

# PENTA18: Pharmacokinetics, safety and efficacy of lopinavir/ritonavir tablets in combination antiretroviral therapy in human immunodeficiency virus-1 (HIV-1) infected children

<b>Submission date</b> 16/06/2009	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 10/07/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 24/06/2015	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

[http://www.ctu.mrc.ac.uk/research\\_areas/study\\_details.aspx?s=71](http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=71)

## Study website

<http://www.pentatrials.org/home.htm>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

PENTA18 version 1.0

## **Study information**

### **Scientific Title**

PENTA18: A study of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in human immunodeficiency virus-1 (HIV-1) infected children

### **Acronym**

PENTA18

### **Study objectives**

The trial will evaluate the pharmacokinetics, safety, efficacy and acceptability of twice- and once-daily dosing of lopinavir/ritonavir tablets (Kaletra®) dosed by weight in human immunodeficiency virus-1 (HIV-1) infected children who are currently taking lopinavir/ritonavir as part of their combination antiretroviral therapy and who are currently achieving virological suppression (less than 50 copies/ml). Specifically:

1. To confirm weight-based dosing recommendations by evaluating the pharmacokinetics of twice-daily lopinavir/ritonavir half strength formulation tablets dosed on body weight and comparing to historical adult and paediatric data of pharmacokinetics of lopinavir/ritonavir soft gel capsules and oral solution respectively
2. To compare the pharmacokinetics of twice-daily lopinavir/ritonavir tablets with once-daily dosing in the same children
3. To evaluate whether once-daily dosing of lopinavir/ritonavir is comparable to twice-daily dosing in terms of virological suppression at 48 weeks. Adherence and acceptability will also be compared.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Trent Research Ethics Committee, 12/01/2010, ref: 09/H0405/49

### **Study design**

Open-label multicentre randomised phase II/III trial

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

**Health condition(s) or problem(s) studied**

Infectious disease - Paediatric HIV

**Interventions**

Children will already be taking lopinavir/ritonavir. Dosage should be adjusted to the FDA approved daily doses (based on weight bands) as part of their combined ART. Children will be randomised to take lopinavir/ritonavir once daily or twice daily (same total daily dose). Children will continue into this dosing unless they reach protocol defined criteria to switch therapy. All children will be followed until the last participant has completed 48 week follow-up.

**Intervention Type**

Drug

**Phase**

Phase II/III

**Drug/device/biological/vaccine name(s)**

Lopinavir/ritonavir (Kaletra®)

**Primary outcome measure**

1. HIV-1 RNA greater than or equal to 400 copies/ml (confirmed) at any of week 4, 8, 12, 24, 36 or 48
2. Area under curve (AUC), Cmin and Cmax values of lopinavir after twice-daily dosing compared to historical adult and paediatric data
3. AUC, Cmin and Cmax values of lopinavir after once-daily and twice-daily dosing (in the same children)

**Secondary outcome measures**

1. HIV-1 RNA less than 400/less than 50 copies/ml at 24 and 48 weeks
2. HIV-1 RNA greater than or equal to 50 and less than 400 copies/ml at any of week 4, 8, 12, 24, 36 or 48
3. Number of HIV mutations present at week 4, 8, 12, 24, 36 or 48 conferring resistance to drugs taken at randomisation or during the trial
4. Change in CD4 (absolute and percentage) from baseline to 24 and 48 weeks
5. Change in ART (defined as any change from the ART regimen at randomisation)
6. ART-related grade 3 or 4 clinical and laboratory adverse events
7. New Centers for Disease Control and Prevention (CDC) stage C diagnosis or death
8. Child and family acceptability of and adherence to twice-daily lopinavir/ritonavir 100/25 mg tablets dosed on body weight, over 48 weeks as assessed by patient/carer completed questionnaires
9. Child and family acceptability of and adherence to once-daily compared to twice-daily dosing

of lopinavir/ritonavir tablets, over 48 weeks as assessed by patient/carer completed questionnaires

**Overall study start date**

30/09/2009

**Completion date**

01/10/2012

## **Eligibility**

**Key inclusion criteria**

1. Aged less than 18 years (up to 18th birthday) with confirmed HIV-1 infection, either sex
2. Weight greater than or equal to 15 kg
3. Able to swallow tablets
4. Stable (i.e. CD4 not declining) on a combination antiretroviral regimen that has included lopinavir/ritonavir for at least 24 weeks, and expected to stay on the same regimen for the next 48 weeks
5. Taking lopinavir/ritonavir dosed twice-daily and be willing at the screening visit to change to tablet formulation (if not currently taking tablets) and to change the lopinavir/ritonavir dose to follow the recommended FDA dosing plan based on body weight bands as necessary; if participating in the PK study, be willing at the screening visit to change to lopinavir/ritonavir half strength formulation tablets (100/25 mg) only, dosed twice-daily and change the lopinavir /ritonavir dose to follow the recommended FDA dosing plan based on body weight bands as necessary
6. Viral suppression (HIV-1 ribonucleic acid [RNA] less than 50 copies/ml) for at least the prior 24 weeks (minimum of two measurements)
7. Children and caregivers willing to participate in the PK study if they are among a minimum of the first 16 children enrolled in each body weight band in the trial, including a second PK assessment if randomised to switch to once-daily lopinavir/ritonavir
8. Parents/carers and children, where applicable, give informed written consent

**Participant type(s)**

Patient

**Age group**

Child

**Upper age limit**

18 Years

**Sex**

Both

**Target number of participants**

160

**Key exclusion criteria**

1. Children on an antiretroviral regimen that includes a non-nucleoside reverse transcriptase inhibitor (NNRTI), fosamprenavir or nelfinavir

2. Children who have previously failed virologically on a protease inhibitor (PI)-containing regimen (where virological failure is defined as two successive HIV-1 ribonucleic acid [RNA] results greater than 1000 copies/ml [confirmed] more than 24 weeks after starting highly active anti-retroviral therapy [HAART], i.e changes for toxicity are not counted as failure)
3. Intercurrent illness
4. Abnormal renal or liver function (grade 3 or above)
5. Receiving concomitant therapy except prophylactic antibiotics
6. Pregnancy or risk of pregnancy in females of child-bearing potential

**Date of first enrolment**

30/09/2009

**Date of final enrolment**

01/10/2012

## **Locations**

**Countries of recruitment**

Austria

Belgium

Brazil

Denmark

England

Germany

Ireland

Italy

Netherlands

Poland

Spain

Sweden

Thailand

United Kingdom

**Study participating centre**

**St Mary's Hospital**  
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## **Sponsor information**

### **Organisation**

The PENTA Foundation (Italy)

### **Sponsor details**

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### **Sponsor type**

Charity

### **Website**

<http://www.ctu.mrc.ac.uk/penta>

### **ROR**

<https://ror.org/00d7mpc92>

## **Funder(s)**

### **Funder type**

Charity

### **Funder Name**

The PENTA Foundation (Italy)

## **Results and Publications**

### **Publication and dissemination plan**

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/03/2014		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No