A Phase III, randomized, multicenter, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRTI-, or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed (study 201636)

Published: 15-04-2015
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Primary: To demonstrate the non-inferior antiviral activity of switching to DTG + RPV once daily compared to continuation of current antiretroviral regimen (CAR) over 48 weeks in HIV-1 infected antiretroviral therapy (ART) experienced subjects....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON47247

Source
ToetsingOnline

Brief title
201636

Condition

- Viral infectious disorders

Synonym
HIV1; HIV

Research involving
Human

Sponsors and support

Primary sponsor: ViiV Healthcare UK Limited
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: dolutegravir, HIV, rilpivirine, switch

Outcome measures

Primary outcome

% of subjects with plasma HIV-1 RNA <50 copies/mL at week 48.

Secondary outcome

CD4+ lymphocyte count, % of subjects with plasma HIV-1 RNA <50 copies/mL at week 24, adverse events, premature discontinuation rate, change in biomarkers and lipids, incidence of resistance, pre-dose plasma concentrations. Previously mentioned variables by 3rd agent treatment class. Symptom distress module, HIV TSQ,

Study description

Background summary

There has been much discussion of NRTI-sparing regimens for long-term treatment of HIV infection as a possible approach to avoid known NRTI-associated adverse drug reactions and long-term toxicities. In addition, while there are no currently approved two-drug regimens to maintain suppression, simplifying treatment has long been a goal to increase treatment compliance and improve the quality of life for patients with HIV. The overall objective of the clinical development program of dolutegravir (DTG) + rilpivirine (RPV) is to develop a

FDC tablet. In addition to this goal, two-drug combination therapy with DTG + RPV may also offer a better tolerability and resistance profile without the requirement for a PK booster in virologically suppressed, treatment-experienced subjects.
Study 201636 is being conducted to establish if HIV-1 infected adult subjects with current virologic suppression on a regimen with 2 NRTIs + a third agent remain suppressed upon switching to a two-drug regimen with DTG + RPV.

Study objective

Primary: To demonstrate the non-inferior antiviral activity of switching to DTG + RPV once daily compared to continuation of current antiretroviral regimen (CAR) over 48 weeks in HIV-1 infected antiretroviral therapy (ART) experienced subjects.
Secondary: immunological activity, antiviral activity, safety and tolerability, biomarkers (renal, bone, CV), effects on lipids, viral resistance, trough plasma concentrations, impact of baseline 3rd agent treatment class (INI, NNRTI, PI) on efficacy and safety, treatment satisfaction.

Study design

Randomized open-label phase III parallel group non-inferiority study.
Randomization (1:1) to:
• DTG + RPV once daily;
• CAR (with 2 NRTIs + a 3rd agent).
Stratification by baseline 3rd agent.
At week 52 patients on CAR will also be switched to DTG + RPV.
Total duration148 weeks.
476 subjects.
Subjects who have fully completed the study may continue with DTG + RPV until the combination is commercially available or until development is discontinued.

Intervention

Treatment with
• DTG + RPV or
• 2 NRTIs plus a 3rd agent (INI, NNRTI or a PI), followed by DTG + RPV.

Study burden and risks

Risk: adverse events of study treatment.
Burden:
Visits: 10 visits in the 1st year, 6 visits in the 2nd year and every 12 weeks thereafter.
Physical examination nearly every visit.
Blood tests during nearly every visit until week 148 (approx. 35-95 ml per

visit), thereof 6 times fasting.
Urine tests 6 times.
ECG at screening.
Questionnaires (1-4).
Optional: genetic testing (6 ml of blood, once).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• HIV1-infected males and females, 18 years and above.
• Uninterrupted current regimen (either the initial or second cART regimen) for at least 6 months.
Acceptable stable cART regimens prior to Screening include 2 NRTIs plus:
• INI

• NNRTI
• PI
See protocol section 5.1 (inclusion criteria) for details.
• Documented evidence of at least two plasma HIV-1 RNA measurements <50 c/mL in the 12 months prior to Screening: one within the 6 to 12 month window, and one within 6 months prior to Screening.
• Plasma HIV-1 RNA <50 c/mL at Screening.
• Females of childbearing potential: adequate method of contraception during study, see protocol section 5.1, item 5.

Exclusion criteria

• Within 6 months prior to Screening and after confirmed suppression to <50 c/mL on current ART regimen, any plasma HIV-1 RNA measurement >=50 c/mL
• Within the 6 to 12 month window prior to Screening and after confirmed suppression to <50 c/mL, any plasma HIV-1 RNA measurement >200 c/mL or 2 or more plasma HIV-1 RNA measurements >=50 c/mL.
• Any drug holiday during the window between initiating first HIV ART and 6 months prior to Screening. Exceptions: see protocol section 5.2, item 4..
• Any switch to a 2nd line regimen due to virologic failure to therapy. See protocol section 5.2, item 5 for details.
• Pregnancy or breastfeeding.
• Any evidence of an active CDC Category C disease. Exceptions: see protocol section 5.2, item 7 for details.
• Severe hepatic impairement, unstable liver disease, evidence of Hepatitis B virus. See protocol section 5.2, item 8 for details.
• Exclusionary treatments: medications associated with Torsades de Pointes, HIV-1 immunotherapeutic vaccine, radiation therapy, cytotoxic chemotherapeutic agents, any immunomodulators that alter immune responses, experimental drug or vaccine, any regimen consisting of only single NNRTI therapy or only single or dual NRTI therapy prior to starting cART, ETR, prohibited medication listed in protocol section 6.8.2. See protocol section 5.2, item 17-25 and 6.8.2 for details (e.g. interval until screening).
• Evidence of viral resistance. See protocol section 5.2, item 26 for details.
• Any verified Grade 4 laboratory abnormality, with the exception of Grade 4 lipid abnormalities.

Study design

Design

Study phase: 3

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-07-2015
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Edurant
Generic name:	rilpivirine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tivicay
Generic name:	dolutegravir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-04-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-05-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-12-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-02-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-02-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-05-2016

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-02-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-09-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	03-04-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-005147-40-NL
CCMO	NL53023.100.15
Other	viiv-clinicalstudyregister.com 201636