

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	Recruitment status No longer recruiting	☐ Prospectively registered
Registration date 12/12/2006	Overall study status Completed	☐ Protocol
Last Edited 08/09/2008	Condition category Nutritional, Metabolic, Endocrine	☐ 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

Contact name

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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 Practice (GCP) and CONSORT guidelines.

Primary study design

Interventional

Study design

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

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 (L'Associazione 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