

# Can Valaciclovir delay the need for initiation of human immunodeficiency virus (HIV) treatment in HIV – infected individuals

<b>Submission date</b>	<b>Recruitment status</b>	<input checked="" type="checkbox"/> Prospectively registered
06/03/2009	No longer recruiting	<input checked="" type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
09/03/2009	Completed	<input checked="" type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
16/04/2019	Infections and Infestations	

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

Dr Sharon Walmsley

### Contact details

Toronto General Hospital  
200 Elizabeth Street  
13EN Room 218  
Toronto, Ontario  
Canada  
M5G 2C4  
+1 416 340 3871  
sharon.walmsley@uhn.on.ca

## Additional identifiers

### ClinicalTrials.gov (NCT)

NCT00860977

### Protocol serial number

MCT-94245

# Study information

## Scientific Title

Valaciclovir in delaying antiretroviral treatment entry: a multicentre, randomised, placebo-controlled, fully blinded clinical trial

## Acronym

VALIDATE

## Study objectives

As of 17-12-2012, the title changed to "Can Valaciclovir delay the need for initiation of human immunodeficiency virus (HIV) treatment in HIV – infected individuals"

As of 10/09/2010 a rollover (off treatment) period was added and the overall trial end date was updated to 01/03/2016

As of 21/09/2015 the overall trial end date has been updated from 01/03/2015 to 30/09/2016 and the recruitment end date has been updated from 01/03/2015 to 11/08/2015.

As of 09/03/2010 this trial has now started to actively recruit participants. The anticipated trial dates of this record have been updated to reflect this; all changes can be found in the relevant fields. The previous anticipated start and end dates were as follows:

Previous anticipated start date: 31/10/2009

Previous anticipated end date: 31/10/2015

As of 18/08/2009 this record has been extensively updated; all updates can be found under the relevant field with the above update date. Please also note that at this time, the anticipated start and end dates of this trial have also been updated; the initial anticipated start and end dates were:

Initial anticipated start date: 01/05/2009

Initial anticipated end date: 30/04/2015

At this time, Argentina was also added as a country of recruitment, and the Sponsor was updated (initial sponsor at the time of registration was Canadian HIV Trials Network (CTN) (Canada)).

Current hypothesis as of 18/08/2009:

Valaciclovir 500 mg orally twice daily delays the time until highly active anti-retroviral therapy (HAART) is recommended or initiated among adults with both stable untreated human immunodeficiency virus (HIV) and herpes simplex virus (HSV) type 2 co-infection.

Initial hypothesis at the time of registration:

Valaciclovir 500 mg orally twice daily delays the time until highly active anti-retroviral therapy (HAART) is recommended or initiated among adults with both stable untreated human immunodeficiency virus (HIV) and infrequent or asymptomatic herpes simplex virus (HSV) type 2 co-infection.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Added 09/03/2010:

University Health Network Research Ethics Board approved on the 22nd September 2009.

**Study design**

Multicentre randomised placebo-controlled fully blinded clinical trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Herpes simplex virus type 2 (HSV-2) and human immunodeficiency virus type 1 (HIV-1) co-infection

**Interventions**

Patients in the intervention group will receive oral valaciclovir 500 mg twice daily, the standard dose used for HSV-2 suppression in HIV-infected individuals. Individuals in the control arm will receive an odourless placebo tablet identical to valacyclovir in appearance and taste, to be taken twice daily.

The anticipated duration of follow-up for both arms of the trial is 3 - 5 years.

**Intervention Type**

Drug

**Phase**

Phase IV

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

Valaciclovir

**Primary outcome(s)**

As or 17/12/2012 primary outcome changed to: Annual rate of change in CD4 count, calculated as the slope of patients' CD4 count change/time.

Initial primary outcome measure:

Time from baseline until reaching the primary endpoint: a composite of either a CD4 cell count less than or equal to 350 cells/mm<sup>3</sup> measured on two consecutive occasions at least 1 month apart, or initiation of HAART for any reason, whichever occurs first.

**Key secondary outcome(s)**

1. Annual rate of change in CD4 count, calculated as the slope of patients' CD4 count change /time
2. Annual rate of change in the CD4 cell count percentage, calculated as the slope of the patient's CD4 count percentage change over time
3. Log<sup>10</sup> plasma HIV viral load at 12, 24 and 36 months of follow-up
4. Treatment-emergent adverse events and laboratory abnormalities (complete blood count [CBC], plasma creatinine, blood urea nitrogen, alanine transaminase, aspartate transaminase, total bilirubin, amylase, international normalised ratio, partial thromboplastin time)

5. Frequency of episodes of HSV reactivations at any anatomic site
6. Proportion of microbiologically confirmed flares of HSV during the trial that are caused by laboratory-confirmed aciclovir-resistant HSV

Added 18/08/2009:

7. Quality of life

As of 17/12/2012 the first secondary outcome changed to: Time from baseline until reaching the primary endpoint: a composite of either a CD4 cell count less than or equal to 350 cells/mm<sup>3</sup> measured on two consecutive occasions at least 1 month apart, or initiation of HAART for any reason, whichever occurs first.

#### **Completion date**

01/03/2016

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 17/12/2012:

1. Adult (aged 18 years or older or as per Local/Provincial Guidelines), either sex, with documented HIV-1 infection
2. Documented HIV-1 infection (determined by EIA and Western blot)
3. No use of chronic anti-HSV therapy for the past 6 months, and not anticipated to require chronic anti-HSV therapy during the study
4. Anti-retroviral naive (no more than 14 days of total prior anti-retroviral [ARV] exposure)
5. CD4 count within the 400-900 cells/mm<sup>3</sup> range (inclusive) on two consecutive occasions, with at least one measurement within 30 days of initiating trial (baseline visit)
6. Does not meet recommendations for initiating ARV therapy according to current guidelines

Initial inclusion criteria at the time of registration:

1. Adults aged over 18 years, either sex, with documented HIV-1 infection
2. Documented HSV-2 seropositivity
3. Maximum of two episodes recurrent symptomatic HSV recurrences per year by self-report
4. Neither currently using nor anticipated to require chronic anti-HSV therapy during the study
5. Anti-retroviral naive (no more than 14 days of total prior anti-retroviral [ARV] exposure)
6. CD4 count within the 400 - 900 cells/mm<sup>3</sup> range (inclusive) on two consecutive occasions, with at least one measurement within 4 weeks of initiating trial
7. Does not meet recommendations for initiating ARV therapy according to current guidelines

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

Current exclusion criteria as of 17/12/2012:

1. Pregnant or actively planning to become pregnant
2. Receiving chemotherapy, chronic steroid therapy or other immunomodulatory medications (e.g. interferon, azathioprine, methotrexate, TNF-alpha antagonists, etc.)
3. Have an estimated creatinine clearance less than 30 ml/min
4. Have another medical condition likely to cause death within 24 months
5. Enrolled in a therapeutic HIV vaccine or immunotherapy trial
6. Enrolled in another trial investigating the impact of another intervention on HIV disease progression
7. HIV elite controller (EC), phenotypically defined here as documented duration of HIV infection of  $\geq 5$  years, a persistent CD4 cell count  $\geq 500$  cells/mm<sup>3</sup>, and a persistent plasma HIV viral load of  $< 1000$  copies/mL in the absence of antiretroviral therapy

Initial exclusion criteria at the time of registration:

1. Pregnant
2. Receiving chemotherapy or chronic steroid therapy
3. Have an estimated creatinine clearance less than 30 ml/min
4. Have an active opportunistic infection
5. Have another medical condition likely to cause death within 24 months
6. Enrolled in a therapeutic vaccine or immunotherapy trial
7. Enrolled in another trial investigating the impact of another intervention on HIV disease progression
8. Fit the phenotype of an HIV elite controller (EC), since the natural history of HIV infection is fundamentally different in such individuals

**Date of first enrolment**

01/03/2010

**Date of final enrolment**

11/08/2015

## Locations

**Countries of recruitment**

Argentina

Brazil

Canada

**Study participating centre**

**Toronto General Hospital**

Toronto, Ontario

Canada

M5G 2C4

# Sponsor information

## Organisation

University Health Network (UHN) (Canada)

## ROR

<https://ror.org/042xt5161>

## Funder(s)

### Funder type

Research organisation

### Funder Name

Canadian Institutes of Health Research (CIHR) (Canada) - <http://www.cihr-irsc.gc.ca> (ref: MCT-94245)

# 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?
<a href="#">Results article</a>	results	01/02/2019		Yes	No
<a href="#">Protocol article</a>	protocol	24/11/2010		Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes