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Genomics to combat resistance against antibiotics for community-acquired lower respiratory tract infection (LRTI) in Europe (GRACE) work package 10: Antibiotic Trial One

Submission date
02/12/2008

Recruitment status
No longer recruiting

Registration date
16/01/2009

Overall study status
Completed

Last Edited
06/11/2015

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
This study is part of a programme of research into cough/chest infections across 12 European countries. Most people with chest infections probably don't benefit from antibiotics and inappropriate antibiotic use drives antibiotic resistance, a major global health problem. Some groups of people however might really benefit from antibiotics. The study aims at understanding which subgroups of individuals with chest infections benefit from antibiotics, but also to study antibiotic resistance after antibiotic treatment.

Who can participate?
Throughout Europe 3000 adult patients presenting to primary care with acute cough or other symptoms that suggest a chest infection will take part in this study.

What does the study involve?
If the participating doctors think there is no definite need for antibiotics, participants will be asked to take a 7-day course of tablets to be taken three times a day. The tablets will be either amoxicillin, a very commonly used and safe penicillin-based antibiotic, or a placebo (a tablet without any medication in it). They will not be able to tell whether they will have the real antibiotic or the placebo. Random numbers are used to decide whether participants get antibiotic or placebo to make sure that they have an equal chance of getting either. This is the best way for us to show scientifically whether antibiotics really make a difference. If it is necessary to know whether participants are using an antibiotic or not, the participating doctors will be able to get that information at any time and change the participant's medication. The participating doctors will also like to take one throat swab at day 8 (extra visit) and at the second study visit (day 28-35). The swab at day 8 will not be taken in all participants. If participants decide they do not want to have a swab taken at day 8 they can still take part in the treatment part of the study.

What are the possible benefits and risks of participating?
The main advantage is that the participating doctors will be well informed about the participants' illness and will monitor them closely. In the future doctors will be able to provide better management for patients with coughs and chest infections, but this will not benefit the participants during this illness. The main disadvantages are the extra time and discomfort related to taking the additional swabs. The patients who will receive amoxicillin can experience the usual side-effects of penicillin: it can cause mild nausea or diarrhoea, and sometimes it can cause a transient skin rash.

Where is the study run from?
University of Southampton (UK).

When is the study starting and how long is it expected to run for?
October 2007 to April 2010.

Who is funding the study?
EC Sixth Framework Programme.

Who is the main contact?
Prof Paul Little

Study website
http://www.grace-lrti.org

Contact information

Type(s)
Scientific

Contact name
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Type(s)
Scientific

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Dr Herman Goossens

Contact details

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2610

Additional identifiers

EudraCT/CTIS number
2007-001586-15

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
GRACE WP10 Protocol v4.1 18/09/2007; GRACE WP10 Protocol v4.2 21/4/2009 (to extend the study with additional networks and a third inclusion period and, only in five networks in the third inclusion period, with an additional objective with associated samples)

Study information

Scientific Title
Genomics to combat Resistance against Antibiotics for Community-acquired lower respiratory tract infection (LRTI) in Europe (GRACE) work package 10: Antibiotic Trial One - a randomised placebo-controlled double-blind trial

Acronym
GRACE AT ONE

Study objectives
This trial aims at understanding which subgroups of individuals with lower respiratory tract infections (LRTI) benefit from antibiotics. A randomised placebo-controlled double-blind trial will be carried out with patients as unit of randomisation to study the clinical effectiveness of antibiotics in community-acquired LRTI.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=4175

Ethics approval required
Old ethics approval format

Ethics approval(s)
GRACE WP10 Protocol v4.1: Southampton and South West Hampshire REC (B), 31/08/2007, ref: 07/H0504/104
GRACE WP10 Protocol v4.2: amendment approved 21/04/2009
The study protocols were approved by ethics committees in all participating countries. The competent authority in each country also gave their approval.

Study design
Randomised placebo-controlled double-blind trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

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
Lower respiratory tract infection (LRTI)

Interventions
1. Amoxicillin capsule, gastroenteral use, 3 g a day for 7 days
2. Placebo

Intervention Type
Drug

Phase
Phase III

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

Primary outcome measure
1. Deterioration of illness: return to doctor with worsening signs, or admission to hospital within 4 weeks of first consultation, measured at one year
2. Symptom severity and duration, duration of symptoms rated moderately bad until symptoms clear, measured by symptom diary (with construct validity), measured at one year

Secondary outcome measures
1. Resource use data, assessed by a review of clinical notes measured at two years
2. Quality of life outcomes for use of economic evaluation (EQ5D), measured at two years

Added 25/11/2014:
3. Antibacterial resistance in oropharyngeal streptococci measured before, immediately after and four weeks after the interventions in five networks in the third inclusion period

Overall study start date

17/03/2006

Completion date
01/04/2010

Eligibility

Key inclusion criteria
1. Aged 18 and over, either sex
2. Acute or worsened cough is the main presentation suggesting LRTI, less than 28 days duration
3. Not been included earlier in the current GRACE trial
4. Able to fill out study materials
5. Immunocompetent
6. Not been on antibiotic treatment in previous month
7. First consultation for this illness episode

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
3000

Key exclusion criteria
1. Allergic to penicillin
2. History/physical examination suggestive of community acquired pneumonia (CAP)
3. Pregnant

Date of first enrolment
15/11/2007

Date of final enrolment
14/04/2010

Locations

Countries of recruitment
Belgium

England

France

Germany

Italy

Netherlands

Poland

Slovakia

Slovenia

Spain

Sweden

United Kingdom

Study participating centre
University of Southampton
Southampton
United Kingdom
SO16 5ST

Sponsor information

Organisation
University of Southampton (UK)

Sponsor details
Research Governance Office
George Thomas Building 37
Room 4001
Highfield
Southampton
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Sponsor type
University/education

Website
http://www.soton.ac.uk/

ROR

https://ror.org/01ryk1543

Funder(s)

Funder type
Government

Funder Name
Sixth Framework Programme

Alternative Name(s)
EC Sixth Framework Programme, European Commission Sixth Framework Programme, EU Sixth Framework Programme, European Union Sixth Framework Programme, FP6

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
We plan to publish on the overall effect of amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected and on a subgroup analysis of potential high-risk groups. Next we plan to publish on the cost-effectiveness of treatment with amoxicillin for acute lower-respiratory-tract infection in primary care and on the selection and persistence of antibiotic resistance in oral streptococci after such treatment.

Participant level data will be stored in a repository, the GRACE Database and Biobank, which is financially supported through the European Science Foundation (ESF), in the framework of the Research Networking Programme TRACE (Translational Research on Antimicrobial resistance and Community-acquired infections in Europe; www.esf.org/trace) and to consult via its chair Herman Goossens.

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2013		Yes	No
Results article	results	01/02/2014		Yes	No
Results article	results	06/03/2015		Yes	No
Results article	results	05/11/2015		Yes	No