A Phase III Randomized, Double-blind Study of the Safety and Efficacy of GSK1349572 50 mg Once Daily Versus Raltegravir 400 mg Twice Daily, Both Administered with an Investigator-selected Background Regimen Over 48 Weeks in HIV-1 Infected, Integrase Inhibitor-NaÃ¯ve, Antiretroviral Therapy-Experienced Adults.

Published: 05-10-2010
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Primary: Antiviral efficacy after 48 weeks of treatment. Secundary: Antiviral efficacy after 24 weeks, safety and tolerability, resistance development, PK, incidence of HIV-associated conditions, gender-, race-, and/or HIV-1 subtype on response to...

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

Summary

ID

NL-OMON38097

Source
ToetsingOnline

Brief title
N/A

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, raltegravir

Outcome measures

Primary outcome

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

Secondary outcome

HIV1-RNA (<50 copies/ml) week 24, sign of resistance, virological and

immunological response, disease progression, adverse events, PK parameters,

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 ART-experienced subjects, the BENCHMRK studies demonstrated the superior efficacy of raltegravir plus optimized background therapy compared to optimized

background alone over 48 weeks. Overall frequencies of drug-related adverse events were similar in the raltegravir and placebo groups. Raltegravir will be administered at the approved dose of 400 mg twice daily. Twice daily dosing is a disadvantage when compared to multiple once daily options. In addition, RAL may have a relatively 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 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-experienced and INI-naïve.

Study objective

Primary: Antiviral efficacy after 48 weeks of treatment. Secundary: Antiviral efficacy after 24 weeks, safety and tolerability, resistance development, PK, incidence of HIV-associated conditions, gender-, race-, and/or HIV-1 subtype on response to GSK1349572, quality of life.

Study design

Multicenter randomized doubleblind phase III non-inferiority parallel group study.
Randomisation (1:1) to treatment with:
2. GSK1349572 50 mg once daily.
2. Raltegravir 400 mg twice daily.
Plus background therapy (not part of study treatment, on prescription), to be chosen by investigator base don resistance tests.
Treatment duration 48 weeks.
Interim-analyse palnned after last subject completed 24 weeks of treatment and after 60% have completed 48 weeks of treatment.
Approx 688 patients.
Patient who did receive GSK1349572 during the study may be eligible for a follow-up study.

Intervention

Treatment with GSK1349572 or raltegravir.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: 11 visits in 48 weeks. Duration 1-4 uur.
Blood tests 11x approx. 10 ml/visit, pregnancy test (if relevant) every visit,
ECG 2x. Questionnaire (EQ 5D, 5 questions) 3x.

Contacts

Public
GlaxoSmithKline

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Scientific
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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.
* Documented resistance to two or more different classes of antiretroviral agents.
* Integrase inhibitor-naïve.
* Safe contraception for women of childbearing potential.

Exclusion criteria

* Screening resistance test result indicates no fully active antiviral agents are available for design of the background regimen.
* Subject-virus is not evaluable using genotype/phenotype/tropism.
* Breastfeeding, pregnancy.
* Any evidence of an active Center for Disease and Prevention Control (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 cutaneous Kaposi's sarcoma, basal cell carcinoma, or resected, non-invasive cutaneous squamous cell carcinoma.
* 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):	16-12-2010
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK1349572

Generic name:	GSK1349572
Product type:	Medicine
Brand name:	ISENTRESS
Generic name:	raltegravir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	05-10-2010
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	18-11-2010
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	26-01-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	17-02-2011
Application type:	Amendment
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:	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:	07-10-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	01-03-2012
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	05-03-2012
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:	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 Rotterdam e.o. (Rotterdam)

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. Registratienummer n.n.b.
EudraCT	EUCTR2009-018001-51-NL
CCMO	NL34068.101.10