

Use of interferon gamma as adjuvant to chemotherapy in patients with pulmonary atypical mycobacteriosis

Submission date
14/02/2007

Recruitment status
No longer recruiting

Prospectively registered

Protocol

Registration date
21/02/2007

Overall study status
Completed

Statistical analysis plan

Results

Last Edited
05/01/2021

Condition category
Infections and Infestations

Individual participant data

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

IG/IGI/MB/0101

Study information

Scientific Title

Use of interferon gamma as adjuvant to chemotherapy in patients with pulmonary atypical mycobacteriosis

Acronym

MACGAM-I

Study objectives

Mycobacteriosis refers to infection by any member of a group of ubiquitous environmental mycobacteria. Mycobacterium Avium Complex (MAC) is the most frequent. It can produce a wide range of disease: Disseminated MAC disease (DMAC) in immunocompromised individuals and MAC Pulmonary Disease (MAC-PD) in immunocompetent adults. MAC disease is associated with substantial morbidity and mortality.

Although DMAC rates declined dramatically after 1995 with the introduction of highly active antiretroviral therapy, pulmonary physicians observed an increase in MAC-PD among Human Immunodeficiency Virus (HIV)-negative patients in the late 1990s and early 2000s. The optimal treatment regimen for MAC-PD has not been fully established. The most clinically efficacious drugs for the treatment of MAC are the new macrolide or azalide antibiotics, clarithromycin or azithromycin, respectively. These drugs are generally part of a multidrug regimen that includes rifamycin and ethambutol. This regimen becomes expensive, is poorly tolerated, and can lead to a variety of side effects. Interferon gamma can enhance the hosts defense mechanism and thus contribute to disease clearance.

Hypothesis:

Adjuvant interferon gamma will increase overall response rate to treatment from 30% in the placebo group to 90%.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approval received from the Ethics Committee of the Benefico Juridico Hospital, Havana, and the Amalia Simoni Hospital, Camaguey. Also approved by the Cuban Regulatory Authority (CECMed) on the 18th March 2002 (ref: 43/05-041-01-B).

Study design

Randomised, double-blind, placebo controlled, parallel group trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Mycobacteriosis

Interventions

Two parallel groups:

Group one: Antibiotic chemotherapy and interferon gamma

Group two: Antibiotic chemotherapy and placebo

Treatment lasted six months, and a further follow up of 12 months occurred. Evaluations were performed at the end of the treatment (six months) and end of the follow up (18 months).

Treatment schedule consists of 1 million IU of human recombinant interferon gamma (produced in *E. coli*, specific activity: 1×10^7 IU/mg of proteins [Heberon Gamma R, Heber Biotec, Havana]) or placebo intramuscularly, daily during four weeks and then three times per week for the next 20 weeks.

All the patients will receive the same conventional antibiotic schedule, orally, daily as follows: azithromycin 500 mg, ciprofloxacin 1000 mg, rifampin 600 mg, and ethambutol 2000 mg.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Human recombinant interferon gamma, azithromycin, ciprofloxacin, rifampin, and ethambutol.

Primary outcome(s)

Composite variable that includes clinical, bacteriological and radiological outcomes:

1. Complete response:
 - a. disappearance of all symptoms
 - b. negative sputum acid-fast-bacilli smear and culture
 - c. pulmonary lesions improvement at X-ray
2. Partial response:
 - a. symptoms decrease
 - b. negative sputum smear and culture
 - c. stable or improvement at X-ray
3. No response:
 - a. symptoms persistence
 - b. positive bacteriological examinations
 - c. lesion progression at X-ray

Key secondary outcome(s)

1. General clinical status:
 - a. good: none or discreet respiratory symptoms without frequent or serious exacerbations, appropriate body weight
 - b. moderate: maintained respiratory symptoms with more acute exacerbations, appropriate body weight
 - c. bad: maintained serious respiratory symptoms (intense dyspnea, cough, and abundant expectoration), low body weight
2. Dyspnea perception:
 - a. score 0: no dyspnea at all
 - b. score 1: dyspnea while climbing hills or stairs
 - c. score 2: dyspnea while walking at a rapid pace on ground level
 - d. score 3: dyspnea while walking at own pace on ground level
 - e. score 4: dyspnea at rest
3. Bacteriology: sputum direct observation and culture: positive or negative
4. Radiology:

- a. lesions extension:
 - i. minimum: if they comprised up to one third of a lung area
 - ii. moderate: up to one lung involvement
 - iii. advanced: more than one lung involved
- b. presence of cavitations
- 5. Time to overall and each response
- 6. Clinical laboratory variables:
 - a. haematocrit
 - b. globular sedimentation rate

Completion date

29/09/2005

Eligibility

Key inclusion criteria

1. Patient's written informed consent
2. To fulfil diagnostic criteria:
 - a. isolation and typification, at least three times, in sputum samples of any of the following species: *M. Avium-intracellulare*, *M. Kansasii*, *M. Xenopi*, *M. Marinum*, *M. fortuitum-chelonae*, *M. simiae*, *M. Scrofulaceum*, *M. Szulgai*, *M. Gorddonae*, *M. Flavescans*, *M. Gastri*, *M. Triviale*, *M. Vaccae*, *M. Smegmatis* or *M. Phlei*
 - b. presence of respiratory symptoms such as cough and expectoration
 - c. tuberculosis-like lesions at thorax radiography
3. Aged more than 18 years old
4. In case of fertile women, to use a non-hormone anti-conception method
5. Not having received any type of interferon during the previous three months

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

Not Specified

Total final enrolment

32

Key exclusion criteria

1. Any other respiratory infection
2. Severe cardiovascular disease
3. Renal or liver failure

4. Malignancies, except for skin basal cell carcinoma and in situ cervix carcinoma
5. Pregnancy or breast-feeding
6. Human Immunodeficiency Virus (HIV) co-infection
7. Hypersensitivity to interferon or other components of the formulations used
8. Treatment with glucocorticoids or other immunosuppressor medication
9. Functional central nervous system alterations
10. Multiple sclerosis or other auto-immune disease

Date of first enrolment

07/10/2002

Date of final enrolment

29/09/2005

Locations

Countries of recruitment

Cuba

Study participating centre

Hospital Benéfico Jurídico

Havana

Cuba

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Sponsor information

Organisation

Centre for Genetic Engineering and Biotechnology (Centro de Ingeniería Genética y Biotecnología) (Cuba)

ROR

<https://ror.org/03qwxgf98>

Funder(s)

Funder type

Research organisation

Funder Name

Centre for Genetic Engineering and Biotechnology (Cuba)

Funder Name

Ministry of Public Health (Cuba)

Alternative Name(s)

Ministry of Public Health (Thailand), , MOPH

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Thailand

Results and Publications

Individual participant data (IPD) sharing plan**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	11/02/2008	05/01/2021	Yes	No