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Trial of Optimal Therapy for Pseudomonas Eradication in Cystic Fibrosis

Submission date
21/05/2009

Recruitment status
No longer recruiting

Registration date
22/05/2009

Overall study status
Completed

Last Edited
23/11/2021

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cystic fibrosis (CF) is a genetic condition in which the lungs and digestive system become clogged with thick sticky mucus. CF patients are at risk of developing infection in their lungs which can cause health problems. A common cause of infection can be a bacteria or germ called Pseudomonas (pronounced sue-doe-moe-nas). When Pseudomonas is first found in the lungs of CF patients they are treated with antibiotics (a type of medicine) to get rid of the germ. There is a choice of treatment that can then be used to get rid of the Pseudomonas – either antibiotics taken by mouth (orally) or given intravenously (by a tube into the vein). These treatments are usually combined with antibiotics that are inhaled as a mist directly into your lungs through a machine called a nebuliser. We know that both treatment types work well at getting rid of Pseudomonas and preventing damage to the lungs, but we don't know if one treatment is better than the other. The only way to find out which of these treatments is better is to carry out a research project called a clinical trial where patients are given either one of two different treatment options at random (50/50 chance of getting either treatment). We have therefore designed a study to compare the two treatments to find out whether there is any difference between two different antibiotic treatments.

Who can participate?
Children over the age of 28 days, older children and adult CF patients with a Pseudomonas infection.

What does the study involve?
You will be randomly allocated to be treated with either antibiotics taken by mouth (orally) or given intravenously (by a tube into the vein). The study will last for 24 months, and during that time your study doctor will collect information about your response to the study treatment and overall medical history. You will also be asked to complete a few short questionnaires at each study visit. During your treatment, the doctor or nurse may take a little bit of blood from your arm, and during your visits they will collect sputum (mucous you cough up from your lungs), ask you how you feel, and get you to blow into a machine to check your lungs. You will be asked to come into hospital for nine study visits. Depending on how frequent your routine clinic visits are, some or all of the study visits will be scheduled to occur at the same time as your routine clinic visits.

What are the possible benefits and risks of participating?
In general, patients who take part in trials do better than those who do not. This is true even if trial patients get a dummy medication (placebo) although we don’t use a placebo in this study! We do not know why trial patients do better. If you take part in this study you will get one of two treatments – both of which we think are effective. The main benefit for you will be knowing you will be helping doctors make the right decisions when they see patients in future. There are some known side effects of the treatment, including the development of an allergic reaction to the antibiotic, which could lead to an itchy rash. Other common side effects are a feeling of sickness and development of loose stools. The full list of possible side effects are available from your CF team. Both of these forms of treatment are available to you whether or not you take part in this study. The study will cause you a little added inconvenience because of the additional questions that you will be asked at a maximum of nine clinic visits. However, some or most of these study visits will take place during your usual clinic visit.

Where is the study run from?
Bristol Royal Hospital for Children (UK).

When is the study starting and how long is it expected to run for?
May 2010 to June 2018.

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK).

Who is the main contact?
Dr Simon Langton-Hewer

Contact information

Type(s)
Scientific

Contact name
Dr Simon Langton-Hewer

Contact details
Bristol Royal Hospital for Children
Paul O'Gorman Building
Upper Maudlin Street
Bristol
United Kingdom
BS2 8BJ

Type(s)
Scientific

Contact name
Dr TORPEDO-CF Trial Co-ordinator

Contact details

Medicines for Children Clinical Trials Unit
Clinical Trials Research Centre
University of Liverpool
Institute of Child Health
Alder Hey Children's NHS Foundation Trust
Liverpool
United Kingdom
L12 2AP
+44 (0)151 282 4714
torpedo@liv.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2009-012575-10

Protocol serial number
HTA 07/51/01

Study information

Scientific Title
Trial of Optimal Therapy for Pseudomonas Eradication in Cystic Fibrosis

Acronym
TORPEDO-CF

Study objectives
This trial will assess whether ten days intravenous ceftazidime with tobramycin is superior to three months oral ciprofloxacin. Both treatment regimes will be in conjunction with three months nebulised colistin.

Please note, as of 14/04/2011 various changes have been to the trial record. These can be found below under the relevant date of update.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London REC, 16/11/2009, ref: 09/H0718/51

Primary study design
Interventional

Study design
Multi-centre parallel-group randomised controlled trial

Study type(s)
Treatment

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

Interventions
Current interventions as of 14/04/2011:
Arm A: 14 days Intravenous (iv) Ceftazidime 50 miligram (mg)/kilogram (kg)/dose, to a maximum of 3 grams (g) three times daily (tds) and IV tobramycin 10mg/kg/dose once daily (od) (maximum 660mg / day)

Arm B: 3 months oral ciprofloxacin twice daily (bd) (Ciprofloxacin dose will be 15 mg/kg/dose twice daily for children aged < 5 years and 20 mg/kg/dose twice daily (maximum 750mg twice daily) for those aged ≥ 5 years)

Both treatment arms will receive three months of nebulised colistin in conjunction to the randomised treatment. Colistin dose will be as recommended by the UK CF Trust: 1,000,000 units twice daily for children aged ≤ 2 years and 2,000,000 units twice daily for children aged >2 years and adults.

Previous interventions:
Arm A: 10 days* Intravenous (iv) Ceftazidime 50 mili gram (mg)/kilo gram (kg)/dose, to a maximum of 3 grams (g) three times daily (tds) and IV tobramycin 10mg/kg/dose once daily (od)

Arm B: 3 months oral ciprofloxacin twice daily (bd) (Ciprofloxacin dose will be 15 mg/kg/dose twice daily for children aged < 5 years and 20 mg/kg/dose twice daily (maximum 750mg twice daily) for those aged ≥ 5 years)

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Ceftazidime, tobramycin, ciprofloxacin

Primary outcome(s)
Successful eradication of P.aeruginosa infection three months after allocated treatment has started, remaining infection free through to 15 months after the start of allocated treatment

Key secondary outcome(s)
Current secondary outcome measure as of 14/04/2011:
1. Time to reoccurrence of original P.aeruginosa infection
2. Re-infection with a different genotype of P.aeruginosa
3. Lung function - FEV1 , FVC, FEF25-75
4. O2 saturation
5. Growth and nutritional status - height, weight and body mass index
6. Number of pulmonary exacerbations
7. Admission to hospital
8. Number of days spent as inpatient in hospital over the three month period after allocated treatment has finished, and between three months and 15 months after eradication treatment

has finished (other than 14 days spent on initial IV treatment)
9. Quality of life (CFQ)
10. Utility (EQ-5D)
11. Adverse events
12. Other sputum/cough Microbiology (Methicillin resistant Staphylococcus aureus (MRSA), Burkholderia cepacia complex, Aspergillus, Candida Infection)
13. Cost per patient (from NHS perspective)
14. Incremental cost effectiveness ratio (cost per successfully treated patient, cost per QALY)
15. Carer burden (absenteeism from school or work)
16. Participant burden (absenteeism from education or work)

Previous secondary outcome measure:
1. Time to reoccurrence of P.aeruginosa infection
2. Time to new P.aeruginosa infection
3. Lung function - FEV1 , FVC, FEF25-75
4. Growth and nutritional status - height, weight and body mass index
5. Number of pulmonary exacerbations
6. Admission to hospital
7. Number of days spent as inpatient in hospital at three months and between three months and 15 months (other than 14 days spent on initial IV treatment)
8. Quality of life (CFQ)
9. Utility (EQ-5D)
10. Adverse events
11. Re-infection with a different strain of P.aeruginosa
12. Other sputum/cough Microbiology
13. Methicillin resistant Staphylococcus aureus (MRSA)
14. Burkholderia cepacia complex
15. Aspergillus
16. Candida Infection
17. Cost per patient (from NHS perspective)
18. Incremental cost effectiveness ratio (cost per successfully treated patient, cost per QALY)
19. Carer burden (absenteeism from school or work)

Completion date
30/06/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/04/2011:
1. Diagnosis of CF
2. Children over the age of 28 days, older children and adult CF participants are all eligible with no upper age limitation
3. Competent adults should provide fully informed written consent to particpiate in the trial
4. Minors should have proxy consent by the parent or legal guardian and should provide assent where applicable to participate in the trial
5. The patient should have isolated P.aeruginosa and should be either:
5.1. P. aeruginosa-naïve (i.e., has never previously isolated P. aeruginosa) or
5.2. P. aeruginosa-free (i.e., a minimum number of four consecutive cough or sputum samples

should be P. aeruginosa free within a 12 month period to satisfy eligibility)
6. The particpiant should be able to commence treatment no later than 21 days from the date of a P. aeruginosa positive microbiology report

Previous inclusion criteria:
1. Diagnosis of CF
2. The patient should have given full written consent, or assent where applicable, to participate in the trial
3. The participant should be able to commence treatment no later than three weeks after the clinical team has been informed that P.aeruginosa has been isolated
4. The patient should have isolated P.aeruginosa and should be either:
4.1. Pseudomonas-naïve (i.e. has never previously isolated P. aeruginosa) or
4.2. Pseudomonas-free i.e. has not isolated P. aeruginosa from cough swab, sputum or bronchoalveolar lavage samples within the previous 12 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
286

Key exclusion criteria
Current exclusion criteria as of 14/04/2011:
1. Antibiotic resistance of the current P.aeruginosa sample to any of: ciprofloxacin, ceftazidime, tobramycin or colistin reported by local microbiology laboratory
2. Known patient hypersensitivity to either ciprofloxacin, ceftazidime, tobramycin or colistin
3. Other known contraindications to any of ciprofloxacin, ceftazidime, tobramycin or colistin including previous aminoglycoside hearing or renal damage
4. Participant receiving P. aeruginosa suppresing treatment, in particular nebulised colistin or tobramycin, or oral ciproflxacin for the previous 9 months. Please note, short courses of oral ciprofloxacin or intravenous antibiotics (with an anti-pseudomonal spectrum of action) are not an exclusion unless they are given to treat proven infections with P. aeruginosa
5. Treatment with other anti-pseudomonal nebuliser
6. Pregnant and nursing mothers (women of child bearing age will be counselled on the risks of becoming pregnant during the trial and will be offered a preganancy test)
7. Previous randomisation in TORPEDO-CF study
8. Previous participation in another intervention trial within four weeks of taking part in TORPEDO-CF

Previous exclusion criteria:
1. Antibiotic resistance of the current P.aeruginosa sample to any of: ciprofloxacin, ceftazidime, or tobramycin reported by local microbiology lab

2. Known patient hypersensitivity to either ciprofloxacin, ceftazidime or tobramycin
3. Other known contraindications to any of ciprofloxacin, ceftazidime or tobramycin, including previous aminoglycoside hearing or renal damage
4. Pregnant women

Date of first enrolment
24/05/2010

Date of final enrolment
30/09/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Bristol Royal Hospital for Children
Bristol
United Kingdom
BS2 8BJ

Study participating centre
66 other centres
United Kingdom
-

Sponsor information

Organisation
University Hospitals Bristol (UK)

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK)

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2020	07/10/2020	Yes	No
Results article		01/11/2021	23/11/2021	Yes	No
Basic results				No	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes