A Phase 3, randomized, double-blind study of the safety and efficacy of GSK1349572 plus abacavir/lamivudine fixed-dose combination therapy administered once daily compared to Atripla over 96 weeks in HIV-1 infected antiretroviral therapy naive adult subjects (ING114467)

Published: 19-11-2010
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Primary: Antiviral efficacy of dolutagravir in combination with Kivexa (abacavir en lamivudine) after 48 weeks of treatment in comparison with Atripla (tenofovir, emtricitabine and efavirenz). Secondary: Antiviral efficacy after 96 and 144 weeks,...

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

Summary

ID

NL-OMON38393

Source
ToetsingOnline

Brief title
ING114467

Condition

- Viral infectious disorders

Synonym
HIV, HIV1

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: GSK1349572, HIV, integrase inhibitor

Outcome measures

Primary outcome

HIV1-RNA (<50 copies/ml) week 48.

Secondary outcome

E.g. the time to viral suppression (<50 copies/mL), the proportion of subjects with plasma HIV-1 RNA <50 copies/mL at Week 96 and 144, the change from baseline in CD4 at week 48, the proportion of subjects with HIV-1 RNA >=1,000 copies/mL at or after 16 and before 24 weeks, or >= 200 copies/mL at 24 weeks, adverse events, quality of life.

Study description

Background summary

Integrase inhibitors (INIs) are a new class of antiretroviral drugs designed to block the action of the integrase viral enzyme, which catalyzes several key steps in the HIV life cycle and is responsible for insertion of the viral genome into the DNA of the host cell. The first INI for the treatment of HIV-1 infected subjects was raltegravir.
In the STARTMRK study, raltegravir demonstrated excellent antiviral activity as first line treatment and was shown to be non-inferior to an

efavirenz-containing (Sustiva) standard of care regimen in the STARTMRK trial. The time to achieve viral suppression was shorter for subjects on raltegravir than on efavirenz. There were fewer drug-related adverse events reported in the raltegravir group and fewer subjects randomized to raltegravir discontinued from the study due to adverse events, highlighting the promise for better long-term tolerability with INI-based therapy. However, RAL requires twice daily dosing, which is a disadvantage when compared to multiple once daily options, and is currently not available in a fixed dose combination (FDC) regimen. In addition, RAL has a low genetic barrier to resistance, given that RAL-associated mutations readily develop in the setting of virologic failure. Therefore, the development of new INIs with different resistance profiles, the potential for higher barrier to resistance, and improved dosing administration is desirable.
GSK1349572 (dolutagravir) is a next-generation INI that may deliver these attributes. Its 14-hour plasma half-life supports once daily dosing. It possesses potent antiviral activity. The compound has no significant CYP P450 enzyme inhibition, and thus has low drug-drug interaction liabilities.
This present study is designed to establish the safety and efficacy of GSK1349572 50 mg once daily in adults infected with HIV-1 who are ART-naïve.
Protocol amendement 04-05: treatment arms from Week 96 to Week 144 in order to collect long term efficacy and safety data for the use of GSK1349572.

Study objective

Primary: Antiviral efficacy of dolutagravir in combination with Kivexa (abacavir en lamivudine) after 48 weeks of treatment in comparison with Atripla (tenofovir, emtricitabine and efavirenz). Secondary: Antiviral efficacy after 96 and 144 weeks, safety and tolerability, resistance development, incidence of HIV-associated conditions, gender-, race-, and/or HIV-1 subtype on response to GSK1349572, quality of life.

Study design

Multicenter randomized double blind phase III non-inferiority parallel group study and open-label extension week 96-144.
Randomization (1:1) to treatment with:
2. Dolutagravir 50 mg plus Kivexa once daily.
2. Atripla once daily.
Treatment duration 144 weeks.
Subjects randomized to receive GSK1349572 plus ABC/3TC therapy and who successfully complete 96 weeks of treatment will be given the opportunity to continue to receive this treatment as part of the study until either GSK1349572 is locally approved and commercially available, they no longer derive clinical benefit, they meet a protocol-defined reason for discontinuation, or the development of the compound is terminated.
Patients from arm 2 will be treated with Atripla until week 144 (1st 96 weeks

in a double blind fashion).
Interim-analysis planned after last subject completed 48 weeks of treatment.
IDMC.
Approx 800 patients.

Intervention

Treatment with GSK1349572 plus Kivexa or Atripla.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: 15 visits in 96 weeks. Thereafter every12 week until week 144 (all patients) or until one of the the stopcriteria defined in the section study design is met (dolutagravir group).Visit duration 1-4 uur.
Blood tests 15x approx. 20-35 ml/visit (total 400 ml in the 1st 96 weeks), pregnancy test (if relevant) nearly every visit, ECG 2x. Questionnaire (EQ 5D, GHO Symptom Distress Module) 4-5x.

Contacts

Public
GlaxoSmithKline

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• HIV-1 infected subjects >=18 years of age.
• HIV-1 infection as documented by HIV-1 RNA >400 c/mL.
• No prior antiretroviral therapy.
• HLA-B*5701 negative.
• Safe contraception for women of childbearing potential.

Exclusion criteria

• Breastfeeding, pregnancy.
• Any evidence of an active CDC Category C disease [CDC, 1993], except cutaneous Kaposi*s sarcoma not requiring systemic therapy or historic or current CD4+ cell count <200 cells/mm3 are not exclusionary.
• History of malignancy within the past 5 years or ongoing malignancy other than the usual exceptions.
• Treatment with an HIV-1 immunotherapeutic vaccine within 90 days of Screening.
• Treatment with any of the following agents within 28 days of Screening: radiation, cytotoxic chemotherapeutic agents, immunomodulators.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-04-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atripla
Generic name:	efavirenz/emtricitabine/tenofovir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dolutagravir
Generic name:	Dolutagravir
Product type:	Medicine
Brand name:	Kivexa
Generic name:	abacavir/lamivudine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-11-2010
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	30-12-2010
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	18-02-2011
Application type:	Amendment

Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	24-02-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	22-03-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	31-03-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	31-05-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	11-07-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	07-11-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	10-11-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO	

Date:	11-05-2012
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	24-05-2012
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	02-11-2012
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	28-11-2012
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	01-05-2013
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	01-05-2014
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek

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
Other	clinicaltrials.gov, regsitratienummer n.n.b.
EudraCT	EUCTR2010-020983-39-NL
CCMO	NL34518.101.10