ISRCTN63659091 https://doi.org/10.1186/ISRCTN63659091

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

Submission date
18/04/2005

Recruitment status
No longer recruiting

Registration date
22/07/2005

Overall study status
Completed

Last Edited
12/02/2019

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00433719

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

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 measure
Mortality at 9 months

Secondary outcome measures
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

Overall study start date
01/04/2005

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

Age group
Adult

Sex
Both

Target number of participants
222

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)

Sponsor details
University Offices
Wellington Square
Oxford
England
United Kingdom
OX1 2JD

Sponsor type
University/education

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

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	01/06/2011		Yes	No