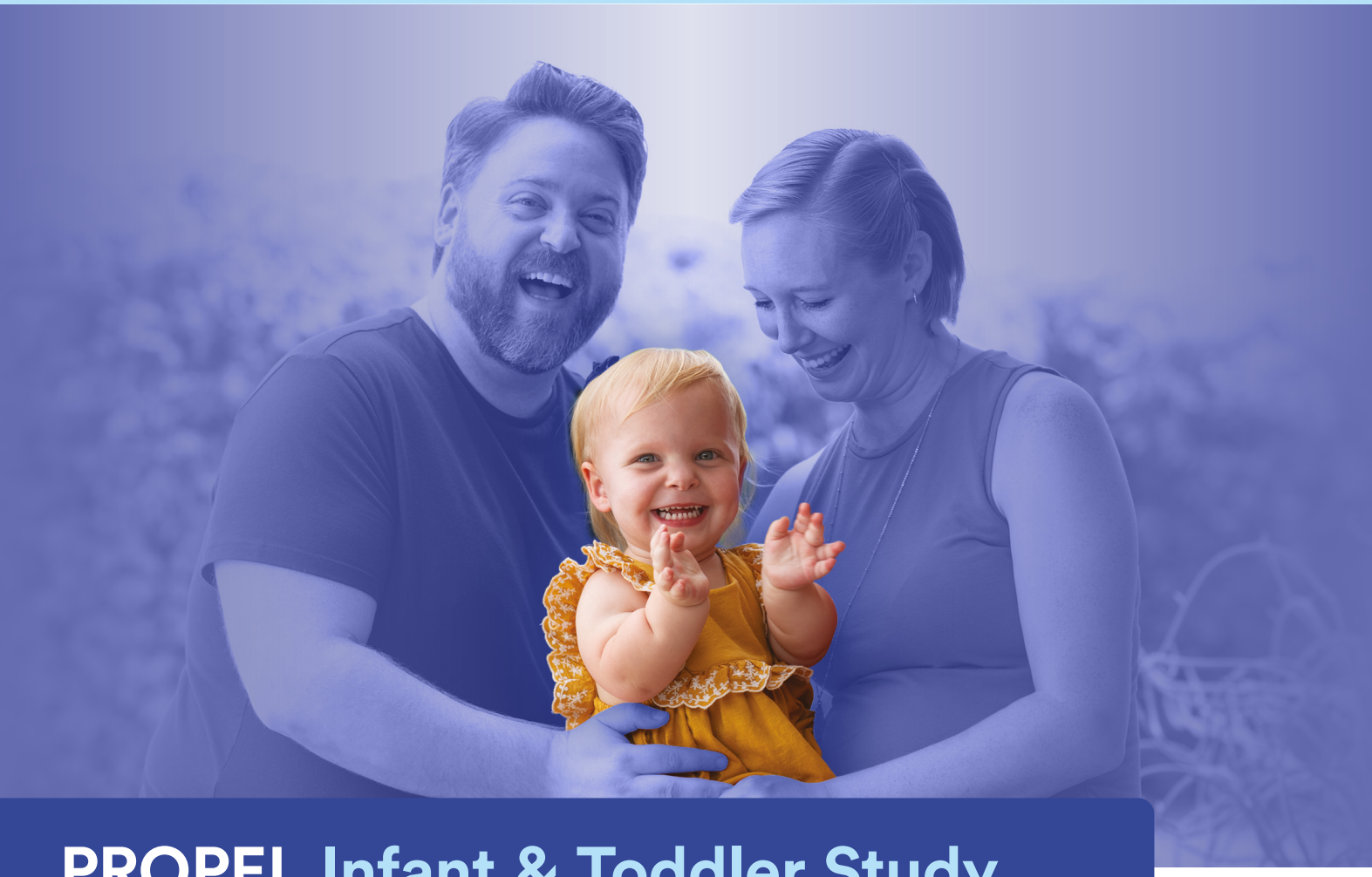


PROPEL Infant & Toddler Study

This plain language overview shares information about achondroplasia (ACH) and infigratinib, an investigational medicine taken by mouth.[1]

The **PROPEL clinical development program** includes ongoing research into the effects of the investigational study drug in **children with ACH who are over 3 but under 18 years of age.**[1–4]

Findings from this research have helped lay the groundwork for the **PROPEL Infant & Toddler study**, which is now exploring the study drug in **children with ACH who are under 3 years of age.**[5]

This overview explains how the study is designed and why researchers are evaluating the investigational medicine in infants and toddlers.

This information is for general awareness and not intended as recruitment.
Infigratinib is an investigational medication that has not been approved by the EMA, US FDA or any regulatory agency. Its safety and efficacy are unknown.

bridgebio

What is ACH?

ACH is the most common type of skeletal dysplasia, a condition that affects how bones and cartilage grow.[6–9]

It occurs in about 1 in 25,000 births.[7]

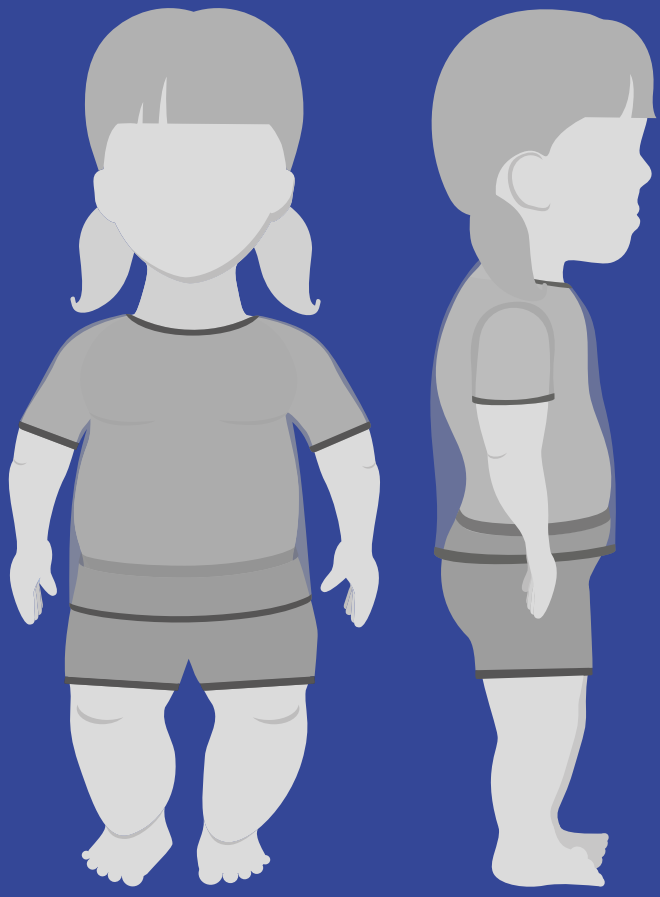
ACH is a genetic condition, but it doesn't always run in families. About 80% of people with ACH are born to parents of average stature.[6,7]

ACH happens because of a change in a gene called fibroblast growth factor receptor 3 (*FGFR3*). This change causes bone growth to slow down, which can lead to disproportionate short stature and may contribute to certain physical characteristics, such as[6–8]:

About **1 in 25,000** births[7]

About 80% born to parents of average stature[6,7]

- **Larger head and prominent forehead**
- **Flat bridge of the nose**
- **Shorter arms and legs** (compared with the torso)
- **Short, broad hands** (sometimes with extra space between the middle and fourth fingers)
- **Bowed legs**
- **Curving or narrowing of the spine**



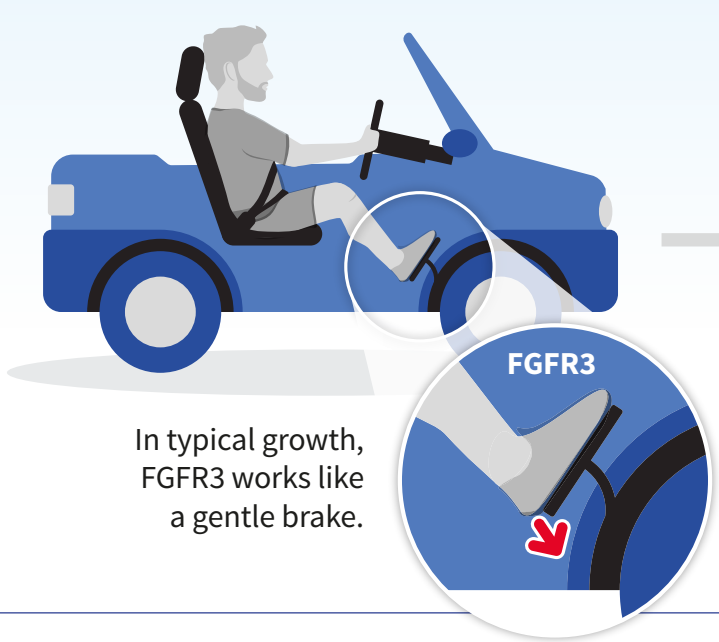
Average adult height in ACH[7]

Women: 125 cm (4 ft 1 in)
Men: 130 cm (4 ft 3 in)

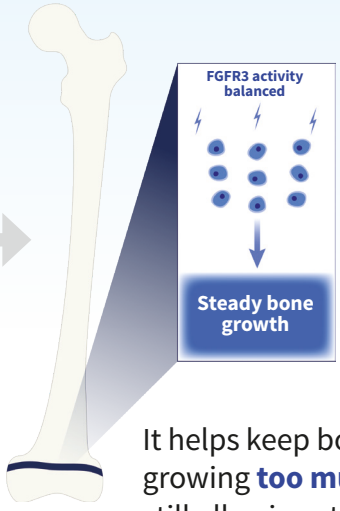
This information is for general awareness and not intended as recruitment.

FGFR3: A “brake” on bone growth

Typical bone growth[2,6,7,9–11]



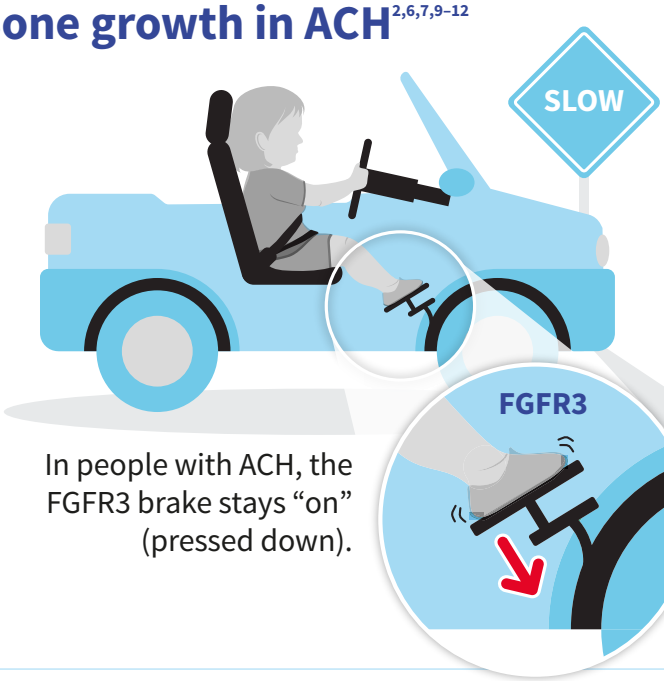
In typical growth, FGFR3 works like a gentle brake.



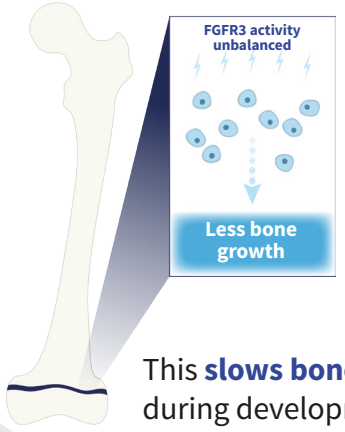
It helps keep bones from growing **too much**, while still allowing steady growth.

Hypothetical illustrations for educational purposes.

Bone growth in ACH[2,6,7,9–12]



In people with ACH, the FGFR3 brake stays “on” (pressed down).



This **slows bone growth** during development, leading to shorter arms and legs and other physical differences.

Hypothetical illustrations for educational purposes.

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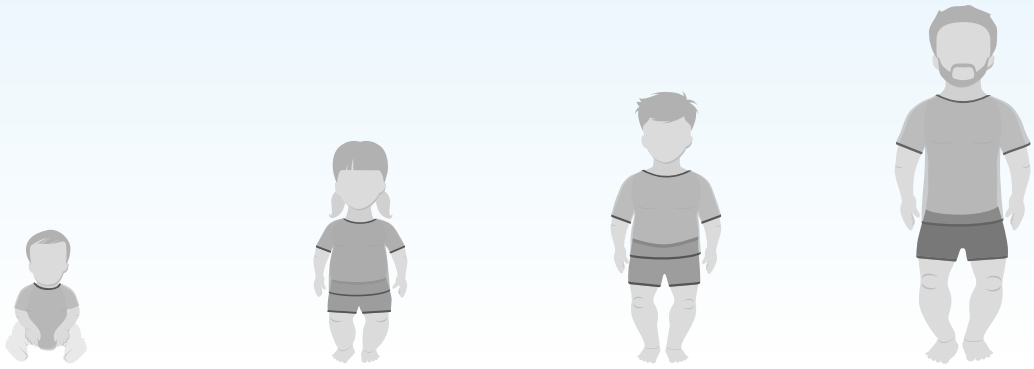
What medical challenges can occur in ACH?[6,13–23]

In addition to physical differences, people with ACH may have medical challenges – some starting in infancy and others appearing later in life.



Infants (0–2 years) | **Children** (3–12 years) | **Teenagers** (13–17 years) | **Adults** (18+ years)

Head & neck
- Fluid build-up in the brain
- Narrowed opening at the base of the skull (foramen magnum)
- Feeding/swallowing challenges
- Frequent ear infections*
- Breathing challenges (especially during sleep)

Spine
- Curved upper spine
- Narrowing of the lower spine
- Back pain & mobility challenges

Arms & legs
- Bowed legs
- Limited movement in the elbows or hips
- Joint pain

*May cause hearing challenges and/or delayed speech development.

Not everyone with ACH will have all these medical challenges. People may experience them differently, and some may occur at different ages. This list does not include every possible medical challenge in ACH.

This information is for general awareness and not intended as recruitment.

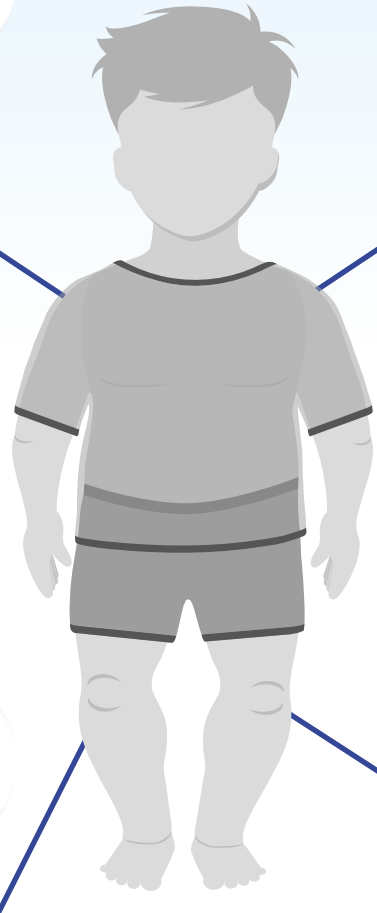
How can ACH affect daily life and well-being?[2,6,13,16,24–29]

Daily life & function

- Some everyday activities (e.g., reaching, driving, getting dressed) may be more challenging
- Pain can make walking and daily tasks more tiring
- Adaptive devices or tools (e.g., step stools, mobility aids) may support independence

Social & emotional

- Bullying or staring from others
  - May affect self-confidence
  - Can lead to anxiety or stress



School & work

- Adjustment or modifications may be required to participate fully

Physical & mobility

- Back or joint pain can affect movement
- Some tasks may take more time or energy

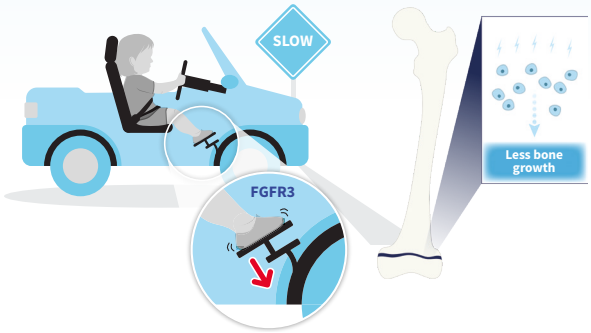
With the right support and adaptations, people with ACH can live full and independent lives.[24]

This information is for general awareness and not intended as recruitment.

What is infigratinib?

Infigratinib is an investigational medicine being studied in children with ACH and also in children with a different form of skeletal dysplasia called hypochondroplasia.[1–5,30] Both conditions are caused by changes in the FGFR3 gene that slow bone growth and lead to disproportionate short stature and other physical features.[6–8,31] Researchers are studying whether infigratinib may help bones grow by reducing FGFR3 activity – like easing your foot off a brake pedal.[1–5,30,32,33] It is not yet known whether infigratinib has any benefit. Research is ongoing to understand its effects.

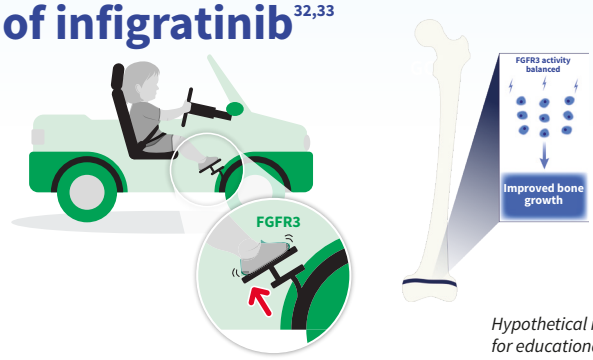
Bone growth in ACH[2,6,7,9–12]



In people with ACH, the FGFR3 brake stays "on" (pressed down).

