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CF START: A national UK trial to determine whether taking an antibiotic (flucloxacillin) every day predisposes infants with cystic fibrosis (CF) to earlier infection with a bug, Pseudomonas aeruginosa, that is resistant to treatment

Submission date
03/10/2016

Recruitment status
No longer recruiting

Registration date
26/10/2016

Overall study status
Ongoing

Last Edited
02/07/2025

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Cystic fibrosis is Cystic fibrosis (CF) is an inherited condition which causes the lungs and digestive system to become blocked with mucus. It is caused by a faulty gene, which is responsible for controlling the movement of water and salts in and out of cells. This leads to a buildup of sticky mucus which clogs the lungs, increasing the sufferer's risk of developing airway infections. This study will determine whether taking a daily dose of the antibiotic flucloxacillin, which is prescribed to prevent infection with a type of bug called Staphylococcus aureus, leads to infants being more likely to have infections caused by a more resistant bug called Pseudomonas aeruginosa. The aim of this study is to find out what the safest and most effective antibiotic approach for infants diagnosed with cystic fibrosis is.

Who can participate?
Infants under 90 days old who have CF.

What does the study involve?
Participants are randomly allocated to one of two groups. Infants in the first group are prescribed flucloxacillin to take twice a day as a liquid at a dose of 125mg until they are 36 months old and then twice a day as a liquid at a dose of 250mg until they are 48 months old. Those in the second group are prescribed antibiotics in a targeted manner for symptoms (prescribed specific antibiotics if they need them) if they are found to have bugs in samples taken in the laboratory and if they require a general anaesthesia (being put to sleep for an operation). Participants in both groups are regularly monitored until they are 48 months old to find out how old they are when they first catch the harder to treat bug Pseudomonas aeruginosa.

What are the possible benefits and risks of participating?
The result of the study will be of benefit to patients with CF, and contribute to a better understanding of the effect of taking flucloxacillin in a “Prevent and Treat” manner, all of which may lead to benefits for infants and others with CF. There are no notable risks involved with participating.

Where is the study run from?
Alder Hey Children’s Hospital and all other cystic fibrosis clinics (UK)

When is the study starting and how long is it expected to run for?
August 2016 to July 2028

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

Who is the main contact?
Mrs Claire Soady
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Study website
http://www.cfstart.org.uk

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Mrs Claire Soady

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Additional identifiers

EudraCT/CTIS number
2016-002578-11

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
31531

Study information

Scientific Title
The cystic fibrosis (CF) anti-staphylococcal antibiotic prophylaxis trial (CF START): A randomised registry trial to assess the safety and efficacy of flucloxacillin as a long-term prophylaxis agent for infants with CF

Acronym
CF START

Study objectives
Use of anti-staphylococcal antibiotic prophylaxis (flucloxacillin) predisposes infants with cystic fibrosis to earlier airway infection with Pseudomonas aeruginosa (PsA) compared to infants treated with antibiotics in more targeted manner.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Liverpool Central, 16/09/2016, ref: 16/NW/0629

Study design
Randomised; Interventional; Design type: Treatment, Prevention, Drug

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cystic fibrosis

Interventions

The randomisation sequence is generated by a computer and the infants are allocated one of two treatment strategies in a 1:1 ratio. The randomisation sequence has been generated to ensure equal allocation in clinics and centres depending on the size of those study sites.

“Prevent and Treat”: Infants are prescribed oral flucloxacillin suspension of 125 mg twice a day until 36 months then 250 mg twice a day until 48 months.

“Detect and Treat”: Infants prescribed antibiotics in a targeted manner for cough; asymptomatic growth of pathogens (bugs) from respiratory cultures, and as cover for a procedure requiring a general anaesthesia.

Infants will receive standard CF care for four years and outcomes will be collected on the national CF Registry.

The only additional (and optional) study measure will be a multiple breath washout undertaken between 40-48 months of age.

