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Phase II study of TYRA-300 in children with achondroplasia

Submission date
11/06/2025

Recruitment status
Recruiting

Registration date
24/11/2025

Overall study status
Ongoing

Last Edited
24/11/2025

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
This study will test a new medicine called dabogratinib (TYRA-300) in children with achondroplasia (ACH) who still have open growth plates, which are the areas of bone that allow for growth. The main goals of the study are to find out if dabogratinib is safe, well-tolerated, and to help identify dose levels that may be effective for children with ACH.

Who can participate?
Children aged between 3 and 10 years who have had a molecular diagnosis of ACH due to the common FGFR3 G380R mutation involves genetic testing to identify the specific mutation in the FGFR3 gene.

What does the study involve?
The study includes three groups of children: the Sentinel Safety Cohort, Cohort 1, and Cohort 2.

The Sentinel Safety Cohort will be the first group to receive dabogratinib. This group will help to understand the safety of the medicine by testing up to four different dose levels, and will include children aged 5 to 10 years . These children can join directly, without first taking part in a natural history (observation) study. After completing the dose-finding stage, participants in this group will continue dabogratinib for 12 months at their assigned dose level.

Cohort 1 will include children aged 3 to 10 years who have not received any previous growth-accelerating treatment. Before beginning dabogratinib, they will take part in a natural history study for at least 6 months to help understand their growth patterns before treatment. After this observation period, they will begin open-label treatment, meaning that all participants will receive dabogratinib at one of the doses found to be safe in the Sentinel group.

Cohort 2 will include children aged 3 to 10 years who have previously received a growth-accelerating treatment. Like Cohort 1, they will take part in a 6-month natural history period before starting dabogratinib at one of the approved dose levels.

All participants will have the option to continue taking dabogratinib for up to 36 months as part of this study. After that, they may also be able to continue treatment in a separate long-term extension study to further evaluate the effects and safety of dabogratinib over time.

What are the possible benefits and risks of participating?
Benefits and risks not given at registration.

Where is the study run from?
Tyra Biosciences Inc.

When is the study starting and how long is it expected to run for?
June 2025 to March 2031

Who is funding the study?
Tyra Biosciences Inc.

Who is the main contact?
Chief Investigator Moira Cheung, moira.cheung@gosh.nhs.uk

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06842355

Clinical Trials Information System (CTIS)
2024-520331-33

Integrated Research Application System (IRAS)
1011484

Protocol serial number
TYR300-201

Study information

Scientific Title
A multicenter, phase 2, dose-escalation/dose-expansion study of TYRA-300 in children with achondroplasia with open growth plates: BEACH301

Acronym
BEACH301

Study objectives
• Evaluation of the safety and tolerability of ascending oral doses of TYRA-300 in children with genetically confirmed ACH with open growth plates.

• Evaluation of annualized growth velocity with ascending oral doses of TYRA-300 in prepubertal children aged 3-10 years old (inclusive) with genetically confirmed ACH with open growth plates, and determine the dose(s) of TYRA-300 for further study.

• Evaluation of changes in height z-score with ascending oral doses of TYRA-300 in prepubertal children aged 3-10 years old (inclusive) with genetically confirmed ACH with open growth plates.

• Characterize sparse PK of TYRA-300 in children with ACH with open growth plates across dose levels.

• Evaluate change from baseline in anthropometric measures in prepubertal children aged 3-10 years old (inclusive) with genetically confirmed ACH with open growth plates.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 15/08/2025, - (-, -, -, United Kingdom; -; -), ref: 25/LO/0490

Primary study design
Interventional

Study design

Phase II multicenter dose-escalation/dose-expansion study

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Achondroplasia with open growth plates
Therapeutic areas: Diseases [C] - Congenital, Hereditary, and Neonatal Diseases and Abnormalities [C16]

Interventions
The BEACH 301 study consists of 3 cohorts of participants: Sentinel Safety Cohort, Cohort 1, and Cohort 2. Participants in each cohort will receive 12 months of open-label TYRA-300 (dabogratinib) at their assigned dose level, after which they will have the opportunity to participate in an optional 36-month treatment extension. TYRA-300 will be administered once daily by the oral route at the following dose levels: 0.125, 0.25, 0.375, and 0.50 mg/kg. The initial dose level in the Safety Sentinel Cohort is 0.125 mg/kg, with dose level escalations based on protocol-specified criteria. Participants in Cohorts 1 and 2 will be assigned to dose levels previously cleared in the Safety Sentinel Cohort.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
TYRA-300-B01

Primary outcome(s)
1. Incidence of treatment-related adverse events as assessed by CTCAE v5.0 throughout the duration of the study
2. Change from baseline in AGV (annualized growth velocity) as assessed by calibrated stadiometer measurements every 6 months in the Treatment Phase and every 12 months in the Optional Long-Term Treatment Extension

Key secondary outcome(s)
1. Change from baseline in height z-score as assessed by calibrated stadiometer every 6 months in the Treatment Phase and every 12 months in the Optional Long-Term Treatment Extension
2. Comparison of single and multiple dose sparse PK parameters as assessed by Cmax, Tmax, AUCO-last, AUCTau, AUC0- ∞, Vd/F, CL/F, and t1 /2 at Day 1, Day 15, Day 30, and every 3 months thereafter in the Treatment Phase
3. Change from baseline in anthropometric measurements as assessed by a calibrated stadiometer every 6 months in the Treatment Phase and every 12 months in the Optional Long-Term Treatment Extension. These include, but are not limited to: standing height; sitting height; upper arm length; lower arm length; tibial length; femur length; arm span proportionality (arm span/height ratio), upper segment/lower segment ratio.

Completion date
21/03/2031

Eligibility

Key inclusion criteria

Participants enrolled in the study must meet all of the following inclusion criteria to be eligible.
1. Informed consent provided by parent(s) or legal guardian(s). As study participants are less than 18 years old, participants are willing and able to provide written assent (where required by local authorities or the Institutional Review Board [IRB]/Independent Ethics Committee [IEC]).
2. Molecular diagnosis of achondroplasia (ACH) (FGFR3 G380R).
3. Radiographically confirmed open growth plates at screening, as determined by the bone age X-ray.
4. Ability to comply with study visits and assessments.
5. Able to cooperate with minimal assistance with anthropometric measurements and able to stand and ambulate independently.
6. Ability to take an oral formulation (sprinkle capsule/mini-tablet) of TYRA-300.
7. Willingness to discontinue consumption of grapefruit, pomelos, star fruit, Seville oranges, or food products containing these ingredients following consent to participate in the study if participating in the Sentinel Safety Cohort or within 1 week prior to initiation of treatment on Day 1 if participating in Cohorts 1 or 2.
8. Females ≥10 years old or have begun menses must have an initial negative serum pregnancy test at screening and be willing to undergo periodic pregnancy testing (serum or urine according to local regulations). Females who turn 10 years old or begin menses during the study period must be willing to undergo periodic pregnancy testing (serum or urine according to local regulations).
9. Participants and their partners who have reached puberty and have been identified by the investigator to be sexually active must practice highly effective contraception. For the purposes of this study, highly effective methods are those that can achieve a failure rate of less than 1% per year when used consistently and correctly.
Inclusion Criteria Specific to Sentinel Safety Cohort:
11. Aged 5 to 10 years old (inclusive) at the time of consent.
Inclusion Criteria Specific to Cohort 1:
12. Aged 3 to 10 years old (inclusive) at the time of consent.
Inclusion Criteria Specific to Cohort 2:
13. Aged 3 to 10 years old (inclusive) at the time of consent.
14. Have received prior growth accelerating therapy (eg, CNP analogs; FGFR pathway inhibitors, including small molecules, antibodies and ligands/ligand traps; human growth hormone [hGH], insulin-like growth factor 1 [IGF-1], anabolic steroids, etc.).

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Child

Lower age limit

3 Years

Upper age limit

17 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Participants must meet none of the following exclusion criteria to be eligible for the study:
1. Have an unstable condition at study entry that is highly likely to require urgent surgical intervention within the first three months of study therapy.
2. In the view of the investigator, presence or history of any uncontrolled or untreated condition that could impact growth or concurrent disease or condition that would interfere with study participation, safety evaluations, or data interpretation, including but not limited to:
2.1. Hypothyroidism or hyperthyroidism
2.2. Insulin-requiring diabetes mellitus
2.3. Autoimmune inflammatory disease
2.4. Renal insufficiency defined as serum creatinine >2 mg/dL
2.5. Chronic anemia
2.6. Cardiac or vascular disease
2.7. Psychiatric disorder
3. Diagnosis of an endocrine condition that alters calcium/phosphate homeostasis.
4. Gastrointestinal conditions that may affect absorption of TYRA-300.
5. Prior limb lengthening surgery or planned or expected to have limb lengthening surgery while enrolled in the study.
6. Thoracolumbar kyphosis angle >60 at screening. If spine X-ray is required to confirm study eligibility, the scheduled Day 1 X-ray assessments (Table 1 [Sentinel Safety Cohort] and Table 3 [Cohorts 1 and 2]) may be performed at the Screening Visit, according to investigator discretion.
7. Taking medications that are strong inhibitors or inducers of cytochrome P450 (CYP) 3A4. Participants who can switch to a medication without a strong CYP3A4 interaction require a 2-week washout period prior to starting TYRA-300 (which can occur during the screening window).
8. Long-term treatment with oral corticosteroids (>3 weeks) in the past 6 months prior to consent. Receiving treatment with a low-dose ongoing inhaled steroid for asthma is permitted.
9. Known allergy to TYRA-300 or excipients of the formulated product.
10. Clinically significant serum phosphorous level greater than the upper limit of normal (ULN) for pediatric age range according to the local laboratory during screening, confirmed by a repeat value, at the discretion of the investigator. Repeat collections should be obtained at least 24 hours after the initial draw.
11. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) level >3x ULN or total bilirubin >2x ULN (except for subjects with known history of Gilbert's disease) at screening.
12. History or current evidence of corneal or retinal disorder/keratopathy.
13. Long bone fracture within 3 months of screening.
14. Presence of guided growth hardware/8 plates. However, prior surgery to correct genu varum is allowed if the growth plate cartilage remains open and 8 plates/guided hardware have been removed at least 6 months prior to study entry.
15. Planned or anticipated orthopedic surgeries (such as genu varum correction) during the study period.
16. Females who are pregnant, breastfeeding, or planning to become pregnant within 180 days after the last dose of TYRA-300 and males who plan to father a child while enrolled in this study or within 180 days after the last dose of TYRA-300.
17. Participation in another clinical study of an investigational therapy or device within 30 days

or five half-lives of another investigational therapy, whichever is shorter, prior to consent.
18. Received prior therapy with TYRA-300.
Exclusion Criteria Specific to Cohort 1:
19. Have received prior therapy growth accelerating therapy (eg, CNP analogs; FGFR pathway inhibitors, including small molecules, antibodies and ligands/ligand traps; hGH, IGF-1, anabolic steroids, etc.) at any time.
Exclusion Criteria Specific to Cohort 2:
20. Receipt of prior growth-accelerating therapy within 3 months of consent.
21. Discontinuation of a prior growth-accelerating therapy due to an FGFR-related toxicity.

Date of first enrolment
20/08/2025

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Australia

Canada

Study participating centre
Great Ormond Street Hospital
Great Ormond Street
London
England
WC1N 3JH

Study participating centre
Sheffield Childrens Hospital
Western Bank
Sheffield
England
S10 2TH

Study participating centre
Guys and St Thomas Hospital
Great Maze Pond
London

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SE1 9RT

Study participating centre
Children's Hospital Colorado
13123 East 16th Avenue
Aurora, Colorado
United States of America
80045

Study participating centre
Nemours Alfred I duPont Hospital for Children
1600 Rockland Road
Wilmington, Delaware
United States of America
19803

Study participating centre
Washington University
660 South Euclid Avenue
St Louis, Missouri
United States of America
63130

Study participating centre
Royal Children's Hospital
50 Flemington Road
Parkville, Victoria
Australia
3052

Sponsor information

Organisation
Tyra Biosciences, Inc.

Funder(s)

Funder type
Industry

Funder Name
Tyra Biosciences Inc.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available