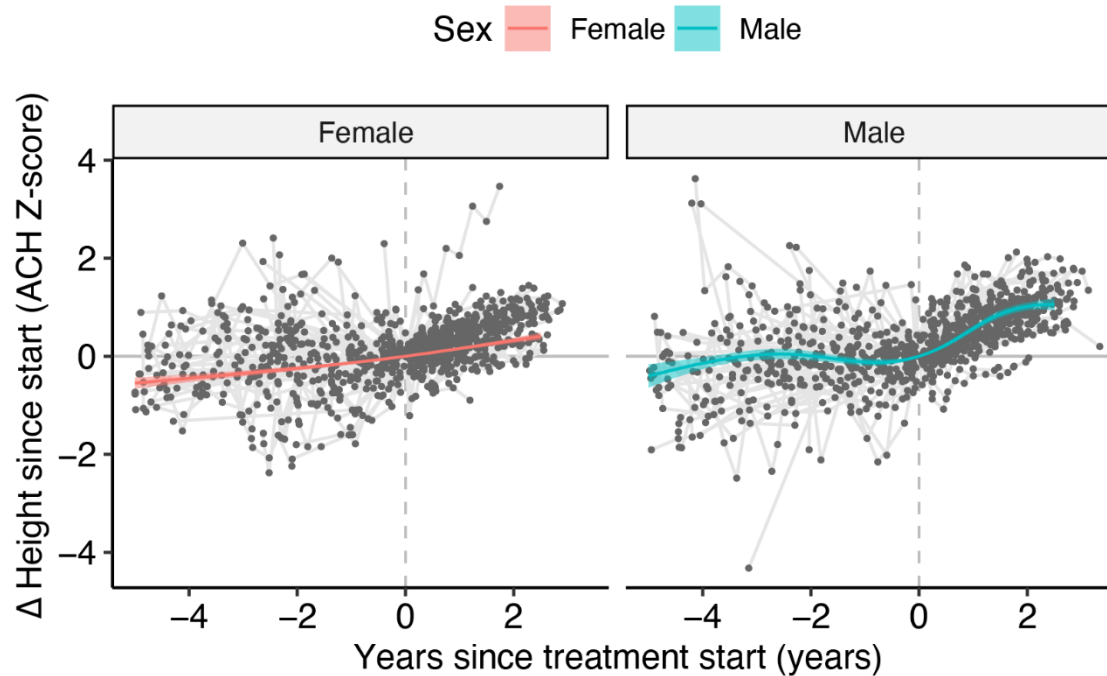
- Among **143** participants (**75** males, **68** females), treated with vosoritide for **12 months**, mean (SD) height increase from baseline was **6.36 (2.13) cm**, with ACH Z-score improvement of **0.7 (1.13)**.
- Furthermore, among **73** participants (**41** males, **32** females) treated with vosoritide for **24 months**, mean (SD) height increase from baseline was **11.86 (2.45) cm**, with ACH Z-score improvement of **1.15 (1.15)**.

*Z-score using achondroplasia reference population.

ACH, achondroplasia.

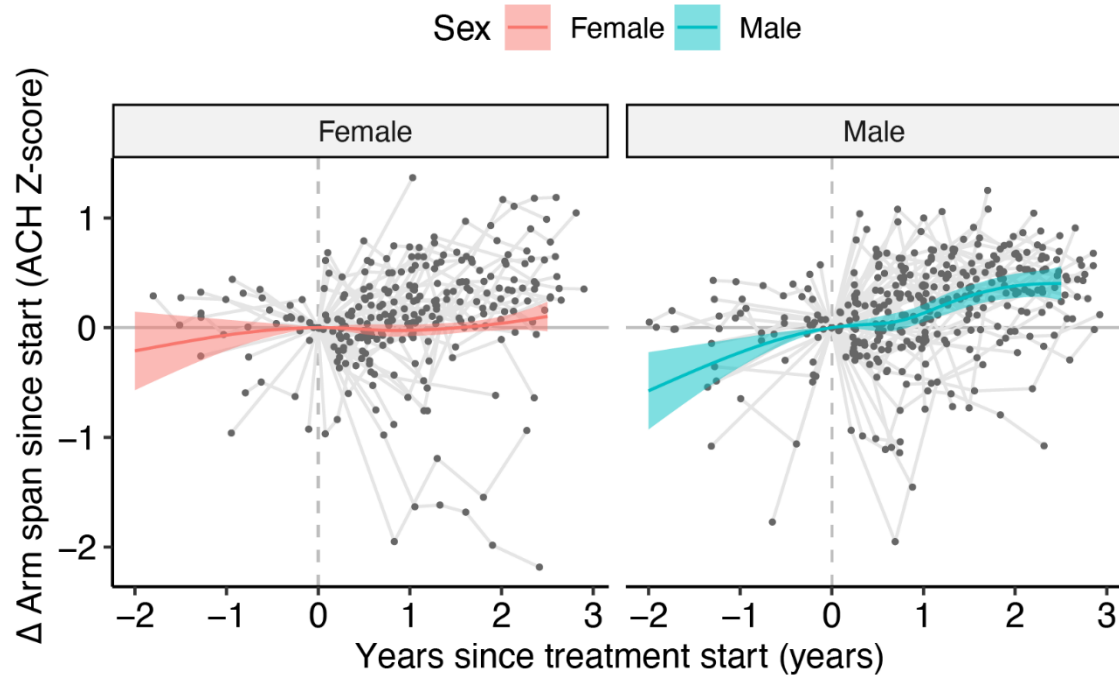
Merker A, et al. *Am J Med Genet A*. 2018;176(8):1723-1734.

ACH Height Z-score Consistently Improved Over 2 Years of Treatment with Vosoritide

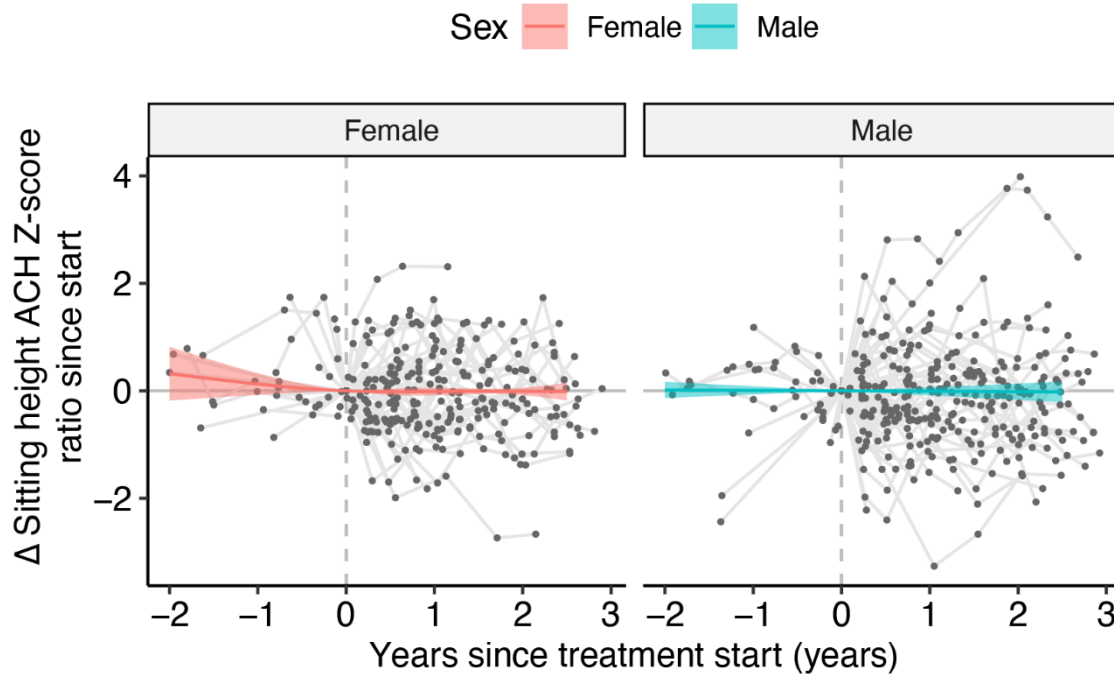


Body Proportion

Arm Span ACH Z-score Improved Over 2 Years of Vosoritide Treatment in Children With Achondroplasia



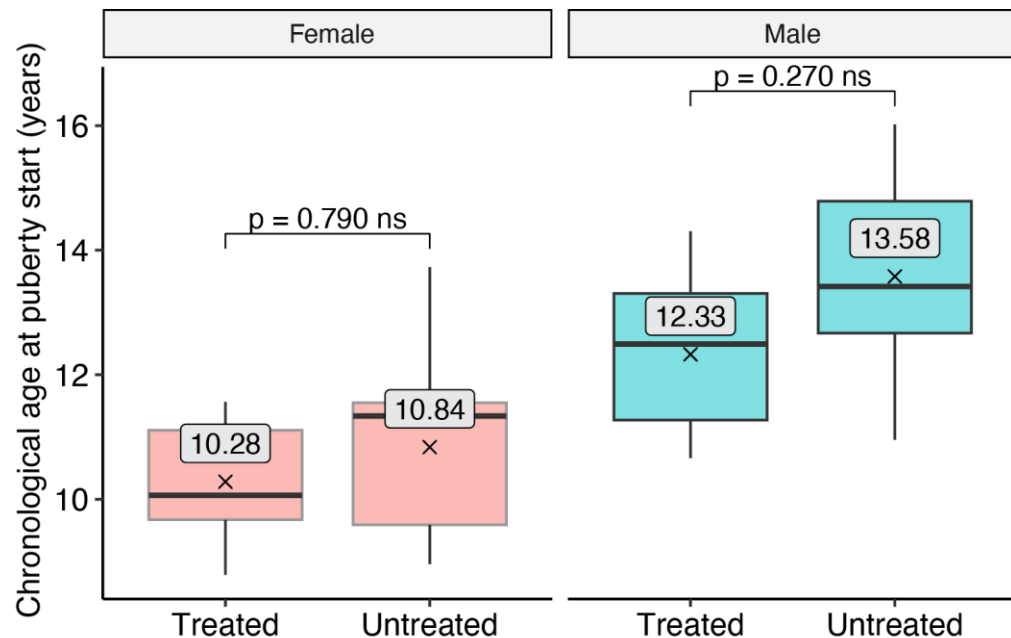
Sitting Height ACH Z-score Ratio Was Consistent in Vosoritide-Treated Children With Achondroplasia



Data suggest that vosoritide treatment led to proportionate growth of both the upper and lower body segment.

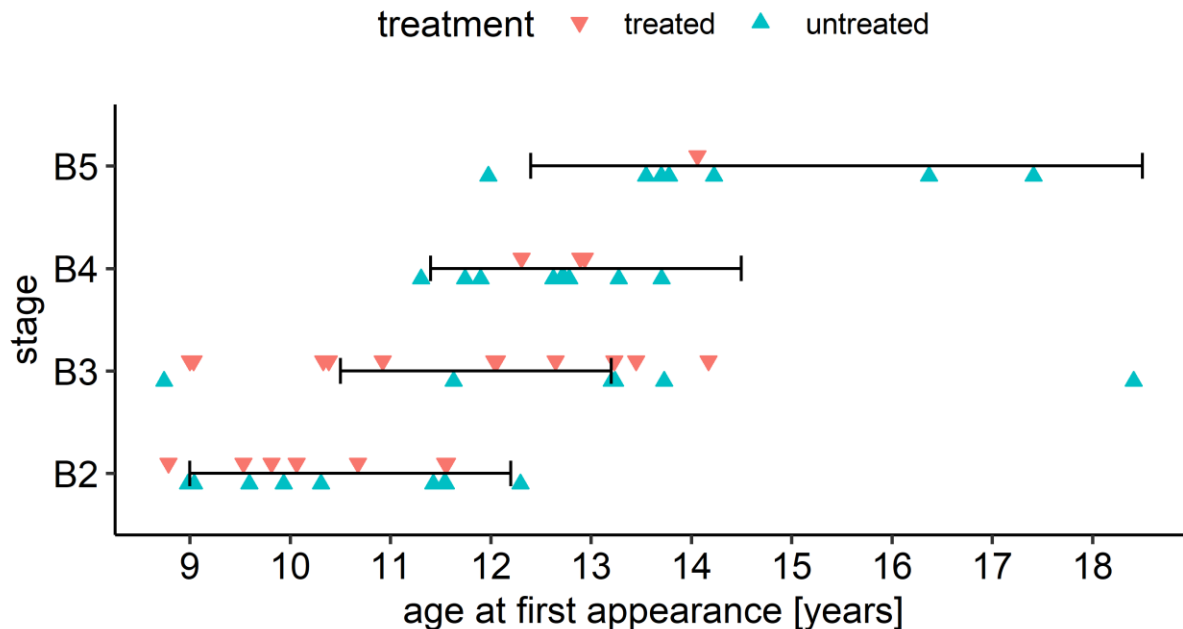
Puberty and Bone Age

Pubertal Stages Are not Affected by Vosoritide Treatment in Achondroplasia



- Testicle volume = 4 ml
- Male: pubic stage = P2
- Female: breast stage = B2
- Bone age: female 11–12, male 13–14

Pubertal Stages Are not Affected by Vosoritide Treatment in Achondroplasia: Breast



Treatment Summary

- CrescNet is a continuously growing multinational registry aiming to monitor growth and development of treated and untreated children with achondroplasia
- Up to two years of vosoritide treatment in children with achondroplasia led to:
 - Improvements in ACH Z-score height of up to 1.15
 - Improvements in proportionality shown by increases in arm span
- Sitting Height/Height ACH Z-score was not affected by vosoritide treatment suggesting proportionate growth in both upper and lower body segment
- Vosoritide treatment had no impact on puberty onset age

Automated Bone Age by AI-tool Deeplasia

...

...

OverviewMaster d...7 Attac...SurveysConsult...SettingsLoggingExport

Cent. to ...Select c...Head girthSitting h...Growth ...daily BMIdaily wei...daily hei...

Upload new image for visit

Visit:*

03/31/2022

Measurement:*

X-ray image (Left hand)

Image:*

Select image file...

Browse

With contrast (0 to 100): ⓘ

0

By uploading an X-ray image, it is automatically analysed with Deeplasia and a bone age is calculated. The resulting value appears in the visit table after a short time. (See also: <http://deeplasia.de/>)

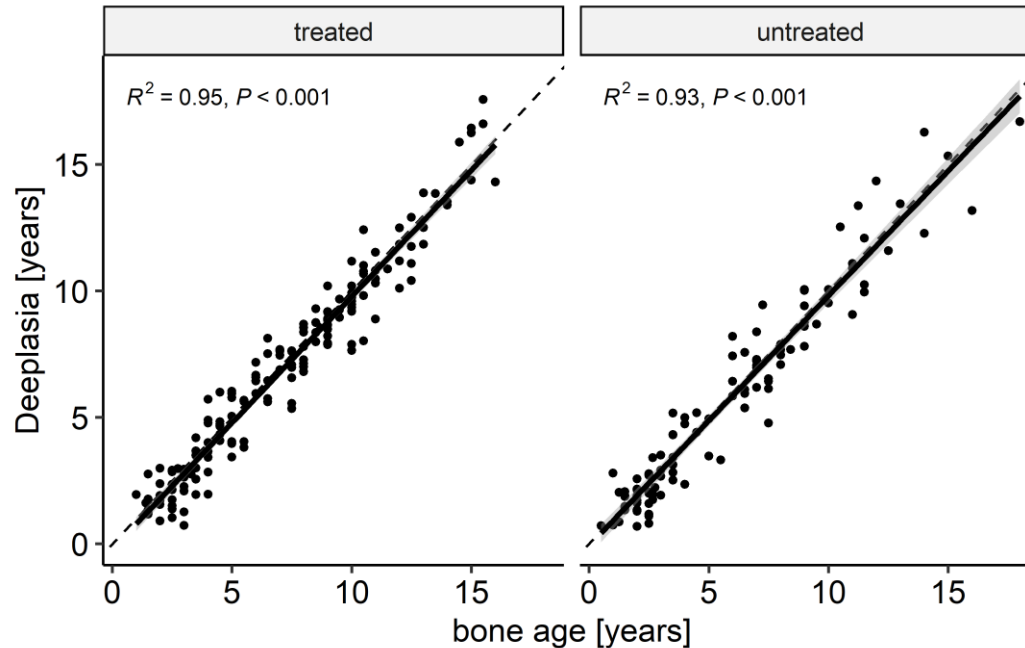
* Mandatory fields

Upload

1. Open attachment
2. Select visit date
3. Upload DICOM, JPG, TIF or other image format
4. Result is displayed direct in visit table



Results of Bone Age in Achondroplasia Assessed With Deeplasia Are Consistent With Greulich/Pyle Method



Results in bone age assessed via Deeplasia are consistent with Greulich and Pyle assessment

- Integration of Deeplasia allows for quick and reliable assessment of bone age

Participating Centres

See also Poster:

K. Wechsung et al.

Real World Effectiveness of Vosoritide in 217 Children with Achondroplasia – Data from a Multicenter European Registry

Poster place: T 20

