ISRCTN47442783 https://doi.org/10.1186/ISRCTN47442783

Follow up at 1 and 2 years of corrected age for participants in the AZTEC study (Azithromycin Therapy for Chronic Lung Disease of Prematurity)

Submission date
07/04/2022

Recruitment status
No longer recruiting

Registration date
12/04/2022

Overall study status
Completed

Last Edited
09/12/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Preterm birth, especially at less than 30 weeks gestation, is significantly associated with respiratory, neurodevelopmental and growth abnormalities. The AZTEC study is registered on ISRCTN (ISRCTN11650227). The AZTEC study has recruited 799 infants born at less than 30 weeks gestation to determine if a ten-day intravenous treatment with azithromycin improves survival without the development of chronic lung disease of prematurity (CLD) at 36 weeks post conceptional age (PCA) when compared to placebo. These follow-up studies will compare respiratory, neurodevelopmental, and growth outcomes from 36 weeks PCA up to 2 years of corrected age between infants who received azithromycin and those who received placebo in the early neonatal period.

Who can participate?
Survivors at 36 weeks PCA who participated in the main AZTEC study and have parental consent will continue to be followed up to discharge from the neonatal unit and to two years of corrected age.

What does the study involve?
Length of stay, rates of home oxygen, length of supplemental oxygen requirement, hospital admissions, drug usage, respiratory illness, neurodevelopmental disability, and death rates will be reported. Data will be collected via parentally completed respiratory and neurodevelopmental questionnaires at one and two years of corrected age respectively and additional information is being obtained from various sources including hospital discharge and clinical letters from general practitioners and hospitals as well as from national databases including the National Database Analyses Unit and from NHS Digital.

What are the possible benefits and risks of participating?
The study may not directly benefit the participants taking part but may lead to knowledge which could potentially help other premature babies in the future. We do not forsee any adverse events as it is a follow up study

Where is the study run from?
Cardiff University (UK)

When is the study starting and how long is it expected to run for?
From October 2019 to December 2025

Who is funding the study?
Aspire Pharma (UK)

Who is the main contact?
Professor Sailesh Kotecha
kotechas@cardiff.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Prof Sailesh Kotecha

Contact details
Professor Sailesh Kotecha
Department of Child Health
School of Medicine
Cardiff University
Heath Park
Cardiff
United Kingdom
CF14 4XN
+44 (0)2920 744187
kotechas@cardiff.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
270464

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number

IRAS 270464, CPMS 44914

Study information

Scientific Title
AZTEC (Azithromycin Therapy for Chronic Lung Disease of Prematurity) follow up studies: AZTEC@1 and AZTEC@2

Acronym
AZTEC@1 and AZTEC@2

Study objectives
It will be important to follow these infants beyond 36 weeks' PCA to monitor any longer-term effects from the early use of azithromycin and ensure longer-term safety. The AZTEC follow-up studies (AZTEC-FU) are assessing death rates, respiratory, neurodevelopmental, and growth outcomes for AZTEC study participants from 36 weeks PCA up to two years of corrected age; they will also document any differences in neurodevelopmental outcomes between the two trial arms. Additional mechanistic elements are investigating underlying mechanisms of azithromycin action by studying the effects of azithromycin on the lung and stool microbiome; tracheal aspirate cytokines and proteome; and antibiotic resistance against azithromycin in lung and stool samples obtained in the first three weeks of life.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/10/2019, Wales Research Ethics Committee 3 (Health and Care Research Support Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff CF11 9AB; +44 (0)29 2078 5735; Wales.REC3@wales.nhs.uk), ref: 19/WA/0267

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prematurity

Interventions
In the main AZTEC study (ISRCTN11650227) infants born at <30 weeks' gestation, within 72 h of birth, were treated intravenously for 10 days with 20 mg/kg azithromycin for 3 days, followed by a further 7 days of 10 mg/kg, or with similarly constituted and administered a placebo. This follow-up study will compare respiratory, neurodevelopmental, and growth outcomes from 36 weeks PCA up to 2 years of corrected age between infants who received azithromycin and those who received a placebo in the early neonatal period.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Azithromycin

Primary outcome(s)
1. Respiratory outcomes measured using parent-reported wheezing at 1 year of corrected age
2. Survival (from birth) without combined moderate/severe neurodevelopmental disability measured using the Bayley Scales of Infant Development/PARCA-R questionnaire at 2 years of corrected age

Key secondary outcome(s))
1. Mortality measured using the total number of deaths occurring during the following periods:
1.1. From birth to one- and two-year corrected age
1.2. From birth to 36 weeks' post-conceptual age (PCA)
1.3. 36 weeks to never discharged
1.4. After discharge.
2. Length of the initial neonatal stay in hospital measured using hospital records at 1 year corrected age
3. Number of children discharged home on domiciliary ambulatory oxygen measured using hospital records at 1 year corrected age
4. Length of oxygen supplementation (including at home) measured using hospital records at 1 year corrected age
5. Respiratory outcomes from discharge to two years of corrected age measured using parent-reported wheeze at 2 years of corrected age
6. Number of respiratory hospital admissions up to one year and two years of corrected age measured using hospital records at 1 and 2 years of corrected age
7. Number of prescribed respiratory drugs measured using hospital records at 1 and 2 years corrected age
8. Survival (from birth) without parent-reported wheeze measured from parent-report at 1 and 2 years of corrected age
9. Moderate/severe neurodevelopmental disability measured using PARCA-R or by using clinical data if PARCA-R scores are missing at 2 years of corrected age. Moderate/severe neurodevelopmental disability is defined, as any of the following:
9.1. Moderate or severe visual impairment (reduced vision uncorrected with aids, blindness in one eye with good vision in the contralateral eye, or blindness or light perception only)
9.2. Moderate or severe hearing impairment (hearing loss corrected with aids, some hearing loss uncorrected by aids, or deafness)
9.3. Moderate or severe gross motor impairment (inability to walk or sit independently)
9.4. Moderate or severe cognitive impairment will be defined using PARCA-R or by using clinical data if PARCA-R scores are missing. Total PARCA-R scores of less than 44 (range, 0 to 158, with lower scores indicating greater impairment) will be used to identify children with moderate or severe developmental impairment
10. Moderate or severe developmental impairment, defined as an Abilities–Revised (PARCA-R) questionnaire score of <44, measured using PARCA-R or by using clinical data if PARCA-R scores are missing at 2 years of corrected age
11. Overall motor skills as well as fine and gross motors scores measured using Bayley Scales of

Infant Development/PARCA-R questionnaire at 2 years of corrected age
12. Overall language scores as well as expressive and receptive language scores measured using Bayley Scales of Infant Development/PARCA-R questionnaire at 2 years of corrected age
13. Overall cognition score measured using PARCA-R or by using clinical data if PARCA-R scores are missing at 2 years of corrected age
14. Growth measured using weight, height, and head circumference after adjusting for sex and gestation at 1 and 2 years of corrected age
15. Adverse Events measured using reports of the rates of reported pyloric stenosis in the active treatment and placebo groups at 1 year of corrected age
16. Cytokine, proteomic, and microbiome profiles of lung or stool samples as well as any modification that occurs in those colonised by Ureaplasma spp. measured using respiratory and stool samples collected during the AZTEC trial at baseline and at 5/7 and 14/21 days

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Participation in the AZTEC trial
2. Survival at 36 weeks PCA
3. Consent provided by the parents/guardians to be contacted for follow-up at 1 and 2 years of corrected age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Total final enrolment
542

Key exclusion criteria
1. Withdrawal from AZTEC
2. Parents/guardians did not provide consent to follow up at one and two years corrected age
3. Death prior to 36 weeks' PCA
4. Survival not confirmed

Date of first enrolment
08/12/2020

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
England
CF14 4XW

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Industry

Funder Name
Aspire Pharma

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		21/09/2022	22/09/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes