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A double-blind, randomised, placebo-controlled phase III study of the efficacy of a bivalent Pseudomonas aeruginosa flagella vaccine in patients with cystic fibrosis

Submission date
17/10/2006

Registration date
12/12/2006

Last Edited
08/09/2008

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
PEI 0169/02

Study information

Scientific Title

Acronym
FLA Vaccine TRIAL

Study objectives
Administration of a bivalent P. aeruginosa flagella vaccine to patients with cystic fibrosis (CF) would significantly lower the frequency of P. aeruginosa pulmonary infection by 66%.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Informed consent was obtained from all patients or their parents, and the study protocol was approved by the institutional review boards at the participating hospitals, the biostatistician, the International Steering Committee, the Supervisory Board and the respective administrative bodies of the European countries Germany, Italy, France and Austria.

The study was conducted according to International Conference on Harmonisation (ICH)/Good Clinical Pratice (GCP) and CONSORT guidelines.

Study design
The phase III study was a randomised, double-blind, placebo-controlled, multi-centre trial.

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
For each patient a package of four pre-filled 1 ml syringes, numbered with the randomisation code, and containing either 40 µg flagella protein (20 µg flagella of subtype a0a1a2 from P. aeruginosa strain 1210 and 20 µg flagella of subtype b from P. aeruginosa strain 5142), 2 mg aluminium hydroxide and 0.1 mg thiomersal, or 2 mg aluminium hydroxide and 0.1 mg thiomersal only, was provided.

The 483 patients were randomised in blocks of 12 patients in a 1:1 ratio between vaccine and placebo using random numbers, generated by the algorithm of Wichmann and Hill, stratified by centre. The patients received the contents of three syringes by intramuscular injection during CF clinic visits, one syringe every four weeks and alternating between the right and left upper arm. After one year the content of a fourth syringe was injected in the left upper arm.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)

Pseudomonas aeruginosa flagella vaccine

Primary outcome(s)
The lower frequency or complete absence of P. aeruginosa pulmonary infection in the vaccine group compared to the placebo group during the two-year observation period of the study. Infection was defined by having one or more P. aeruginosa positive throat swabs or positive serum antibody titres against the P. aeruginosa antigens alkaline proteinase, elastase and exotoxin A (primary endpoint one). The primary endpoint two was defined as three positive throat swabs and/or three positive serum antibody titres against the P. aeruginosa antigens alkaline proteinase, elastase and exotoxin A within a 12 month period during the study, to assess chronic P. aeruginosa infection in the patient groups.

Key secondary outcome(s))
Secondary criteria for efficacy were:
1. A difference between the vaccine and the placebo groups in specific serum antibody titres against the inoculated antigens;
2. The distribution of P. aeruginosa flagella subtype strains between the vaccine and the placebo groups.

Completion date
19/04/2003

Eligibility

Key inclusion criteria
1. Cystic fibrosis that has been diagnosed according to conventional criteria
2. Patients aged between two and 18 years
3. No infection with P. aeruginosa as assessed by a negative throat swab culture and negative serum antibody titres against the P. aeruginosa antigens exotoxin A
4. Alkaline protease and elastase in enzyme-linked immunosorbent assays (ELISAs)
5. A forced expiratory volume in one second (FEV1) of at least 70% of the predicted value
6. A weight-to-height ratio of at least 90%
7. An oxygen saturation of at least 92%

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 years

Upper age limit
18 years

Sex

Not Specified

Key exclusion criteria
1. A known allergy to thiomersal or mercury
2. A prolonged bleeding time or a pathological partial thromboplastin time (PTT) value
3. Were using immunosuppressive drugs such as systemic corticosteroids
4. Participating in other clinical studies

Date of first enrolment
06/05/1997

Date of final enrolment
19/04/2003

Locations

Countries of recruitment
Austria

France

Germany

Italy

Study participating centre
Wilhelmstrasse 31
Tuebingen
Germany
72074

Sponsor information

Organisation
The Society for the fight of Cystic Fibrosis (The Gesellschaft zur Bekämpfung der Mukoviszidose e.V.) (Germany)

ROR
https://ror.org/028ew8k17

Funder(s)

Funder type
Research organisation

Funder Name
The study was supported by grants from:

Funder Name
The Society for the fight of Cystic Fibrosis (The Gesellschaft zur Bekämpfung der Mukoviszidose e.V.) (Germany)

Funder Name
Cystic Fibrosis Association (Vaincre la Mucoviscidose) (France)

Funder Name
The Association for Cystic Fibrosis of Lombardia (LAssoziazione de la Fibrosi Cistica Lombardia) (Italy)

Funder Name
Hospital Meyer (Ospedale Meyer) (Italy)

Funder Name
Association for Cystic Fibrosis (Verband der Cystischen Fibrose) (Austria)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration