Study on Pharmacokinetics of newly developed ANtiretroviral agents in HIV-infected pregNAnt women (PANNA)

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This study has been transitioned to CTIS with ID 2024-515487-31-00 check the CTIS register for the current data. The primary objective of this study is to describe the pharmacokinetics of antiretroviral agents, for which no or limited available...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON54597

Source
ToetsingOnline

Brief title
PANNA

Condition

- Viral infectious disorders
- Pregnancy, labour, delivery and postpartum conditions

Synonym
HIV-infection

Research involving
Human

Sponsors and support

Primary sponsor: Apotheek Klinische Farmacie
Source(s) of monetary or material Support: bedrijven,Gilead

Sciences,GlaxoSmithKline,Merck Sharp & Dohme (MSD),Penta

Intervention

Keyword: antiretrovirals, HIV, pharmacokinetics, pregnancy

Outcome measures

Primary outcome

Pharmacokinetics (AUC, Cmax, Cmin) of the agents under study in the second,

third trimester of pregnancy related to the pharmacokinetics (AUC, Cmax, Cmin)

at 4-6 weeks after delivery.

Secondary outcome

Viral load of the pregnant female at screening, week 20, 33 of pregnancy and at

4-6 weeks post-partum.

Viral infection of the neonate.

Transfer of antiretrovirals to breast milk (milk to blood ratio)

Study description

Background summary

Due to the potential for pregnancy-induced changes in the pharmacokinetics of medication, one cannot assume that the currently licensed doses of the medication to be tested under this protocol lead to adequate exposure in an HIV-infected pregnant woman. For the agents under study no or limited pharmacokinetic data during pregnancy are available.
Recently women living with HIV are given the option to breastfeed their children, under certain circumstances. For most antiretrovirals passage into breastmilk is unknown. Therefore, if a mother decides to breastfeed and is using at least one of the compounds mentioned in appendix 1, we will collect breastmilk, maternal plasma and infant plasma (for cabotegravir/rilpivirine regimen only) at at least one visit they have to report to the hospital for viral load checks (generally done monthly during breastfeeding period).
The rationale for the current study is to evaluate the pharmacokinetics of agents with unknown (or unclear) pharmacokinetic profiles during pregnancy when

their use is indicated in pregnant women by the treating physician.

Study objective

This study has been transitioned to CTIS with ID 2024-515487-31-00 check the CTIS register for the current data.

The primary objective of this study is to describe the pharmacokinetics of antiretroviral agents, for which no or limited available pharmacokinetic data during pregnancy is available, in the 2nd, 3rd trimester of pregnant HIV-infected women and at 4-6 weeks post-partum.
In addition, the pharmacokinetics will be determined in the infant as well in case of post-exposure prophylaxis with one of the agents tested.
To describe breastmilk transfer in case of breastfeeding and assess exposure in child if breastfeeding.
Secondary objective of this study is to describe the safety of the antiretroviral agents during pregnancy and the efficacy in terms of viral load response of the mother and prevention of mother to child transmission.

Study design

This is a non-randomized, open-label, parallel-group, multi-center phase-IV study in HIV-infected pregnant women recruited from HIV treatment centers in Europe.

Patients treated with one or more of the agents listed below during pregnancy will be screened and the PK evaluation will take place in Week 33 of the pregnancy, representing the 2nd, 3rd trimester and between 4 and 6 weeks post-partum (if medication use continues after delivery). Patients will use a HAART regimen containing one or more of the agents mentioned below continuously during pregnancy (at least two weeks prior to the first PK evaluation). Safety and antiviral efficacy (including MTCT) will be evaluated too.

Agents under study:
raltegravir QD, tenofovir alafenamide fumarate, dolutegravir, bictegravir (new), doravirine (new), etravirine, enfuvirtide, fosamprenavir, etravirine, maraviroc, efavirenz, rilpivirine, abacavir, atazanavir, emtricitabine, tenofovir (TDF), tirpanavir, indinavir, (cobicistat boosted darunavir and elvitegravir arms have been closed).

Study burden and risks

Adverse effects of the HIV medication administered (the patients have to use this medication to treat their HIV-infection, this medication is not provided for this study).
The needles used for blood collection can induce pain or discomfort at the

injection site. Qualified personell will peform the blood sampling.

The patients are not treated with different medication for this study (the regimen is not adapted). They will be admitted to the hospital two days for blood collections. The total volume of blood collected is not large (max 140 mL). Future treatment of HIV-infected pregnant females will be better.
The same applies for neonates. The maximum blood volume collected from neonates will be 12 mL.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Newborns

Inclusion criteria

1. HIV-infected as documented by positive HIV antibody test and confirmed by Western Blot.

2. Subject is at least 18 years of age at screening.
3. Subject is able and willing to sign the Informed Consent Form prior to screening evaluations.
4. Treated with an HAART regimen containing at least one agent which is mentioned in Appendix 1; this agent has been taken for at least 2 weeks before the day of first PK curve evaluation.
5. Duration of pregnancy not longer than 33 weeks at the day of screening
6. Subject is able to adhere to food intake recommendations.

Exclusion criteria

1. Relevant history or current condition that might interfere with drug absorption, distribution, metabolism or excretion.
2. Inability to understand the nature and extent of the study and the procedures required.
3. Presence of grade III/IV anemia (i.e. Hb <4.6 mmol/L or <7.4 g/dL)
4. Using oral cabotegravir/rilpivirine.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-11-2009
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	09-12-2008
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-02-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-07-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-06-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-06-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-06-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-04-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-02-2015

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-03-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-12-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-07-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-05-2023

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EU-CTR	CTIS2024-515487-31-00
EudraCT	EUCTR2008-006158-16-NL
CCMO	NL26028.091.08