

# Learning to Grow: A Year in the Life of Queensland's Vosoritide Multidisciplinary Clinic for Achondroplasia



Zoë Cotton (Physiotherapist) Elle Weston (Clinical Nurse)



# The Journey So far

- Who: Brief introduction to Achondroplasia and Vosoritide
- Where: Our clinic
- What: Our approach to this precision treatment advance
- Why: Hearing the Progress to date
- How... will future directions go?





Article

# Consensus Guidelines for the Use of Vosoritide in Children with Achondroplasia in Australia

Louise Tofts <sup>1,\*</sup>, Penny Ireland <sup>2,3,4</sup>, Tracy Tate <sup>5</sup>, Supriya Raj <sup>4</sup>, Theresa Carroll <sup>2</sup>, Craig F. Munns <sup>2,6</sup>, Stephen Knipe <sup>7</sup>, Katherine Langdon <sup>8,9</sup>, Lesley McGregor <sup>10</sup>, Fiona McKenzie <sup>11,12</sup>, Andreas Zankl <sup>13,14,15</sup> and Ravi Savarirayan <sup>4,16</sup>

## Achondroplasia

- Most common form of short-limbed dwarfism
- Estimated 1 in 25,000-30,000 live births
- Heterozygous FGFR3 mutation (c.1138G>A; p.Gly380Arg)
- 80% of achondroplasia cases occur de novo (Horton, et al., 2007)
- ➤ Downregulation of growth plate chondrocyte proliferation and differentiation → reduced endochondral bone growth
  - Rhizomelia, radial head subluxation, elbow contractures, trident hands, genu varum (Ireland, et al., 2011)
  - → difficulty with self-care tasks
  - Foramen magnum stenosis, macrocephaly (midface hypoplasia)
    - → central sleep apnoea, cranial nerve compression, weakness, motor delays, risk of sudden death, recurrent ear infections (assoc. hearing loss)
  - Spinal canal stenosis and nerve root compression
  - → pain, sensory and motor deficits, bladder and bowel dysfunction





Cheung MS. Arch Dis Child. 2021 Feb;106(2):180-184.

Horton WA Lancet. 2007 Jul 14;370(9582):162-172.

### **Our Clinic**

- Our clinic is for the 'whole' patient (not only about a drug)
- Dedicated achondroplasia vosoritide clinic based in the Department of Endocrinology and Diabetes

Fortnightly clinics

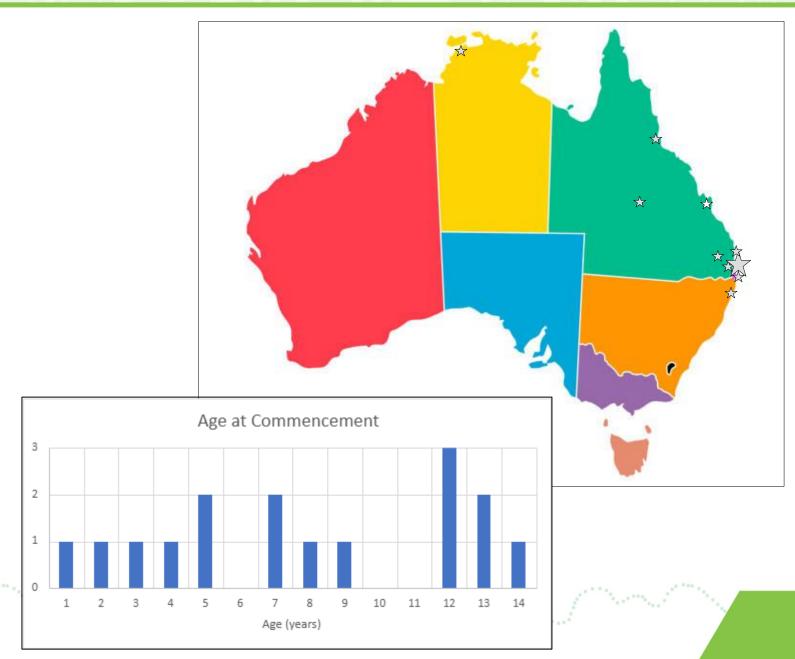
• Multidisciplinary team:



