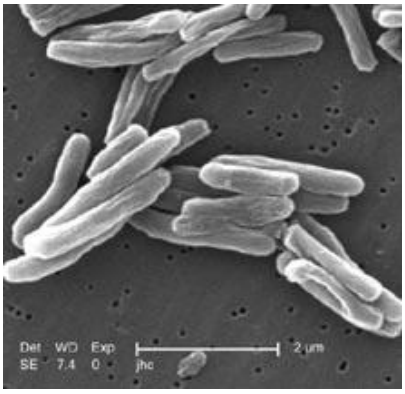
TBCT Clinical Trial Study 29 Evaluating Rifapentine Drug in Tuberculosis Treatment

2008-2013

Background



The World Health Organization estimates that there are 175,000 new cases of tuberculosis (TB) in Vietnam every year, 7,000 of which are new multi-drug resistant cases and 6,400 new HIV/TB cases. Although the Government of Vietnam has made considerable progress in expanding TB services and treatment through its National Tuberculosis Program, the rate of new cases of TB per population has yet to show a significant decline over the last decade (WHO, 2009).

One of the goals of the Tuberculosis Trials Consortium (TBCT) is to conduct research that expands clinical and epidemiologic knowledge of TB and facilitates the diagnosis, clinical management, and prevention of tuberculosis infection and disease. In an effort to contribute to TB control program and in an effort to reduce the duration of TB treatment, TBCT is in the process of implementing Study 29. The purpose of the study is to evaluate the antimicrobial activity and safety of an experimental intensive phase (first 8 weeks of treatment) tuberculosis treatment regimen in which rifapentine is substituted for rifampin.

In conjunction with Westat, ISMS researchers are contributing to Study 29 by monitoring the overall implementation process of study sites in Hanoi.

Objectives

Primary Objective

To compare the antimicrobial activity and safety of the standard daily regimen to that of an experimental regimen.

Secondary Objectives

1 To determine and compare for each regimen the time to culture-conversion, using data from 2-, 4-, 6-, and 8-week cultures (10, 20, 30, 40 doses).

2 To determine and compare for each regimen the proportion of patients with any Grade 3 or 4 adverse reactions.

3 To determine the correlation of the MGIT liquid culture growth index and other mycobacterial and clinical biomarkers with time to culture conversion and treatment failure.

4 To store serum for future assessment of biomarkers of TB treatment response and hypersensitivity to study drugs.

5 To compare adverse events and 2-month culture conversion rates among HIV-infected patients vs. HIV-uninfected patients.

Study Design & Methodology

The study was a prospective, multi-center, open-label, phase 2 clinical trial in which participants were randomly assigned to receive either the experimental intensive phase tuberculosis treatment regimen or the standard intensive phase tuberculosis treatment regimen. Randomization was stratified by presence/absence of cavitation on baseline chest radiograph, and by geographic continent.

- Standard Regimen: Rifampin (approximately 10 mg/kg/dose) + isoniazid + pyrazinamide + ethambutol (RHZE)

- Experimental Regimen: Rifapentine (approximately 10 mg/kg/dose) + isoniazid + pyrazinamide + ethambutol (PHZE)

All doses of study drugs were given under direct observation and administered 5 days per week. After a subject completed intensive phase therapy, he/she was treated with a non-

experimental continuation phase tuberculosis treatment regimen. Subjects had their blood drawn for one pharmacokinetic determination of rifapentine concentration towards the end of intensive phase therapy.

Study Subjects & Sites

Participants in the study were adults aged 18 and older suspected of having pulmonary tuberculosis who met eligibility criteria (willingness to be HIV-tested, Karnofsky score of at least 60, not pregnant, signed informed consent, etc.)

Role of ISMS

With training and support from Westat, ISMS researchers are serving as monitors of Study 29. In this role, they must ensure that the implementing partners – The University of California, San Francisco (UCSF), The National Lung Hospital and Hanoi Lung Hospital – are in compliance with protocol procedures, federal regulations and IRB guidelines in recruiting patients, upholding confidentiality, offering treatment, etc. They also assure that good clinical practices are maintained and provide support and training to Study sites as needed. All the site monitoring reports written for the study are reviewed by Westat and submitted to CDC.

Donors and Partners

ISMS researchers are working in collaboration with Westat and the University of California, San Francisco. Study 29 is funded by the US Centers for Disease Control and Prevention and the Department of Veterans Affairs.

UCSF University of California San Francisco

Westat

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