Intervention Type
Other

Primary outcome measure
Age at first growth of Pseudomonas aeruginosa on a respiratory culture taken as a standard part of CF clinical care and recorded on the national CF Patient Registry

Secondary outcome measures
1. Lung clearance index measured by multiple breath washout at age 40-48 months
2. Number of courses (and days) of extra antibiotics (oral, intravenous or aerosolised) measured on the CF registry as a routine part of CF care
3. Number (and type) of respiratory cultures taken as a routine part of CF care during the 48 month trial period and recorded on the national CF Patient Registry (is measured using … at …)
4. Number of positive respiratory cultures for Staphylococcus aureus from samples taken as a routine part of CF care during the 48 month trial period and recorded on the national CF Patient Registry (is measured using … at …)
5. Number of positive respiratory cultures for Pseudomonas aeruginosa from samples taken as a routine part of CF care during the 48 month trial period and recorded on the national CF Patient Registry
6. Number of positive respiratory cultures for other significant CF pathogens from samples taken as a part of routine CF care during the 48 month trial period and recorded on the national CF Patient Registry
7. Chronic infection rate, as defined by “more than 50% of respiratory cultures are positive for the same pathogen during any 12 month period during the trial” during the 48 month trial period and recorded on the national CF Patient Registry
8. Number of inpatient stays (and number of days) during the 48 month trial period and recorded on the national CF Patient Registry
9. Adverse events occurring during the 48 month trial period and recorded on the national CF Patient Registry
10. Nutritional parameters (weight, height and weight for height percentile) are measured as a part of standard clinical care and recorded on the national CF Patient Registry during the last 8 months of the trial (age 40-48 months)
11. CF Banding (annual cost band allocated to infants in the study each year) is measured using data from the CF Registry

Overall study start date
01/08/2016

Completion date
30/07/2028

Eligibility

Key inclusion criteria
Current inclusion criteria as of 13/04/2021:
1. A confirmed diagnosis of cystic fibrosis through one of the following three routes:
1.1. Two CF-causing mutations are identified
OR
1.2. One or no CF- causing mutations identified and a sweat chloride test result greater than 59 mmol/L
OR
1.3. Two CFTR mutations (not known CF-causing mutations) and a sweat chloride test result greater than 29 mmol/L
2. Age 90 days or less
3. Consent for inclusion on the national UK CF Registry
4. Consent for inclusion in the CF START trial

Previous inclusion criteria:
1. A confirmed diagnosis of cystic fibrosis through one of the following three routes:
1.1. Two CF-causing mutations are identified
OR
1.2. One or no CF- causing mutations identified and a sweat chloride test result greater than 59 mmol/L
OR
1.3. Two CFTR mutations (not known CF-causing mutations) and a sweat chloride test result greater than 29 mmol/L
2. Age 70 days or less
3. Consent for inclusion on the national UK CF Registry
4. Consent for inclusion in the CF START trial

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
Planned Sample Size: 480; UK Sample Size: 480

Total final enrolment
485

Key exclusion criteria
1. An inconclusive diagnosis after newborn screening (NBS)*
2. A condition (non-CF) that, in the opinion of the recruiting investigator will impact on the long-term management and outcome of a participant with CF**
3. Previous growth of PsA from respiratory culture
4. Infants with a history of hypersensitivity to β-lactam antibiotics (e.g. penicillins) or excipients
5. Infants with a history of flucloxacillin associated jaundice/hepatic dysfunction

*Infants with an inconclusive diagnosis after NBS (termed 'CF Screen Positive Inconclusive Diagnosis (CFSPID)') should not receive standard CF care and should not be recruited into CF START (Munck et al 2015).
The two situations that result in a diagnosis of CFSPID after NBS are
1. Two CFTR mutations recognised, one or both of which are not characterised as CF-causing and the sweat chloride is less than 30 mmol/L
2. The sweat chloride is repeatedly between 30-59 mmol/L and only one or no CFTR mutations are recognised

**Significant non-CF conditions might include chromosomal abnormality (for example, Down syndrome), cerebral palsy, chronic lung disease (oxygen requirement) following pre-term birth and other significant congenital anomalies (for example, severe cardiac disease, tracheo-oesophageal fistula, diaphragmatic hernia).

Date of first enrolment
01/11/2016

Date of final enrolment
04/05/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Alder Hey Children's Hospital
East Prescot Road
West Derby
Liverpool
United Kingdom
L14 5AB

Sponsor information

Organisation

Alder Hey Children's NHS Foundation Trust

Sponsor details
Alder Hey Hospital
Eaton Road
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England
United Kingdom
L12 2AP

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00p18zw56

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
30/07/2029

Individual participant data (IPD) sharing plan

This is a Registry trial. Data will be collected as part of routine clinical care and will remain on the UK Registry after completion of the study. These data will be available on request from the registry steering committee.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No