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

Submission date	Recruitment status	[X] Prospectively registered
06/03/2009	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
09/03/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] 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

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00860977

Secondary identifying numbers
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 or 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

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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 measure
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^3 measured on two consecutive occasions at least 1 month apart, or initiation of HAART for any reason, whichever occurs first.

Secondary outcome measures
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^10 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^3 measured on two consecutive occasions at least 1 month apart, or initiation of HAART for any reason, whichever occurs first.

Overall study start date
01/03/2010

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. 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/mm^3 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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
230

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
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M5G 2C4

Sponsor information

Organisation
University Health Network (UHN) (Canada)

Sponsor details
200 Elizabeth Street
Toronto, Ontario
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Sponsor type
Research organisation

Website
http://www.uhn.ca/index.htm

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

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?
Protocol article	protocol	24/11/2010		Yes	No
Results article	results	01/02/2019		Yes	No