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A clinical study testing if a daily low dose of an antibiotic, ciprofloxacin, given during the first part of chemotherapy treatment to children with newly diagnosed ALL would reduce the risk of infection

Submission date 08/01/2021	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 20/01/2021	**Overall study status** Ongoing	
Last Edited 04/12/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims:
Acute Lymphoblastic Leukaemia (ALL) is one of the commonest forms of childhood cancer. Treatment has improved and survival rates are now high. ALL treatment involves chemotherapy which reduces the child's ability to fight infections. Infection is now one of the commonest causes of death in children with ALL, and this is most likely to happen in the first five weeks of treatment – called "Induction".
In children with other types of leukaemia and in children whose ALL has come back after treatment (relapsed), it has been shown that giving a daily, low dose of antibiotics every day can reduce the risk of infection by about a half, but nobody has tested it in children the first time they have treatment for ALL.
A new research study to look at how best to treat childhood ALL called ALLTogether-1 is open in the UK and across Europe. Our study, called CiproPAL, will work alongside the ALLTogether-1 study in the UK. CiproPAL will aim to answer the question "Does adding a daily, low-dose antibiotic (called ciprofloxacin) during the first part of chemotherapy treatment (induction) reduce the risk of infection in children, age 1-17 years old, with new ALL?"

Who can participate?
Children, aged 1-17 years with new ALL and are taking part in the ALLTogether-1 research study. They will have give their consent to take part in CiproPAL or their parents give consents on their behalf.

What does the study involve?
Each child will receive either the antibiotic or no antibiotic – the decision will be made randomly by a computer. We will then look at whether they get infections.
We will do tests to see if the infections that make children unwell and whether the bacteria that usually live in us are more resistant to antibiotics. This will help to decide whether using

ciprofloxacin is a good idea. The tests to see if the infections that make children unwell are resistant to antibiotics will be done as part of the normal care of the children – we will just collect the information to be used. The test for bacteria that live in us will be done by taking a sample of stool, or if the patient is finding it difficult to poo, a swab (a bit like cotton wool on a stick) that is rubbed onto the bottom. It does not hurt. The swab can be done by the patient, their carer, or a healthcare professional. It can be done when they are awake or when they are having an anaesthetic (for their other leukaemia treatment). We will ask for 5 of these samples to be done for each child over a year from when they join CiproPAL. These samples (of stool or swabs) will be optional – patients can still take part in CiproPAL whether they are done or not.

What are the possible benefits and risks of participating?
Giving children regular antibiotics might change how well the infections respond to antibiotics in the future ("resistance"). Tests will be done to look at whether this happens on CiproPAL. We hope that children who receive the antibiotics will have less infections during the induction stage of their treatment.

Where is the study run from?
CiproPAL is being run in NHS children's hospitals in the UK, who are also seeing patients for the ALLTogether-1 research study.

When is the study starting and how long is it expected to run for?
December 2020 to December 2031

Who is funding the study?
National Institute of Health Research (NIHR) (UK)

Who is the main contact?
Stephanie Argue (public), ctc.cipropal@ucl.ac.uk
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Contact information

Type(s)
Public

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Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04678869

Clinical Trials Information System (CTIS)
2021-000341-40

Integrated Research Application System (IRAS)
293372

National Institute for Health and Care Research (NIHR)
130848

Protocol serial number
129038, ,1004004

Study information

Scientific Title
CiproPAL (Ciprofloxacin Prophylaxis in Acute Leukaemia): a randomised trial to assess the use of ciprofloxacin prophylaxis to prevent bacterial infection in children treated on the induction phase of the ALLTogether-1 treatment protocol

Acronym
CiproPAL

Study objectives
1. To assess the efficacy of ciprofloxacin prophylaxis in the reduction of infection during the induction phase of treatment for paediatric Acute Lymphoblastic Leukaemia within the ALLTogether-1 Trial
2. To evaluate the impact of ciprofloxacin prophylaxis on antimicrobial resistance, both of invasive infections and colonising organisms

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 20/08/2020, HCRW Wales (2 Redman Place, Cardiff, CF14 7EF, United Kingdom; +44 (0)292 2940931; HCRW.approvals@wales.nhs.uk), ref: 20/WM/0205

2. Approved 25/11/2021, London – Brent REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048131; brent.rec@hra.nhs.uk), ref: 21/LO/0752

Primary study design
Interventional

Study design
Interventional randomized controlled trial with internal pilot study

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Reduction in risk of infection during the induction phase of treatment for paediatric acute lymphoblastic leukaemia

Interventions
Treatment arm:
Drug - Ciprofloxacin
Intervention - Prophylactic ciprofloxacin (10mg/kg BD, enteral/IV), to be given daily during the induction phase (over 4 weeks)

Control arm:
Drug: Antibiotic
Control - Standard of care antibiotic as per local policy

Following pre-randomisation assessments, using an electronic randomisation system, eligible patients will be allocated to an intervention arm stratified by intensity of chemotherapy (low-intensity vs high-intensity), age (<10 years vs >10 years), antibiotic use at randomisation (patients given antibiotics at diagnosis for proven/suspected infection vs no antibiotics) and trial centre. Both arms will be followed up for at least 72 months in total (12 months of active follow-up and at least 60 months of passive follow-up)

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)

Rate of sterile site bacterial infections during induction, measured at approximately 1 month from randomisation until the start of consolidation, discontinuing protocol, antileukaemic therapy or death post induction, using patient records

Key secondary outcome(s)

Current secondary outcome measures as of 10/01/2025 were assessed using patient records unless otherwise noted:
1. Febrile episodes, febrile neutropenia, severe infection (defined as the need for organ support or critical care intervention) and infection-related death.
1.1. Fever is defined as temperature ≥38°C (as per CTCAE v5.0).
1.2. Febrile neutropenia is defined as neutrophil count ≤0.5x109/L and either a single temperature of >38.3°C or a sustained temperature of >38°C for more than one hour.
2. Antibiotic exposure relating to infections which result in an inpatient hospital stay: This will be reported as days on therapy per 100 patient days per antibiotic.
Total exposure for IV antibiotics and IV+oral will be described. Separate analysis will be performed looking specifically at the differences:
2.1. Prophylactic antibiotics include ciprofloxacin (intervention), prophylaxis for Pneumocystis jirovecii infection (usually with co-trimoxazole on two days per week), and prophylaxis against urinary or respiratory infections.
2.2. Empirical antibiotics are those given prior to the identification of a specific infection and are usually defined within a centre's febrile neutropenia protocol.
2.1. Treatment antibiotics are those targeted at a particular clinically or microbiologically defined infection.
3. Patterns of antimicrobial resistance and their changes over time in A) bacterial isolates from blood cultures or other sterile sites, B) stool or peri-rectal swab isolates.
3.1. Local sites to analyse, looking at standard resistance patterns and report for each antibiotic class as resistant, intermediate or sensitive.
4. Secondary infections: Clostridium difficile infections (see current definitions) and invasive fungal infections (following the 2020 EORTC definition).
5. Specific quinolone adverse effects, including tendinitis and tendinopathy, visual disturbance, seizures, polyneuropathy and hepatic dysfunction which should be coded as per CTCAE v5.0.
6. Health economic analysis to assess the cost-effectiveness of ciprofloxacin prophylaxis versus no prophylaxis for patients receiving induction therapy for ALL.

Measured using patient records unless otherwise noted:
1. Rate of febrile episodes during induction, measured at approximately 1 month from randomisation until the start of consolidation, discontinuing protocol, antileukaemic therapy or death post induction
2. Rate of febrile neutropenia during induction, measured at approximately 1 month from randomisation until the start of consolidation, discontinuing protocol, antileukaemic therapy or death post induction
3. Rate of severe infection and infection-related deaths during induction, measured at approximately 1 month from randomisation until the start of consolidation, discontinuing protocol, antileukaemic therapy or death post induction
4. Rates of AMR (antimicrobial resistance) measured from randomisation until end of trial declaration (approximately 10 years) measured using results from stool samples or peri-rectal swab cultures
5. Rate of antibiotic exposure during induction, measured at approximately 1 month from randomisation until the start of consolidation, discontinuing protocol, antileukaemic therapy or death post induction
6. Rate of secondary infections during induction, measured at approximately 1 month from

randomisation until the start of consolidation, discontinuing protocol, antileukaemic therapy or death post induction
7. Quinolone side effects during induction, measured at approximately 1 month from randomisation until the start of consolidation, discontinuing protocol, antileukaemic therapy or death post induction
8. Cost-effectiveness of ciprofloxacin prophylaxis versus no prophylaxis - model-based health economic analysis measured using the EQ-5D (5L) questionnaire which is being collected on the ALL Together-1 study, on which the CiproPAL participants are enrolled

Completion date
31/12/2031

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 10/01/2025:
1. Paediatric patients (1-17 years inclusive) with de-novo Acute Lymphoblastic Leukaemia treated on ALLTogether1 in the UK as soon as possible after commencing induction, preferably in the first 5-8 days of therapy, up to 14 days is acceptable.
2. Written informed consent.

Previous participant inclusion criteria as of 15/11/2023 to 10/01/2025:
1. Paediatric patients (1 - 17 years inclusive) with de-novo acute lymphoblastic leukaemia treated on ALLTogether-1 in the UK in the first 14 days of therapy (but ideally day 5-8)
2. Written informed consent

Previous participant inclusion criteria:
1. Paediatric patients (1 - 17 years inclusive) with de-novo acute lymphoblastic leukaemia treated on ALLTogether-1 in the UK in the first 5 days of therapy
2. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
1 Years

Upper age limit
17 Years

Sex
All

Total final enrolment

0

Key exclusion criteria
1. Non-participants of the ALLTogether-1 trial
2. Patients with Down syndrome who already receive ciprofloxacin prophylaxis
3. Patients with chronic active arthritis
4. Other contraindication to fluoroquinolones

Date of first enrolment
29/06/2022

Date of final enrolment
31/12/2027

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
University College London Hospital
225 Euston Road
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Study participating centre
Addenbrooke's Hospital
Hills Road
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Study participating centre
Royal Manchester Children's Hospital
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M13 9WL

Study participating centre
Bristol Royal Hospital for Children and Bristol Haematology and Oncology Centre
Upper Maudlin Street
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Study participating centre
Royal Victoria Infirmary
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Study participating centre
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L12 2AP

Study participating centre
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Study participating centre
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Study participating centre
Great Ormond Street Hospital for Children
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Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Requests for de-identified data should be made in writing to the Trials Group Lead at the CR UK and UCL Cancer Trials Centre. Please see the UCL CTC website for access criteria and link to contact http://www.ctc.ucl.ac.uk/DataSampleSharing.aspx

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1	22/09/2021	15/12/2021	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes