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

Submission date 16/06/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 10/07/2009	**Overall study status** Completed	
Last Edited 24/06/2015	**Condition category** Infections and Infestations	

Plain English summary of protocol
http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=71

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
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

Primary study design
Interventional

Study design
Open-label multicentre randomised phase II/III trial

Study type(s)
Treatment

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(s)
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)

Key secondary outcome(s)
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. Cchild 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

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

Healthy volunteers allowed
No

Age group
Child

Upper age limit
18 Years

Sex
All

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
United Kingdom

England

Austria

Belgium

Brazil

Denmark

Germany

Ireland

Italy

Netherlands

Poland

Spain

Sweden

Thailand

Study participating centre
St Mary's Hospital
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Sponsor information

Organisation
The PENTA Foundation (Italy)

ROR
https://ror.org/00d7mpc92

Funder(s)

Funder type
Charity

Funder Name
The PENTA Foundation (Italy)

Results and Publications

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?
Results article	results	01/03/2014		Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes