

A European clinical pharmacology network to investigate the Pharmacokinetics of newly developed ANtiretroviral agents in HIV-infected pregNAnt women

panna

Radboud University Nijmegen Medical Centre
The Netherlands

Investigator meeting in Glasgow 8-Nov-2010

1st PANNA Investigators Meeting: Paris, June 2008

2nd PANNA Investigators Meeting: Boston, Feb 2009

3rd PANNA Investigators Meeting: Venice, May 2009

4th PANNA Investigators Meeting: San Francisco, Feb 2010

5th PANNA Investigators Meeting: Glasgow, Nov 2010

Agenda PANNA investigator meeting 8 November 2010

- Welcome & introduction of attendants
David Burger 17:00 - 17:10
- General introduction and update including first results
Angela Colbers 17:10 – 17:30
- Interactive part: problems to be solved
Angela Colbers 17:30 – 18:00
- Questions and closure
David Burger 18:00 – 18:10

Thanks to the sponsors of PANNA

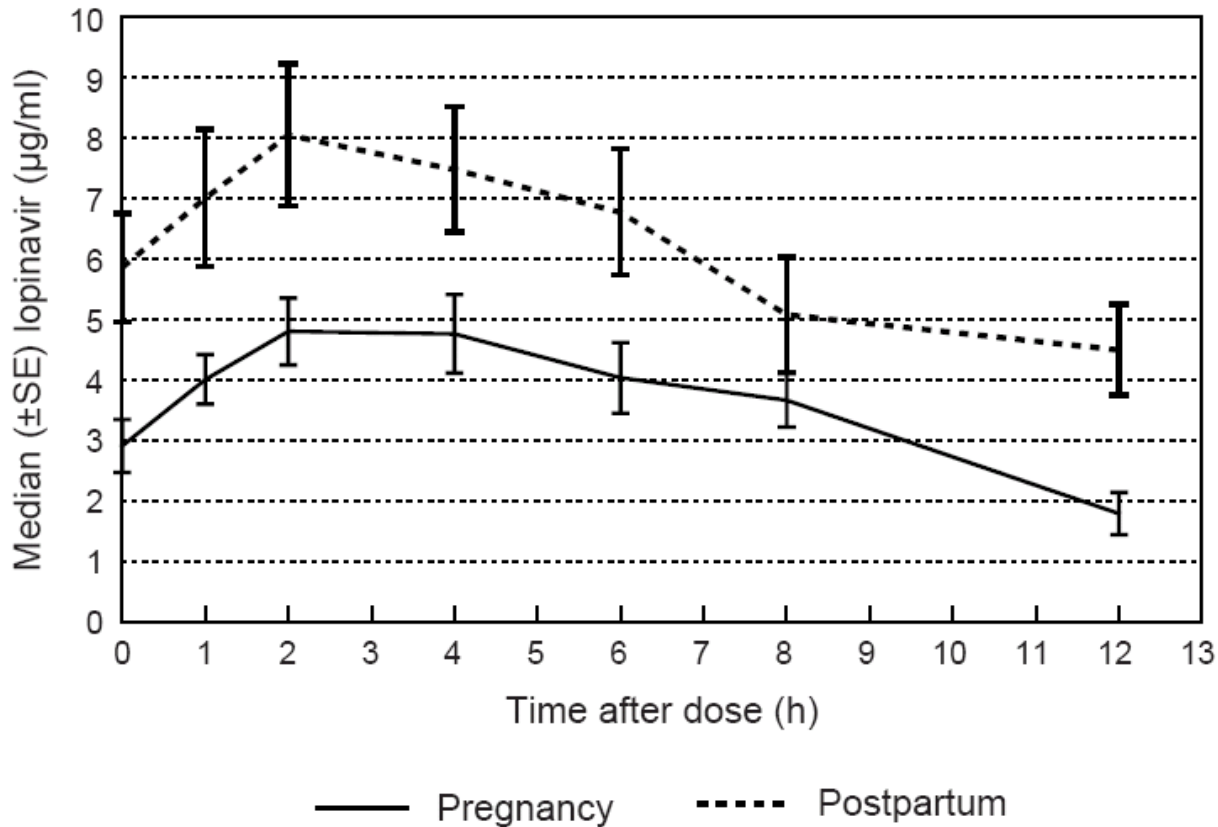
- NEAT/PENTA
- Merck
- BMS
- CTN (Canada)
- Negotiations with other companies are ongoing

Why study pharmacokinetics of ARVs in pregnant women?

- Pregnancy may induce changes in PK of ARVs:
 - Increased volume of distribution
 - Reduced absorption from GI tract
 - Increased hepatic blood flow
 - Increased enzyme activity
 - Reduced protein binding
- In many cases lower plasma concentrations are the result
- Adequate exposure to ARVs is necessary to maximize VL reduction
- Low VL is needed to prevent MTCT

Reduced lopinavir exposure during pregnancy

Alice M. Stek^a, Mark Mirochnick^b, Edmund Capparelli^c,
 Brookie M. Best^c, Chengcheng Hu^d, Sandra K. Burchett^e,
 Carol Elgie^f, Diane T. Holland^c, Elizabeth Smith^g,
 Ruth Tuomala^h, Amanda Cotterⁱ and Jennifer S. Read^j
 for the PACTG 1026s study team*



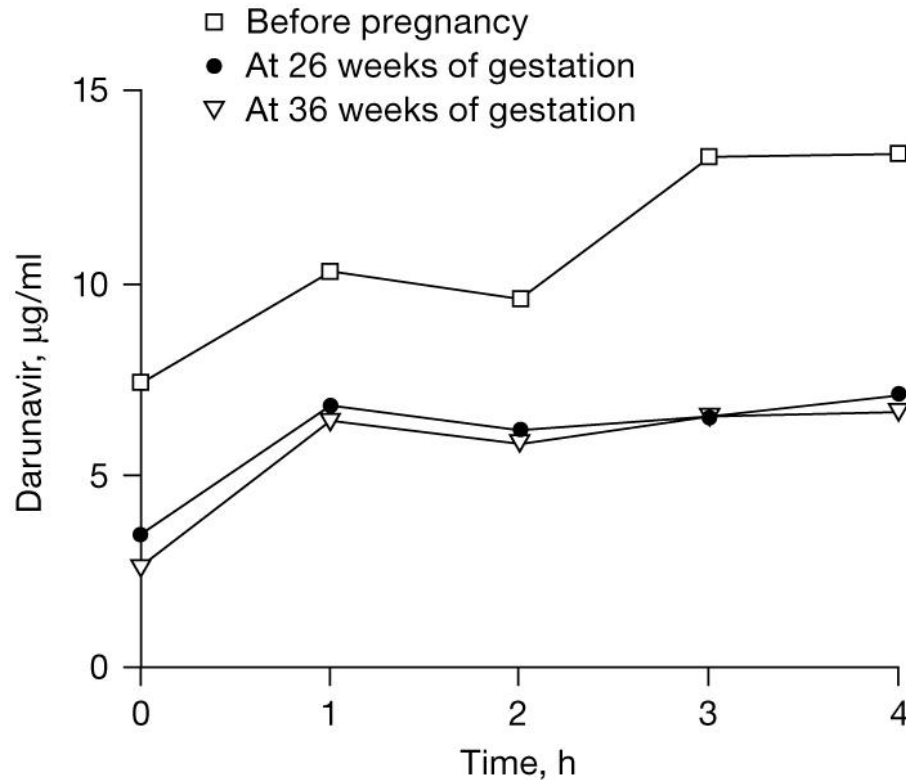
AUC: -28%
 Cmin: -56%

AIDS 2006, **20**:1931–1939

Case report

Decreased plasma levels of darunavir/ritonavir in a vertically infected pregnant woman carrying multiclass-resistant HIV type-1

*Carmela Pinnetti**, *Enrica Tamburrini¹*, *Enzo Ragazzoni²*, *Andrea De Luca¹*, *Pierluigi Navarra²*



AUC: -45%
 Cmin: -61%

PANNA's mission:
Evidence-based dose
recommendations for all ARVs
to be used in pregnancy

Compounds under investigation

NNRTI

- Etravirine (class B) 200mg BID
- Efavirenz (class D) 600mg QD, UK/Ireland only

NRTI

- Emtricitabine (class B) 200mg QD
- Tenofovir (class B) 245mg QD

PI

- Atazanavir (class B) 300mg/100mg RTV QD; 400mg QD; 400/100mg QD
- Fosamprenavir (class C) 700mg/100mg RTV BID; 1400mg/200mg RTV QD
- Darunavir (class B) 600mg/100mg RTV BID; 800/100mg QD
- Tipranavir (class C) 500mg/200mg RTV BID
- Indinavir (class C) 800mg TID; 800mg/100mg RTV BID

Integrase inhibitor

- Raltegravir (class C) 400mg BID

Entry inhibitor

- Enfuvirtide (class B) 90mg BID
- Maraviroc (class B) 300mg BID

PANNA network collaboration

- Selection of sites capable of doing 12h or 24h PK recordings
 - Large site (preferably >40 deliveries/year)
 - Multidisciplinary team
 - Research unit/clinical ward & lab facilities (handling, storage)
 - Regional collaboration preferred
 - European (NEAT) & Canadian sites
- Target: sufficient sites to cover >500 deliveries/year

PANNA network

← Canada

Dublin

London
3 centres

Nijmegen
Rotterdam
Amsterdam

Brussels

Amadora

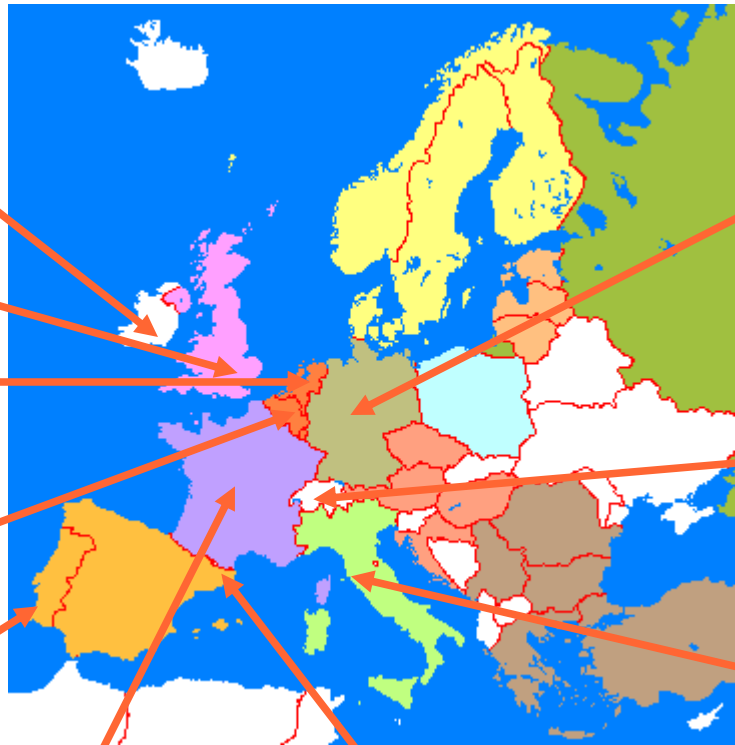
Paris

Barcelona

Cologne
Bonn
Berlin
München
Frankfurt

Geneva

Roma
Torino
Padua





Outline PANNA study protocol

- General study protocol, not specified per drug
 - Patient is eligible if HAART contains at least one drug from the list (no or limited PK information): efavirenz in UK and Ireland only
 - PK at third trimester (preferably Week 33) **and** >2 weeks PP (pref week 4-6)
 - N=16 per drug
 - Cord blood sampling at delivery
 - Safety/efficacy/adherence measurements
 - Central PK lab or local lab with sufficient QA/QC

Website: www.pannastudy.com

panna

Home Contact

PANNA study
Inclusion
Study centres
Participate as a new study centre

PANNA

PANNA is the name of the study of Pharmacokinetics of newly developed ANTiretroviral agents in HIV-infected pregnant women (PANNA). The purpose of the study is to collect pharmacokinetic data (PK curves) in pregnant HIV-infected women using newly developed antiretroviral agents.

Setting up a European-Canadian network

The group of pharmacist David Burger (Radboud University Nijmegen Medical Centre, The Netherlands) has set up a European-Canadian network of centres that are willing and able to participate in this study.

This website gives information about the study, how physicians can include patients and how centres can participate in the PANNA study.

Deutsch
Espagnol
Français
Italiano

Sponsors

Disclaimer Sitemap

Participate as a new
study centre

PANNA network



is at the discretion of the treating physician.

Inclusion criteria

1. HIV-infected as documented by positive HIV antibody test and confirmed by an antigen test.
2. Subject is at least 18 years of age at screening.
3. Subject is willing and able 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. Subject is pregnant.
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 anaemia (i.e. Hb <4.6 mmol/L or <7.4 g/dL).

Test products

Below you will find an overview of the antiretroviral agents that we will investigate in the PANNA study. The number of patients still needed is mentioned in the last column. Please contact the [study centre](#) near you to include a patient treated with one of these agents.

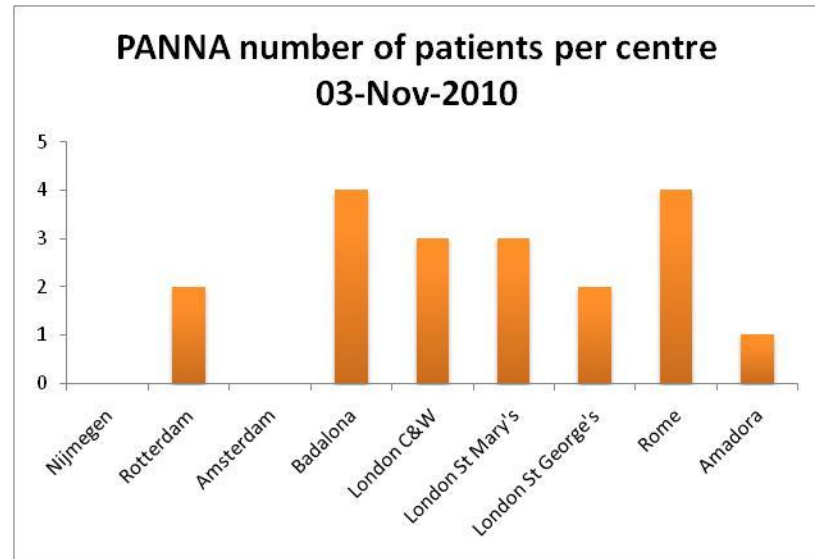
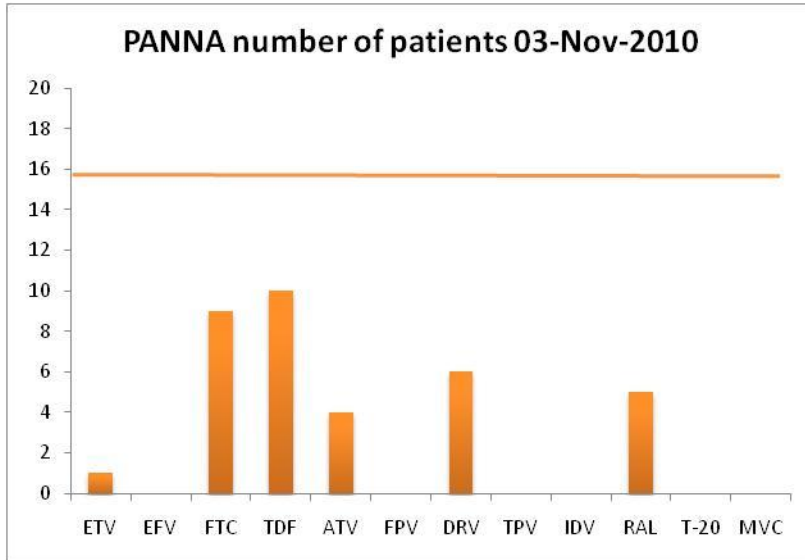
Inclusion of patients

Drug name	Class	Dose and frequency	# pt included	# patients needed (16-#included)
Efavirenz, Stocrin®, EFV	NNRTI	600mg QD	0	16
Etravirine, Intelence®, TMC125	NNRTI	200mg BID	1	15
Emtricitabine, Emtriva® or FTC	NRTI	200mg QD	5	11
Tenofovir, Viread®, TDF	NtRTI	245mg QD	5	11
Atazanavir, Reyataz®	PI	300/100mg RTV QD 400mg QD 400/100mg RTV QD	3	13
Fosamprenavir, Telzir®, FPV	PI	700mg/100mg RTV BID 1400mg/200mg RTV QD	0	16
Darunavir, Prezista®, TMC114	PI	600mg/100mg RTV BID 800mg/100mg QD	5	11
Tipranavir, Aptivus®, TPV	PI	500mg/200mg RTV BID	0	16
Indinavir, Crixivan®	PI	800mg TID 800mg/100mg RTV BID	0	16
Raltegravir, Isentress®	integrase inhib	400mg BID	5	11
Enfuvirtide, Fuzeon®	entry inhibitor	90mg BID	0	16
Maraviroc, Celsentri®	entry inhibitor	300mg BID	0	16

Status and milestones

- The Netherlands, Spain, Italy, UK, Germany, Ireland (?), Canada (Ottawa) open for inclusion
- Portugal, Belgium, France: NA and ethics being worked on
- December 2012 TARGET:
 - For 5 drugs: data from 16 patients
 - Other agents: 5-10 patients
- November 2010:
 - Included 19 patients; 4 dropped out prior to first curve; 2 did not have a post partum curve
 - 6 compounds

Status and milestones



Preliminary results

Presented at the meeting, confidential data, not for the public (yet)

Problems to be discussed

- Patients who take the medication once daily and at night

Change this to morning intake for one week (starting one week before the curve day):

Monday evening

Tuesday-Sunday morning

Monday CURVE day morning

Tuesday morning AND evening

Wednesday evening etc.

- Other solutions: evening/night curve? Start 15:00 h and skip 12h sample?

- Meals

Preferably the meal mentioned on the CRF; however: most important is that the patient takes the same breakfast each PK day

Problems to be discussed

- Logistics regarding cord blood sampling

Examples of how to arrange it. Different for each site.

- Reporting serious adverse events

If a patient has been admitted to the hospital due to complications: this should be reported as SAE.

- Reporting adverse events

All adverse events must be reported.

- Atazanavir amendment

Extra blood sample (trough) for patients on ATV/r 300/100 mg QD at 12 weeks post partum. This has been added on request of BMS. Amendment (+ adapted subeject information) accepted in UK, Germany, The Netherlands, Spain. Italy?

Problems to be discussed

- Convince the patient to have the post partum curve taken

Tips from the centres?

Contact details

- Project coordinator: Mrs Angela Colbers:
A.Colbers@akf.umcn.nl
- Principal Investigator: Dr David Burger:
D.Burger@akf.umcn.nl