#### Assessment Pathway - First clinic visit Refer for MRI requirements targeted Genetic <2 years testing???|nvitae Baseline MRI Brain+ C spine /referral to ASFM score 1-2:proceed genetics ASFM score 3-4: repeat MRI 2-5 years Satisfactory MRI (ASFM score 1-2) within 2y: proceed with Vosoritide No or unsatisfactory MRI (ASFM) Specialist in Achondroplasia: score 3-4); refer for MRI >5 years Confirm Genetic diagnosis MRI only if clinical concern before Medical history, identification proceeding of complications: Craniocervical compression, Sleep Assessment of Growth disordered breathing: management of complications Growth data indicating as required growth >1.5 cms year Physical examination Tanner Stage Baseline Growth YES NO investigations No growth data or <1.5 cms Proceed with Vosoritide Radiographic Nursing (completed by OP Assessments nurse): Baseline Xray (proximal BP, pulse tibia + distal femur) Height (standing) Weight Head Circumference POTENTIAL OUTCOMES OF FIRST VISIT Awaiting Not eligible Progress to Physiotherapist: medical prescription of STEMS assessment management of Vosoritide Developmental check list complications WeeFim referrer PQoL Functional Assessment Rebook into Sitting heights/LL endocrinology clinic measurements

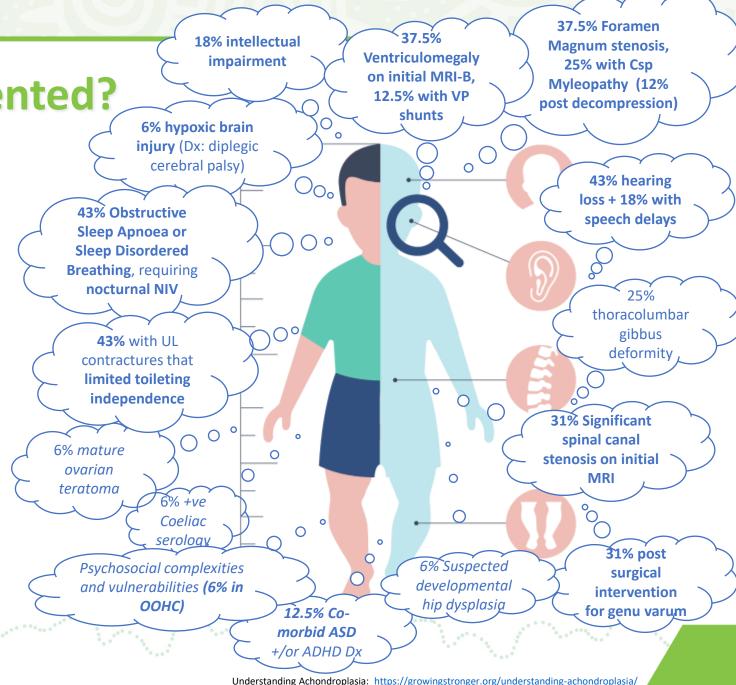
## **Progress to date**

- Commenced seeing patients July 2023
- 16 patients commenced Vosoritide (age range: 14 months to 15 years old)
  - x2 assessed as eligible <1yo</li>
     (@ 6m & 9m respectively)
- 11 have reached 12 months of treatment
- No reports of serious adverse events to date
  - Minor redness and swelling at injection site
  - 1x episode of mild self-limiting hypotension at initiation
- No patients have discontinued treatment



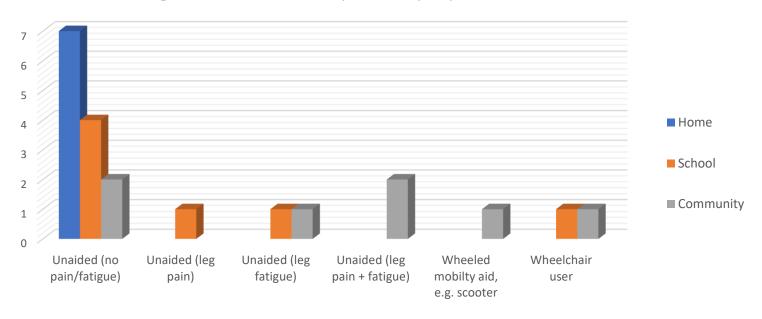
How has our cohort presented?

The Application of Clinical Genetics **Dove**press A Open Access Full Text Article REVIEW Optimal management of complications associated with achondroplasia This article was published in the following Dove Press journal: The Application of Clinical Genetics Penny J Ireland Abstract: Achondroplasia is the most common form of skeletal dysplasia, resulting in Verity Pacey<sup>2,3</sup> disproportionate short stature, and affects over 250,000 people worldwide. Individuals with Andreas Zankl achondroplasia demonstrate a number of well-recognized anatomical features that impact on growth and development, with a complex array of medical issues that are best managed through Priya Edwards<sup>1</sup> a multidisciplinary team approach. The complexity of this presentation, whereby individual Leanne M Johnston<sup>5</sup> impairments may impact upon multiple activity and participation areas, requires consideration Ravi Savarirayan<sup>6</sup>

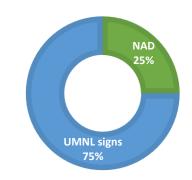


# How has our cohort presented?

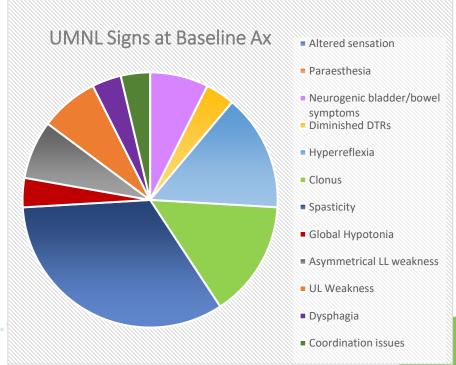
#### Screening Tool for Mobility and Symptoms (STEMs)



## INITIAL NEUROLOGICAL EXAMINATION







Ireland, P.J., Savarirayan, R., Pocovi, T. *et al.* Development of the Screening Tool for Everyday Mobility and Symptoms (STEMS) for skeletal dysplasia. *Orphanet J Rare Dis* **16**, 40 (2021). https://doi.org/10.1186/s13023-021-01681-z

## First disease-specific Rx: Vosoritide

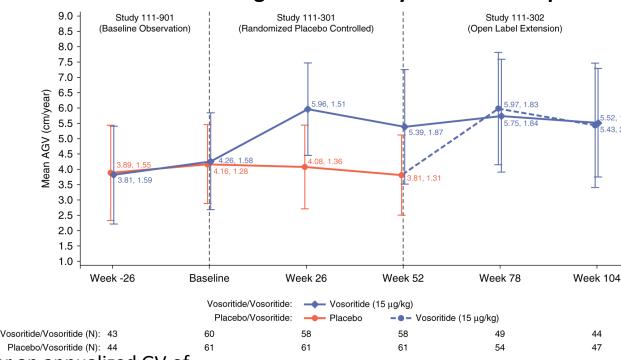
- Trade name VOXZOGO® (BioMarin Pharmaceuticals)
- On PBS for achondroplasia since 2023
- Available for children 0-2 years old since 2024
- Cost approx. \$300,000 per year
- Daily subcut injection
- Safe & efficacious at making long-bones longer in Achondroplsia

So they can grow, but does it improve anything else?

#### **PBS Criteria:**

- Diagnosis of achondroplasia, confirmed by genetic testing
- Must not have growth plate closure (based on bilateral knee x-ray or an annualized GV of >1.5cm/year)
- Must be treated by a medical specialist experienced in the management of achondroplasia OR a paediatrician in consultation with an experienced specialist

#### Mean annualized growth velocity Vosoritide vs placebo



## **Consumer's Goals for Vosoritide**

"I'd love to see him make more **progress** across all **developmental domains**, because he's quite delayed currently."

(mother of a 4yo Male)

"...to put on and take off my **shoes**without as much **back pain**."

(13yo Male)

"I'd like to run faster.

I'd like to be able to get my togs [swimsuit] on over my shoulders more easily **by myself**.

I'd like to be able to pull down and pull back up my undies and shorts when I'm all **sweaty** after lunchbreak.

It'd also be cool to reach further, like the taps in the toilets at the shopping centre, **all on my own**." (9yo Female)

"Reaching things in my wardrobe by myself.

Managing stairs with less tiredness.

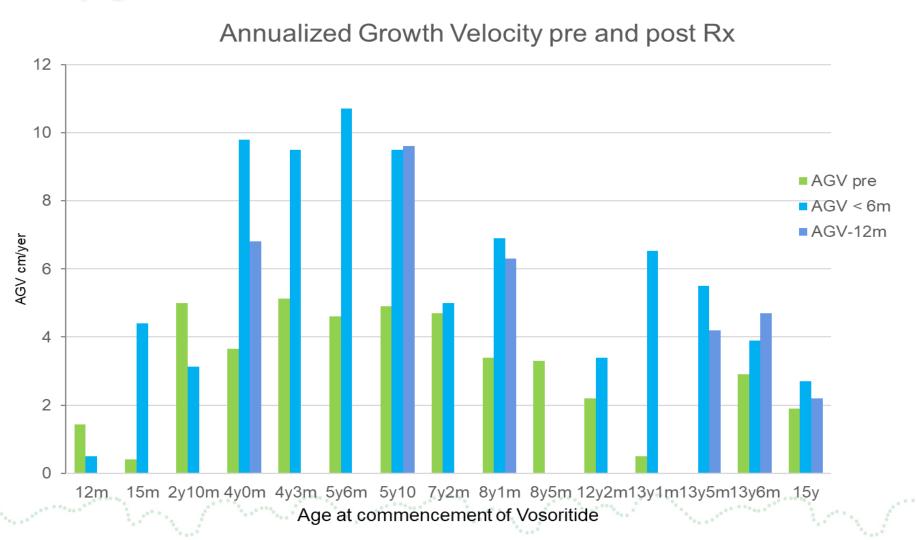
And long term, getting a part-time job, —
e.g. fast food." (14yo Male)



Outcomes to date

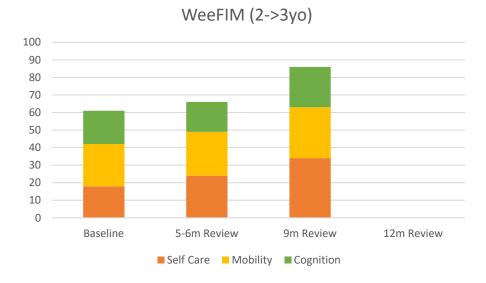


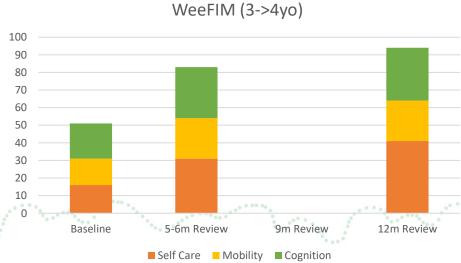
# **Preliminary growth data**



## **An Overview of 12m Functional Data**







#### Activities Scales for Kids (ASK-30)





## **Key Learnings & previously unexplained benefits**

- Increased energy levels/stamina (& appetite)
- Incidence of pain
  - just living with it all haven't known any differently... until it's not there...?
- Developmental progress across domains
  - Unknown mechanism / pathophysiology
  - Unknown relationship (coincidence or not?)
- Incidence of radiculopathy and neurological compromise
  - Asymmetrical LL neuro-orthopaedic
- Checking Paralympic Classification criteria\*
  - Class 8, Short Stature (S-SB6 or S-SB7)
  - Safe & Legal as a 'growth enhancer'

"He's making leaps and bounds with his gross motor development. This has been his most rapid period of progress (since commencing Vosoritide)." (Community Physiotherapist)

"His vocabulary has exponentially increased since starting on Vosoritide. He's picking up words from his peers, such as "lame" – the other day, my husband and I said, 'he's sounding like a teenager now'!". (patient's mother)



#### **Key Qns remaining:**

- Impact on foramen magnum stenosis?
  - Foramen magnum grows rapidly in first months of life will we see any change if vosoritide is commenced in infancy?
  - Impact on developmental timeline?
  - Impact on sleep disordered breathing or ENT issues?
- Impact on musculoskeletal segualae, such as genu varum or spinal canal stenosis?
- Mechanism for impact on reducing pain?



> Contributing to national Ax standardization

## **Acknowledgements**

#### Our patients & families!

- Dr Karissa Ludwig
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- A/Prof Penny Ireland
- Emma Pendlebury
- Dr Theresa Carroll
- Dr Tony Huynh

## **Questions?**



Contact the MDT here: QBAMS@health.qld.gov.au

If you think you have someone who might be interested, get in touch!