

# The TILT Study: A pilot trial of antiretroviral Therapy Interruption with and without use of interLeukin-Two

<b>Submission date</b> 18/10/2000	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
<b>Registration date</b> 18/10/2000	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 30/07/2009	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## 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

G0000198

# Study information

## Scientific Title

## Acronym

TILT

## Study objectives

Primary: To gain experience in antiretroviral therapy interruptions in patients with viral suppression and increased CD4 count, with and without use of Interleukin-2 (IL-2). In particular, to test the ability to maintain the CD4 count at a level above 150/mm<sup>3</sup> during interruption, to evaluate the length of time off therapy that can be safely achieved and to evaluate the ability to "re-suppress" viral load if and when antiretroviral therapy is restarted. This information will be used to guide the design of a larger trial.

Secondary: To obtain preliminary data comparing the three strategies with regard to:

1. CD4 count decline to less than 150/mm<sup>3</sup> to the power of three or new Acquired Immune Deficiency Syndrome (AIDS) disease or death
2. Virological failure of therapy (viral load greater than 1000 after having been on antiretroviral therapy for over 16 weeks) by two years
3. Changes in levels of lactates, lipids and bicarbonates
4. Quality of life using the Medical Outcomes Study health status questionnaire for HIV (MOS-HIV)

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Not provided at time of registration

## Study design

Randomised controlled trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

## Health condition(s) or problem(s) studied

Human Immunodeficiency Virus (HIV), Acquired Immune Deficiency Syndrome (AIDS)

## Interventions

An open, randomised, three arm, controlled trial to study interruption of antiretroviral therapy with or without IL-2 therapy, in individuals with HIV-1 infection and nadir CD4 cell counts greater than  $100 \times 10^6/l$ , current CD4 count greater than  $300 \times 10^6/l$  and currently receiving antiretrovirals and with a viral load less than 50 copies/ml for greater than three months.

Participants will be randomly allocated 1:1:1 ratio to either:

1. Continue with antiretroviral therapy. If drugs need to be switched for any reason, this should be done without a complete interruption, or
2. Interrupt antiretroviral therapy. Restart with the same regimen when the clinician and patient feel this is warranted. Treatment should certainly be restarted before the CD4 count falls below  $200/mm^3$ . Further treatment interruptions should be considered when viral load is less than 50 for 12 weeks or more and if CD4 count is more than or equal to  $300/mm^3$ , or
3. Give two cycles of IL-2, eight weeks apart, while still on antiretroviral therapy. Then interrupt antiretroviral therapy. Use new cycles of IL-2 and/or reintroduction of antiretroviral therapy if the clinician and patient feel that this is warranted. New cycles of IL-2 and/or antiretroviral therapy should certainly be given before the CD4 count falls below  $200/mm^3$ .

Last patient will complete follow up in July 2006.

## Intervention Type

Drug

## Phase

Not Specified

## Drug/device/biological/vaccine name(s)

interLeukin-Two

## Primary outcome measure

1. CD4 decline to less than 100 or new AIDS disease after death
2. Virological failure of therapy at two years after baseline
3. Virological failure of therapy at any time during the two year period after randomisation
4. Changes in levels of total cholesterol
5. Changes in severity of lipodystrophy/ quality of life
6. Incidence of grade three or four adverse

## Secondary outcome measures

Not provided at time of registration

## Overall study start date

20/02/2001

## Completion date

31/08/2006

## Eligibility

**Key inclusion criteria**

1. HIV seropositive
2. Adult (18 years or older) HIV-infected therapy naïve patients
3. On Highly Active Anti-retroviral Therapy (HAART) (more than or equal to three ARTs of any of the three main classes) with viral load less than 50 copies/mL for 12 weeks or more
4. CD4 count nadir more than 50/mm<sup>3</sup>
5. CD4 lymphocyte count more than or equal to 300/mm<sup>3</sup>
6. Signed informed consent obtained

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

90 - Closed to recruitment - in follow-up

**Key exclusion criteria**

1. Patients on hydroxyurea or interferons or any immunomodulating agent besides IL-2
2. Age less than 16
3. Prior IL-2 therapy
4. Use of any approved or experimental antiretroviral drug within four months prior to study therapy
5. Concurrent malignancy other than mucocutaneous Kaposi sarcoma or malignancy treated within the past five years
6. Any concurrent or history of AIDS defining illness
7. Use of systemic corticosteroids, chemotherapy or experimental cytotoxic drugs within four weeks prior to study therapy
8. Use of any agent approved or experimental with clinically significant immunomodulatory effects
9. Any Central Nervous System (CNS) abnormality that requires treatment with anti-seizure medication
10. Patients with current or historical Crohn's disease, psoriasis or other autoimmune /inflammatory diseases with potential life threatening complications
11. Pregnant or lactating women
12. Use of recreational drugs/alcohol that in the opinion of the investigator would affect patient safety and/or compliance
13. Patients with any serious psychiatric, medical and/or cognitive disturbance or illness that in the opinion of the investigator may affect safety, compliance or ability to provide written informed consent

**Date of first enrolment**

20/02/2001

**Date of final enrolment**

31/08/2006

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

Department of Thoracic Medicine

London

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## **Sponsor information**

**Organisation**

Medical Research Council (MRC) (UK)

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**Sponsor type**

Research council

**Website**

<http://www.mrc.ac.uk>

## **Funder(s)**

**Funder type**

Research council

**Funder Name**

Medical Research Council (MRC) (UK)

**Alternative Name(s)**

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**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?
<a href="#">Results article</a>	results	30/03/2008		Yes	No