

Study of immediate versus deferred antiretroviral therapy in human immunodeficiency virus-associated tuberculous meningitis

Submission date 18/04/2005	Recruitment status No longer recruiting	☐ Prospectively registered
Registration date 22/07/2005	Overall study status Completed	☐ Protocol
Last Edited 12/02/2019	Condition category Infections and Infestations	☐ Statistical analysis plan
		☒ Results
		☐ Individual participant data

Plain English summary of protocol

Background and study aims

Infection with human immunodeficiency virus (HIV) can lead to an increased risk of developing tuberculous meningitis (TBM), a condition where infection with bacteria called *Mycobacterium tuberculosis* leads to life-threatening inflammation in the brain and spinal cord. HIV is treated with a life-long drug course called antiretroviral therapy (ART), which can be highly toxic. If a patient is found to have HIV when they are diagnosed with TBM there are concerns that beginning ART immediately could be bad for patients because they are taking a lot of drugs at the same time. Beginning HIV treatment too late, however, can cause the patient to die from other infections because their ability to fight infections is too weak. This study examines when to begin ART in patients with TBM who are also found to have HIV .

Who can participate?

Patients had to be over 15 years old, HIV-positive and diagnosed with TBM.

What does the study involve?

The patients were randomly assigned into two groups. In addition to their treatment for TBM, one group received ART within 72 hours of study entry (immediate ART) and the other group received ART two months after study entry (deferred ART). The patients were then monitored daily in the hospital for general health, fever, coma and other negative health events. At the end of three months, the patients were discharged and followed up monthly as part of the national tuberculosis program. A final follow-up visit took place at 12 months from study entry.

What are the possible benefits and risks of participating?

The patient will not have to pay for anything other than the normal costs of routine inpatient care. All medication and tests related to the study will be paid for. Having a blood test or a lumbar puncture done can be uncomfortable and may cause a bruise. Common side effects of

the drug include orange discolouration of body fluids, nausea, vomiting, abdominal pain and headache. While in hospital, the patient will be closely monitored by the study doctor. After the patient leaves hospital, they will be followed up in the clinic every month.

Where is the study run from?

The study was run by researchers at the Oxford University Clinical Research Unit in Vietnam, in partnership with the Hospital for Tropical Diseases and the Pham Ngoc Thach Hospital in Ho Chi Minh City.

When is the study starting and how long is it expected to run for?

The study ran from April 2005 to December 2008.

Who is funding the study?

The Wellcome Trust (UK).

Who is the main contact?

Clinical Trials Unit at the Oxford University Clinical Research Unit in Vietnam

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Contact information

Type(s)

Scientific

Contact name

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District 5

Additional identifiers

ClinicalTrials.gov (NCT)

NCT00433719

Protocol serial number

076224; OXTREC 023-04

Study information

Scientific Title

Study of immediate versus deferred antiretroviral therapy in human immunodeficiency virus-associated tuberculous meningitis

Acronym

DK Study

Study objectives

Human Immunodeficiency Virus (HIV) infection is associated with an increased risk of Tuberculosis (TB); in particular Tuberculous Meningitis (TBM). There are limited data describing the influence of HIV infection on the clinical presentation, response to treatment, frequency of adverse events, outcome or the impact of Anti-Retroviral Therapy (ART) in HIV-associated TBM. The optimal time to initiate ART is unknown. There are concerns that immediate ART may worsen rather than improve outcome, because of the development of an Immune Reconstitution Inflammatory Syndrome (IRIS) or combined drug toxicities. Conversely, delaying ART may result in increased HIV-related deaths. We therefore propose to conduct a clinical trial of immediate versus deferred ART in HIV-infected patients presenting with TBM, to assess effect on survival.

As of 13/02/2007 the anticipated end date of this trial was shortened to 20/09/2008.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Oxford Tropical Research Ethics Committee (OxTREC), 07/02/2005, ref: OxTREC 023-04

Study design

Randomised controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

HIV-associated tuberculous meningitis

Interventions

Randomised double-blind placebo-controlled trial with two parallel arms: immediate Highly Active Anti-Retroviral Therapy (HAART) and deferred HAART (two months). Patients will also receive standard treatment (anti-tuberculous chemotherapy and adjunctive dexamethasone) for tuberculous meningitis.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Highly Active Anti-Retroviral Therapy (HAART)

Primary outcome(s)

Mortality at 9 months

Key secondary outcome(s))

1. Mortality at 12 months
2. Fever clearance time
3. Coma clearance time
4. Neurological relapse
5. Progression to new or recurrent Acquired Immuno-Deficiency Syndrome (AIDS) defining illness
6. Any grade three or four adverse event
7. CD4 count response
8. Plasma HIV-1 RiboNucleic Acid (RNA) response
9. Neurological disability: neurological disability will be assessed using the 'simple questions' and Rankin score

Completion date

01/12/2008

Eligibility**Key inclusion criteria**

1. Patients aged 15 or over
2. HIV seropositive
3. Anti-retroviral naive
4. Presenting with tuberculous meningitis

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Key exclusion criteria

1. Positive Cerebrospinal Fluid (CSF) Gram or India ink stain
2. Known or suspected pregnancy
3. Anti-tuberculous treatment eight to 30 days immediately prior to recruitment
4. Previous antiretroviral therapy
5. Laboratory contraindications to anti-retroviral or anti-tuberculous therapy
6. Lack of consent

Date of first enrolment

01/04/2005

Date of final enrolment

20/09/2007

Locations

Countries of recruitment

Viet Nam

Study participating centre

Oxford University Clinical Research Unit

Ho Chi Minh City

Viet Nam

District 5

Sponsor information

Organisation

University of Oxford (UK)

ROR

<https://ror.org/052gg0110>

Funder(s)

Funder type

Charity

Funder Name

Wellcome Trust

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype

International organizations

Location

United Kingdom

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	01/06/2011		Yes	No