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

Submission date	Recruitment status	[_] Prospectively registered
14/02/2007	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
21/02/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
05/01/2021	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Secondary study design
Randomised controlled trial

Study setting(s)

Not specified

Study type(s)
Treatment

Participant information sheet

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 x 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 measure
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

Secondary outcome measures

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

Overall study start date
07/10/2002

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

Age group
Adult

Lower age limit
18 Years

Sex
Not Specified

Target number of participants
34

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 glucocoticoids 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
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10800

Sponsor information

Organisation

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

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Sponsor type
Research organisation

Website
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ROR
https://ror.org/03qxwgf98

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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