This limits bone growth during development, resulting in features commonly seen in people with ACH, such as shorter arms and legs.

Potential action of infigratinib[32,33]



Hypothetical illustrations for educational purposes.

Researchers are studying if with infigratinib, the FGFR3 "brake" signal may be reduced – like easing your foot off the pedal.

This may allow the growth plate to work more typically by reducing the "slow-down" signal. It is not yet known whether infigratinib has any benefit. Research is ongoing to understand its effects.

How is infigratinib taken?

Infigratinib is an investigational medicine taken by mouth. In clinical studies, the form and amount of medicine given depend on a child's age and weight.[1–5,30]

For infants under 6 months of age[34]

Liquid medicine

For children 6 months of age and older[1,34]

A sprinkle capsule with tiny minitablets inside

Swallowed whole or sprinkled on soft food

This information is for general awareness and not intended as recruitment.
Infigratinib is an investigational medication that has not been approved by the EMA, US FDA or any regulatory agency. Its safety and efficacy are unknown.

Earlier studies researched infigratinib in children with ACH ages 3 to under 18 years old

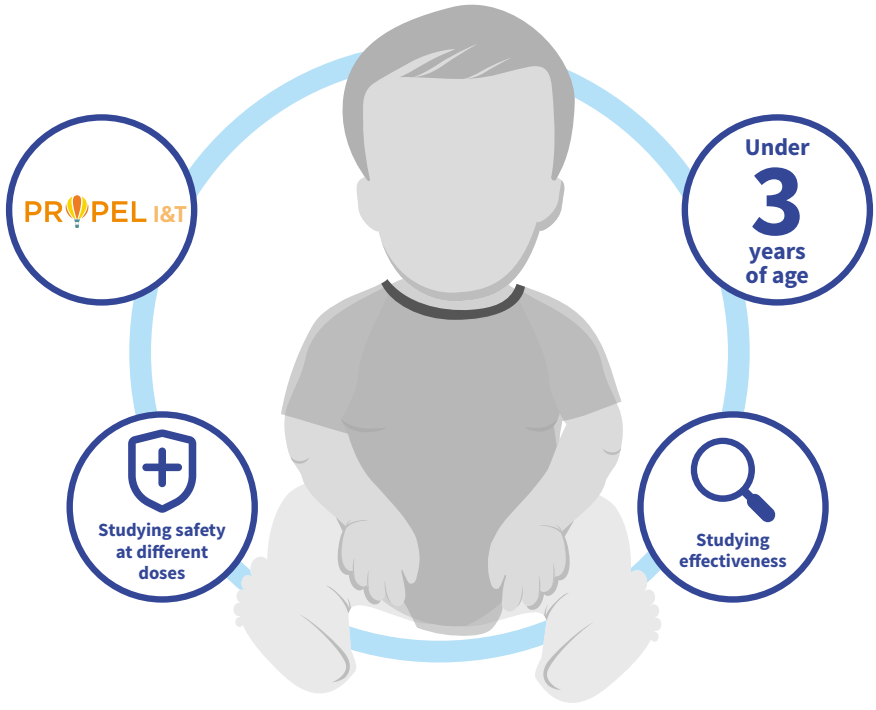
In pediatric clinical research, new medicines are often studied first in smaller groups and in older children. This process helps researchers learn about the safety profile and potential benefits before testing in larger groups and, eventually, in younger children.

The **PROPEL clinical development program** investigated the effects of infigratinib in children with ACH who were over 3 but under 18 years of age. Now, BridgeBio is studying younger age groups in the **PROPEL Infant & Toddler study**, which is investigating the effects of the study drug in children under 3 years of age.[1–5]

What is the PROPEL Infant & Toddler study?

The **PROPEL Infant & Toddler study** is a **global clinical research study** sponsored by BridgeBio.

It is exploring **the safety profile of infigratinib and how it works** in children with ACH who are under **3 years of age**.



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Why is infigratinib being studied in infants and toddlers?

Researchers are studying infigratinib in infants and toddlers with ACH to[2,6]:

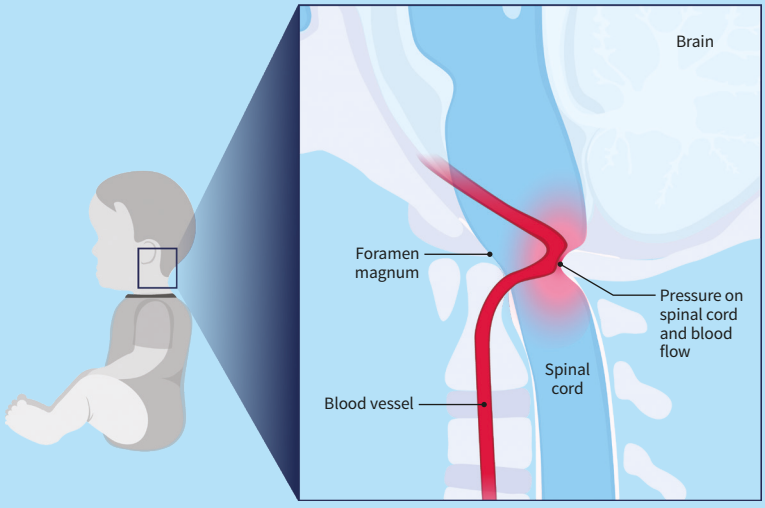
- **Learn about its safety profile in infants and toddlers in this age group**
- **Understand its potential impact on medical complications associated with ACH**, such as foramen magnum stenosis (FMS)
- **Measure its potential impact on growth and body proportions**
- **Evaluate its potential impact on quality of life**

What is FMS?

The foramen magnum is an opening at the base of the skull where the spinal cord passes from the brain to the body.[35]

In children with ACH, this opening is often smaller than what is typical. This narrowing is called FMS.[35]

In some instances, this opening is so small that it can squeeze the spinal cord and nerves, which may cause breathing or feeding problems, delays in development, or (in rare cases) life-threatening complications.[2,13,35,36]



About **1 in 5 children** with ACH **need surgery** for FMS. Early detection and treatment are key to preventing serious complications.[14]

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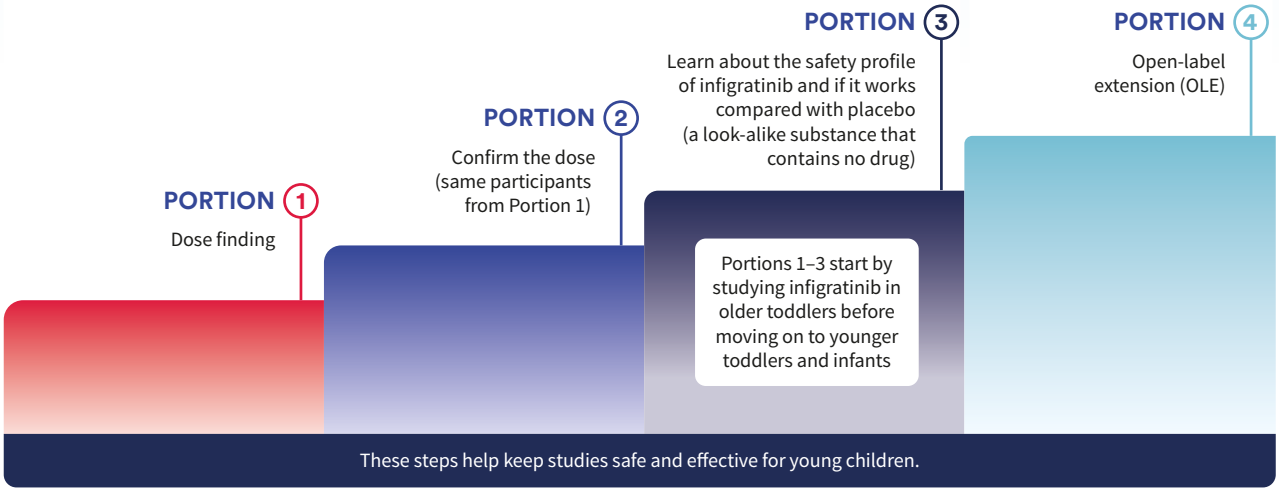
How is the PROPEL Infant & Toddler study designed?[5,34]

The PROPEL Infant & Toddler study is designed like a staircase, with each portion building on the one before it.

The first steps (Portions 1–3) focus on finding the appropriate dose of infigratinib to continue to study. Older participants are studied first, followed by younger age groups, with each step tested before moving forward.

Participants from Portions 1–3 who are under 3 years of age may continue into Portion 4, where researchers will gather additional information on if infigratinib works and its safety profile over a longer period.



How are studies different for infants & toddlers?[37-41]

Infants and toddlers are not just "smaller" versions of older children – their bodies develop and respond to medicines differently, and they need to be monitored in ways that fit their age.

In this study, special considerations for infants and toddlers include:

- Investigating **lower doses based on weight**
- Investigating **age-appropriate dosage forms** like liquids and mini-tablets
- Using **assessments that fit their age**, like measuring growth lying down and tracking certain developmental milestones
- **Using scans,** such as MRIs, to understand how their bodies are developing

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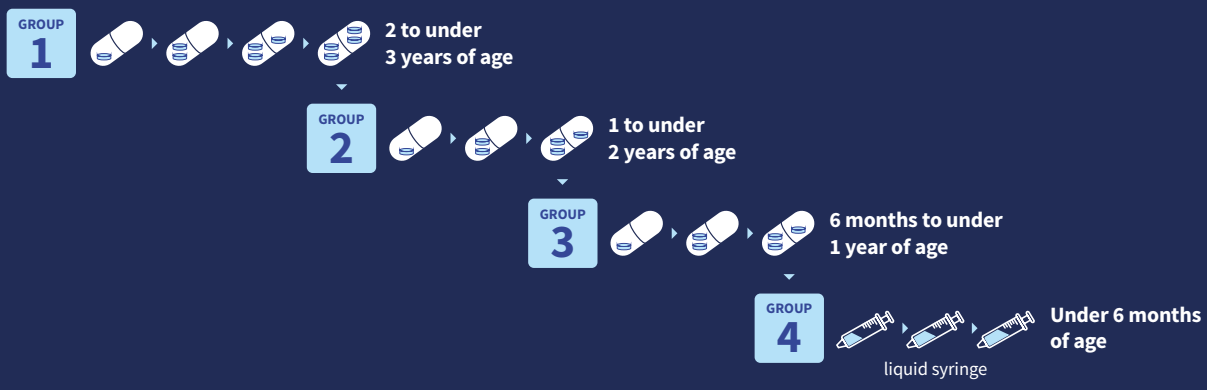
Portion 1: Dose finding[5,34]

Goal: Identify the dose of infigratinib to be used in Portion 2

The study begins with older participants and moves step-by-step to younger participants.

- There will be 4 groups based on age (about 5 participants per group)
- Within each age group, 3 or 4 dose levels of the study drug are tested for safety, starting at the lowest dose. Each participant receives a single dose*
- Each younger group begins only after all doses are evaluated to be safe in the older group



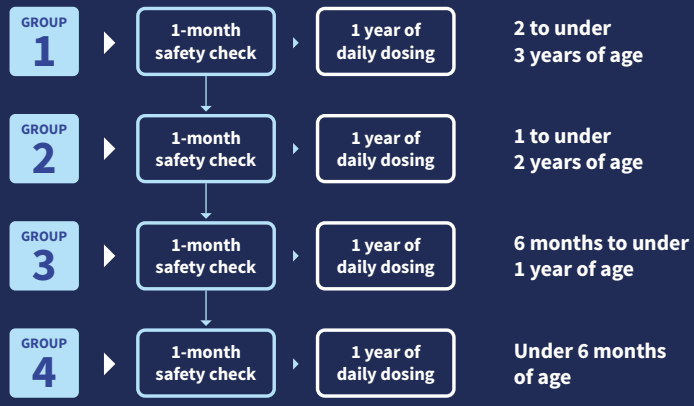
*In some cases, a participant may receive a second single dose at a higher level.

Portion 2: Confirm the dose (same participants from Portion 1)[5,34]

Goal: Confirm the dose for each age group before moving on to Portion 3

Each age group takes part one at a time, from oldest to youngest.

- Participants take infigratinib at the dose chosen in Portion 1 once daily for 1 month, while safety and how the medicine moves through the body are measured
- After those results are confirmed, the next youngest age group begins
- All participants then continue taking the study drug once daily for 1 year



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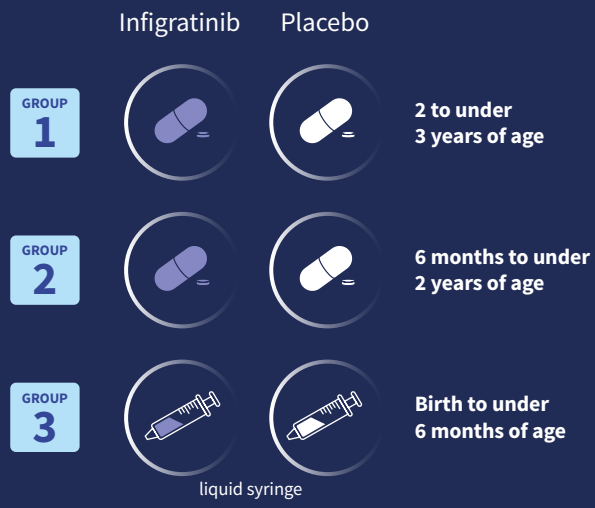
Portion 3: Learn about the safety profile of infigratinib and if it works compared with placebo, a look-alike substance that contains no drug (all new participants)[5,34]

Goal: Study the safety profile of infigratinib and if it works over 1 year compared with placebo, using the dose determined in Portion 2

This portion of the study will include 56 **new infants and toddlers with ACH who did not participate in Portions 1 or 2**.

- Researchers will compare infigratinib with a placebo (a look-alike substance that contains no drug) to study its safety profile and potential impact on medical complications, growth, body proportions, and quality of life
- Participants will join in 3 age groups and be randomly assigned to receive infigratinib (at the dose confirmed in Portion 2) or placebo for 1 year
  - Half of the participants will receive the study drug and half will receive placebo
  - Neither the participants nor the researchers will know which one is given

The use of a placebo makes it easier to understand if a medication works and its safety profile.



Each age group in Portion 3 will begin only after 1-month safety results from Portion 2 are reviewed.

Portion 4: Open-label extension (OLE)

(participants who completed 1 year in Portion 2 or 3)[5,34]

Goal: Continue to collect information about the safety and effectiveness of infigratinib in participants who completed 1 year in Portion 2 or 3

Participants who completed 1 year in Portion 2 or 3 and are under 3 years of age may continue in Portion 4 so that researchers can keep studying the safety profile of infigratinib and if it works over a longer period.

- Participants receive the study drug until they reach 3 years of age
- After turning 3, they may continue in the PROPEL OLE study until final adult height is reached
- All participants in Portion 4 will receive the study drug, even if they received placebo in Portion 3

Portion 2 or 3
Under 3 years of age after 1 year of participation
→ **Portion 4**
PROPEL Infant & Toddler OLE
All participants receive infigratinib until 3 years of age

Portion 2 or 3
Over 3 years of age after 1 year of participation
→ **PROPEL OLE**
All participants receive infigratinib until final adult height is reached

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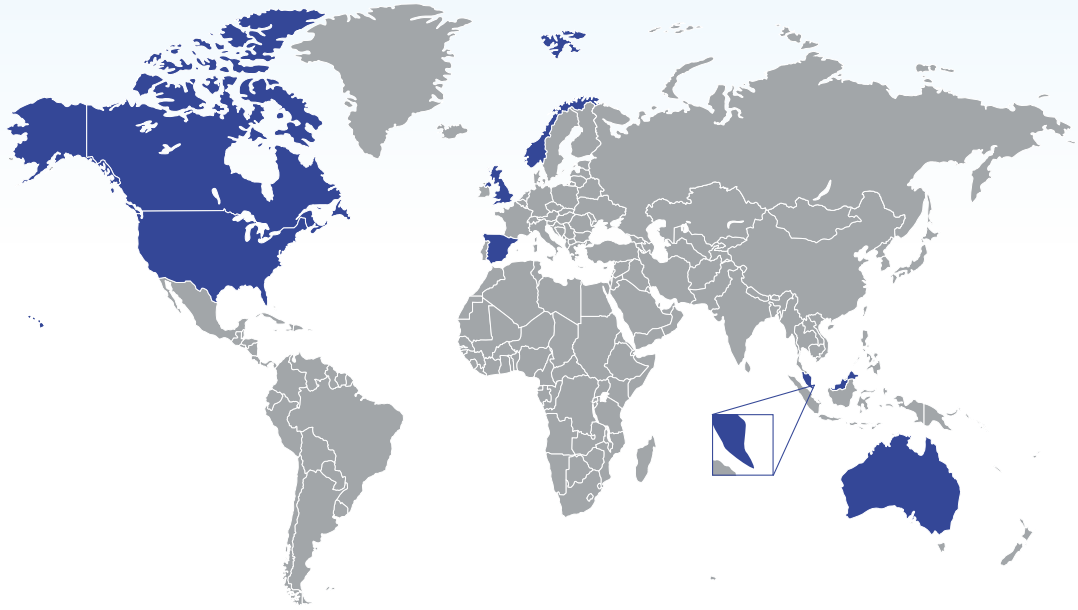
Infigratinib is an investigational medication that has not been approved by the EMA, US FDA or any regulatory agency. Its safety and efficacy are unknown.

Where will the PROPEL Infant & Toddler study take place?[5]

The PROPEL Infant & Toddler study will take place in several countries around the world, including:

- Australia
- Canada
- Norway
- Singapore
- Spain
- UK
- US



Where can I learn more?

For additional information about the **PROPEL Infant & Toddler study**, including details about the study population, visit:
https://clinicaltrials.gov/study/NCT07169279

This information is for general awareness and not intended as recruitment.

Abbreviations

ACH, achondroplasia; FGFR3, fibroblast growth factor receptor 3; FMS, foramen magnum stenosis; OLE, open-label extension.

Acknowledgments

BridgeBio thanks the children and families who participated in earlier studies that helped to inform this research, including PROPEL 2.

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