A Phase III, Randomized, Multicenter, Parallel-group, Open-Label Study Evaluating the Efficacy, Safety, and Tolerability of Long-Acting Intramuscular Cabotegravir and Rilpivirine for Maintenance of Virologic Suppression Following Switch from an Integrase Inhibitor Single Tablet Regimen in HIV-1 Infected Antiretroviral Therapy Naive Adult Participants (study 201584, FLAIR)

Published: 22-09-2016
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Primary:To demonstrate the non-inferior antiviral activity of switching to a two drug CAB LA 400 mg + RPV LA 600 mg regimen every 4 weeks compared to remaining on ABC/DTG/3TC (or DTG and an approved dual-NRTI scheme) over 48 weeks.Secondary:To...

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

Summary

ID

NL-OMON50519

Source
ToetsingOnline

Brief title
study 201584, FLAIR

Condition

- Viral infectious disorders

Synonym
HIV1; HIV

Research involving
Human

Sponsors and support

Primary sponsor: ViiV Healthcare
Source(s) of monetary or material Support: ViiV Healthcare

Intervention

Keyword: Cabotegravir, HIV, longacting injections, Rilpivirine

Outcome measures

Primary outcome

Proportion of participants with a *virologic failure* endpoint (see protocol page 28-29 for details) at Week 48.

Secondary outcome

Proportion of participants with plasma HIV-1 RNA <50/200 c/mL at week 48/96, virologic failure at week (48-)96. Absolute values and change from baseline in plasma HIV-1 RNA at week 48/96. Absolute values and changes from Baseline in CD4+ cell counts over time. Incidence of disease progression. Adverse events. Lipids. Incidence of treatment emergent genotypic and phenotypic resistance to CAB, RPV, and other on-study ART at Week 48/96. PK parameters. Outcomes questionnaires (HAT-QoL, treatment satisfaction score, SF-12, ACCEPT, Numeric Rating Scale injection tolerability).

Study description

Background summary

This study, the First Long-Acting Injectable Regimen * FLAIR study, is being conducted to establish if HIV-1 infected adult participants whose virus is virologically suppressed on an integrase inhibitor single tablet regimen (INI STR) will remain suppressed after switching to a two-drug intramuscular (IM) longacting (LA) regimen of cabotegravir (CAB) and rilpivirine (RPV) once every 4 weeks. In this study, the INI STR will be limited to abacavir/dolutegravir/lamivudine (ABC/DTG/3TC, trade name: Triumeq) for HLA-B*5701 gene negative subjects. Subjects who are HLA-B*5701 positive at the screening visit are allowed to enter the study on DTG and an approved dual-nucleoside reverse transcriptase inhibitor (NRTI) scheme that does not contain abacavir.
The FLAIR study is being conducted in parallel with the 201585 (ATLAS) study with the aim to pool data generated from FLAIR and ATLAS, in order to evaluate key program objectives.

Study objective

Primary:
To demonstrate the non-inferior antiviral activity of switching to a two drug CAB LA 400 mg + RPV LA 600 mg regimen every 4 weeks compared to remaining on ABC/DTG/3TC (or DTG and an approved dual-NRTI scheme) over 48 weeks.
Secondary:
To demonstrate the antiviral and immunologic activity, safety and tolerability, effects on fasting lipids, development of viral resistance, pharmacokinetics, pain and injection site reactions, quality of life, treatment satisfaction and acceptance, health status.

Study design

Open label multicenter parallel group study of 120 weeks.
1. Induction phase (ABC/DTG/3TC for 20 weeks).
2. Subjects who are HLA-B*5701 positive at the screening visit are allowed to enter the study on DTG and an approved dual-nucleoside reverse transcriptase inhibitor (NRTI) scheme that does not contain abacavir.
3. Participants who have an HIV-1 RNA <50 c/mL will be randomized (1:1) into the maintenance phase to either continue ABC/DTG/3TC (or DTG and an approved NRTI scheme) for at least 100 weeks or to begin oral therapy with CAB 30 mg + RPV 25 mg once daily for 4 weeks, followed (in case of acceptable tolerability) by CAB LA (400 mg) + RPV LA (600 mg) injections every 4 weeks (loading dose 600/900 mg resp.).
4. Participants from the ABC/DTG/3TC arm (or DTG and an approved NRTI scheme)

who successfully complete Week 100 will be given the option to switch to the LA arm in the extension phase (no predefined length).
5. Participants on the CAB LA + RPV LA regimen in the maintenance phase will enter the extension phase as well.
6. Any participant who receives at least a single dose of CAB LA and/or RPV LA and discontinues the CAB LA + RPV LA regimen for any reason will enter a 52 week follow-up phase on suppressive highly active antiretroviral therapy.
Independent Data Monitoring Committee.
620 participants.

Intervention

Treatment with ABC/DTG/3TC and CAB LA + RPV LA.

Study burden and risks

Risk: Adverse events of the study medication. Resistance development.
Burden:
Visits every 4 weeks in case of LA injections. In case of tablets: every 4-8 weeks up to extension period, during extension period every 4 weeks.
Al least 33 visits.
Physical examination: every visit.
Blood draws (occasionally fasting): nearly every visit (avg 40 ml blood).
Pregnancy test: every visit.
ECG: 10-11 times.
Questionnaires:SSRS (Columbia) 20 times, others up to 17 times.
Optional: blood sample for pharmacogenetics, PK sampling.

Contacts

Public
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Scientific
ViiV Healthcare

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* HIV-1 infected, ART-naive men or women aged 18 years or older.
* HIV-1 infection as documented by Screening plasma HIV-1 RNA *1000 c/mL.
* Antiretroviral-naïve (*10 days of prior therapy with any antiretroviral agent following a diagnosis of HIV-1 infection). Any previous exposure to an HIV integrase inhibitor or NNRTI will be exclusionary.

Exclusion criteria

* Women who are pregnant, breastfeeding, or plan to become pregnant or breastfeed during the study.
* All active CDC stage 3 diseases at screen are exclusionary, except cutaneous Kaposi*s sarcoma (not requiring systemic therapy) or historic or current CD4+ cell count <200 cells/mm3.
* Known moderate to severe hepatic impairment.
* High risk of seizures, see protocol page 70 for details.
* Significant suicide risk, see protocol page 70-71 for details.
* Evidence of Hepatitis B virus, see protocol page 71 for details.
* Asymptomatic individuals with chronic hepatitis C virus infection will not be excluded, see protocol page 71 for details.
* Untreated syphilis infection, see protocol page 72 for details.
* Clinically significant cardiovascular disease, see protocol page 72 for details.
* Concomitant medications, see protocol page 72 for details.
* Any evidence of primary resistance to NNRTIs, see protocol page 73 for details.
* HLA-B*5701 positive and are unable to use an NRTI backbone that does not contain abacavir, see protocol page 73 for details.

* Any verified Grade 4 laboratory abnormality.
* Estimated creatinine clearance <50 mL/min/1.73m2.
* Currently participating in or anticipating to be selected for any other interventional study.

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):	05-01-2017
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	cabotegravir longacting (IM injections)
Generic name:	cabotegravir longacting (IM injections)
Product type:	Medicine
Brand name:	Edurant
Generic name:	rilpivirine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	rilpivirine longacting (IM injections)

Generic name:	rilpivirine longacting (IM injections)
Product type:	Medicine
Brand name:	Tivicay
Generic name:	dolutegravir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Triumeq
Generic name:	abacavir/dolutegravir/lamivudine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-09-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-11-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-02-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-03-2017
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:	04-04-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-05-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-08-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-08-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-05-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-06-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-07-2018

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-07-2018
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:	02-10-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-10-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-11-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-06-2020
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-01-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-01-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-01-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	12-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-12-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-03-2022
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	EUCTR2016-001646-25-NL
Other	http://www.gskclinicalstudyregister.com, 201584
CCMO	NL59040.100.16