

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

Submission date 06/03/2009	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
Registration date 09/03/2009	Overall study status Completed	<input checked="" type="checkbox"/> Protocol
Last Edited 16/04/2019	Condition category 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

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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 of 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/mm³ 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. Log¹⁰ 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/mm³ 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/mm³ 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/mm³ 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 ≥ 5 years, a persistent CD4 cell count ≥ 500 cells/mm³, 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?
Results article	results	01/02/2019		Yes	No
Protocol article	protocol	24/11/2010		Yes	No