Completed essay summary form

Applicant information

Notifier:

Promoter ☐

Promoter legal representative ☐

Person or organization authorized by the promoter to make the request ☒

Contact information

C.1.1.1 Contact person or organization name: **Clinical Trial Unit_Hospital Virgen del Rocío**

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Trial Information:

EudraCT number: 2012-005409-38

Promoter protocol code: **TriSulfa-FPI-1**

Title of the trial:

Pilot study phase III to evaluate the efficacy and safety of Trimethoprim sulfamethoxazole in the treatment of idiopathic pulmonary fibrosis

Name or abbreviated title of the trial, if applicable:

Introduction / Justification:

First study to test the validity of the treatment of idiopathic pulmonary fibrosis, which causes inflammation and fibrosis (scarring) of the lung tissue, with cotrimoxazole.

Cotrimoxazole may improve the clinical course of the disease through eradication of Pneumocystis jiroveci colonization and other mechanisms as inhibiting the activation of alveolar macrophages and producing alterations in the surfactant system which favours the persistent activation of the inflammatory response and the development of pulmonary fibrosis.

Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease that is clinically manifested by the appearance of effort dyspnea and impaired lung function.

The natural history of the disease is poorly understood and there is no clear consensus as to the most appropriate markers for predicting patient outcome.

This pilot-controlled trial aims to test the efficacy and safety of cotrimoxazole in the treatment of IPF. This novel therapeutic strategy, with very encouraging preliminary data is based on its pathophysiological basis, primarily related to the elimination of Pneumocystis colonization. That elimination, could serve as a potent weapon for reducing morbidity and mortality and the cost associated with this devastating disease.

Summary: **Relevant objectives, Variables, Design, scope and period of study, work plan, inclusion / exclusion criteria, patients / sample size, statistical analysis, economic and ethical aspects.**

Primary Outcome Measure:
1. Evaluate the efficacy of oral cotrimoxazole versus placebo in idiopathic pulmonary fibrosis (IPF).
Decline of the FVC ≥ 5% at 24 weeks and / or hospitalization for respiratory causes.
[Time Frame: 24 weeks]
Secondary Outcome Measure:
2. Evaluate the safety of oral cotrimoxazole versus placebo in IPF.
• Time to progression
• Any cause of hospitalization
• Overall mortality
• Incidence and severity of adverse events.
[Time Frame: At 24 weeks]
3. Evaluate the effect of cotrimoxazole on the natural history of Pneumocystis colonization in patients with IPF.
- Molecular diagnosis of colonization by Pneumocystis jiroveci.
[Time Frame: 24 weeks]
4. Identify the effects of cotrimoxazole systemic level of inflammatory activity in patients with IPF.
• Acute exacerbation of IPF
• Scales of dyspnea
• Reduction > 50% in the values of different proinflammatory cytokines
• Reduction > 50% in the values of surfactant proteins.
• Reduction > 50% in the values of chemokine CCL-18.[Time Frame: At 24 weeks]

Inclusion Criteria:
• **Patient, regardless of gender, aged 18 to 80 years.**
• Well-established diagnostic criteria of the Idiopathic Pulmonary Fibrosis (IPF) as ATA/ERS/JRS/ALAT 2011.
• Ability to obtain a sample of sputum or oropharyngeal washing.
• Forced Vital Capacity (FVC) above 50% from the theoretical value expected.
• Patient compliance or legal guardian to participate in this study by signing the informed consent.
Exclusion Criteria:
• Allergy / hypersensitivity or known gastrointestinal intolerance to cotrimoxazole.
• Use of immunosuppressants or corticosteroids in the previous 90 days at baseline.
• Exacerbation of IPF and / or pneumonia in the 90 days prior to baseline.
• Presence of autoimmune diseases or asthma.
• Patients with other significant diseases other than IPF. It is considered significant disease any disease or condition that, in the investigator's opinion, may jeopardize the patient's health participating in the study or influence the results of the study or the patient's ability to participate in the study.
• Pregnant or lactating or of childbearing potential not using medically approved contraceptive methods at least three months before or during trial.
• Participation in another trial with an investigational drug within 30 days or six half-lives (the larger of the two) above the baseline.

Sample size 56 patients

Authorization date:	Initial estimate of the duration of the trial:
2014/05/22	**2 years**
Expected completion date	**Actual end date**
2016/05/22	2015/02/27

Number of subjects expected to be included in the trial	Number of subjects finally included
56	7

Definition of the end of the trial in the protocol, and justification, in case it does not coincide with the last visit of the last subject recruited into the trial:

-LPLV is considered the final procedure for the study

Is it an early completion of the trial? yes ☒ no ☐

If the answer is yes, indicate the date (YYYY/MM/DD):
Specify reasons for early termination

Safety
yes ☐ no ☐

Lack of effectiveness
yes ☐ no ☐

The trial never started yes ☐ no ☐

Expected subjects were not recruited ☒

Other yes ☐ no ☐

If the answer is yes to any of the above questions, briefly describe (free text):
Seven patients were included in the screening phase of the clinical trial and three patients completed the study protocol. Two of them were assigned to the experimental treatment arm (cotrimoxazole) and one to the placebo arm.
The two patients who received cotrimoxazole were colonized by Pneumocystis at the beginning of the study and during the 24 weeks of treatment they remained stable with respect to the main variable of efficacy and had no adverse events. The patient assigned to the placebo group also was colonized by Pneumocystis at the beginning of the study and presented at week 18 of follow-up a primary event of progression (hospitalization for respiratory causes) that conditioned the withdrawal of the study.

It was not possible to carry out an efficacy assessment as the necessary sample size was not reached or a number of patients that would allow a preliminary analysis of the variables defined on the study.

The security information collected during the notification period did not create the need to take any action, or modify the available information on the safety information of the drug 8Summary of products characteristics).

Are only partial results available? yes ☐ no ☒