



## Clinical trial results:

**A monocenter, non-controlled, non-randomized IST to compare bioavailability of Kaletra softgelcapsules or -suspension to Kaletra tablets in pediatric patients – C2T**

### Summary

EudraCT number	2010-021622-35
Trial protocol	DE
Global end of trial date	07 May 2014

### Results information

Result version number	v1 (current)
This version publication date	23 June 2022
First version publication date	23 June 2022

### Trial information

#### Trial identification

Sponsor protocol code	C2T
-----------------------	-----

#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	University Hospital of Goethe University Frankfurt
Sponsor organisation address	Theodor-Stern-Kai 7, Frankfurt am Main, Germany, 60590
Public contact	Principal investigator- Dr Koenigs, University Hospital of Goethe University Frankfurt, 49 696301-83030, christoph.koenigs@kgu.de
Scientific contact	Principal investigator- Dr Koenigs, University Hospital of Goethe University Frankfurt, 49 696301-83030, christoph.koenigs@kgu.de

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 December 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	07 May 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Comparison of pharmacokinetic parameters of the different formulations (tablets, capules and oral solution)

Protection of trial subjects:

When planning the study, care was taken to keep the burden and risk for the patients as low as possible. The study participants were exposed to the following stresses:

- A screening visit that could be combined with a routine visit to the outpatient clinic.
- As part of pharmacokinetics, the patients had to spend one day (12-13 hours) in the outpatient clinic. On this day they had to appear sober.
- Blood was taken at different time points on this PK day via an intravenous access, so that the children and young people only had to be "pricked" once. A blood volume of 1.6 ml was required.
- The testing and questionnaires to record the neurocognitive abilities were carried out on the PK day and do not represent an additional time burden.

Kaletra® is approved as a medicinal product and was administered to patients in the usual routine dosage. The therapy is not changed in the study, so that no further study-related risks were expected.

Background therapy:

Kaletra® is an antiretroviral drug and is used in combination with other drugs to treat HIV1 infection. It belongs to the group of Protease inhibitors and consists of a combination of two active substances lopinavir and ritonavir. In this study, drug levels of lopinavir/r after taking Kaletra® tablets were assessed and compared. Patients received this medication as part of their HIV therapy already prior to start the study. As part of the study only the drug levels after taking the regular medication were measured so that no additional or different drugs were administered. The regular intake of medication was continued unchanged.

Evidence for comparator:

Comparison of pharmacokinetic parameters of the different Kaletra formulations (tablets, capules and oral solution) in pediatric patients with confirmed HIV infection.

Actual start date of recruitment	31 July 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	5
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

First patient in study on 12.Sep.2011. Last patient completed the study on 13.May.2012.  
Recruitment was mono-centric in Germany. 15 patients completed the study.

### Pre-assignment

Screening details:

Patients were recruited consecutively at the study site. The investigator reviewed the inclusion and exclusion criteria of the patients.

### Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

### Period 1

Period 1 title	PK1 and PK2 all patients (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	PK1 and PK2 all patients
-----------	--------------------------

Arm description:

PK1: retrospective data collection of a PK under capsule or oral solution intake after screening visit  
PK2: 4 weeks ( $\pm$  5 days) after screening

Arm type	PK Arm Routine Medication
Investigational medicinal product name	Kaletra
Investigational medicinal product code	ATC-Code: J05AE 06
Other name	
Pharmaceutical forms	Capsule, Oral solution, Tablet
Routes of administration	Oral use

Dosage and administration details:

Kaletra (Capsule): 133mg Lopinavir and 33mg Ritonavir  
Kaletra (Oral Solution): 80mg Lopinavir and 33mg Ritonavir /ml  
Kaletra (Tablet): 200mg Lopinavir and 50mg Ritonavir  
Kaletra (Tablet) for children: 100mg Lopinavir and 25mg Ritonavir

Dosing (according to IB): twice per day according to BSA

Number of subjects in period 1	PK1 and PK2 all patients
Started	15
PK1	15
PK2	15
Completed	15



## Baseline characteristics

### Reporting groups

Reporting group title	PK1 and PK2 all patients
-----------------------	--------------------------

Reporting group description: -
--------------------------------

Reporting group values	PK1 and PK2 all patients	Total	
Number of subjects	15	15	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
1.86-5.41	0	0	
8.76-12.79	15	15	
Gender categorical			
male and female			
Units: Subjects			
Female	6	6	
Male	9	9	

### Subject analysis sets

Subject analysis set title	PK1 Lopinavir all patients
----------------------------	----------------------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:
-----------------------------------

PK1 and PK2 all patients
--------------------------

Subject analysis set title	PK2 Lopinavir all patients
----------------------------	----------------------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:
-----------------------------------

PK2 all patients
------------------

Subject analysis set title	PK1 Ritonavir all patients
----------------------------	----------------------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:
-----------------------------------

Ritonavir PK level at PK1
---------------------------

Subject analysis set title	PK2 Ritonavir all patients
----------------------------	----------------------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:
-----------------------------------

Ritonavir PK level at PK2
---------------------------

<b>Reporting group values</b>	PK1 Lopinavir all patients	PK2 Lopinavir all patients	PK1 Ritonavir all patients
Number of subjects	15	15	15
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
1.86-5.41	15	0	15
8.76-12.79	0	15	0
Gender categorical			
male and female			
Units: Subjects			
Female	6	6	6
Male	9	9	9

<b>Reporting group values</b>	PK2 Ritonavir all patients		
Number of subjects	15		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
1.86-5.41	0		
8.76-12.79	15		
Gender categorical			
male and female			
Units: Subjects			
Female	6		
Male	9		

## End points

### End points reporting groups

Reporting group title	PK1 and PK2 all patients
Reporting group description: PK1: retrospective data collection of a PK under capsule or oral solution intake after screening visit PK2: 4 weeks ( $\pm$ 5 days) after screening	
Subject analysis set title	PK1 Lopinavir all patients
Subject analysis set type	Per protocol
Subject analysis set description: PK1 and PK2 all patients	
Subject analysis set title	PK2 Lopinavir all patients
Subject analysis set type	Per protocol
Subject analysis set description: PK2 all patients	
Subject analysis set title	PK1 Ritonavir all patients
Subject analysis set type	Per protocol
Subject analysis set description: Ritonavir PK level at PK1	
Subject analysis set title	PK2 Ritonavir all patients
Subject analysis set type	Per protocol
Subject analysis set description: Ritonavir PK level at PK2	

### Primary: PK1 (retrospective) and PK2 (prospective) Lopinavir

End point title	PK1 (retrospective) and PK2 (prospective) Lopinavir
End point description:	
End point type	Primary
End point timeframe: PK1: retrospective data collection of a PK under capsule or oral solution intake after screening visit PK2: 4 weeks ( $\pm$ 5 days) after screening	

End point values	PK1 Lopinavir all patients	PK2 Lopinavir all patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	15		
Units: AUC (ng*h/ml)				
geometric mean (confidence interval 90%)	30791 (19261 to 49223)	84144 (73083 to 96878)		

Attachments (see zip file)	LPV PK1 and PK2/LPV_PK1_PK2_C2T.png
----------------------------	-------------------------------------

### Statistical analyses



<b>Statistical analysis title</b>	Kaletra PK1 and PK2 all patients
Statistical analysis description: Comparison of pharmacokinetic parameter (AUC) among different Kaletra drug formulations at PK1 and PK2	
Comparison groups	PK2 Lopinavir all patients v PK1 Lopinavir all patients
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
P-value	< 0.0001
Method	t-test, 1-sided

Notes:

[1] - Lopinavir level at PK1 compared to PK2

### Primary: PK1 (retrospective) and PK2 (prospective) Ritonavir

End point title	PK1 (retrospective) and PK2 (prospective) Ritonavir
End point description:	
End point type	Primary
End point timeframe:	
PK1: retrospective data collection of a PK under capsule or oral solution intake after screening visit	
PK2: 4 weeks (± 5 days) after screening	

End point values	PK1 Ritonavir all patients	PK2 Ritonavir all patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	15		
Units: AUC (ng*h/ml)				
geometric mean (confidence interval 90%)	1556 (983.5 to 2460)	5285 (4125 to 6771)		

<b>Attachments (see zip file)</b>	RTV PK1 and PK2/RTV_PK1_PK2_C2T.png
-----------------------------------	-------------------------------------

### Statistical analyses

<b>Statistical analysis title</b>	PK1 and PK2 Ritonavir
Comparison groups	PK1 Ritonavir all patients v PK2 Ritonavir all patients
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other <sup>[2]</sup>
P-value	< 0.0001
Method	t-test, 1-sided

Notes:

[2] - Ritonavir PK level at PK1 compared to PK2

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12/Sep/2011 - 13/Mai/2012

Adverse event reporting additional description:

Adverse events must be documented from inclusion until end of the study (Pharmacokinetic day). The investigator asks the patients about adverse events and assesses the intensity as mild, moderate or severe. The "DAIDS Grading Scale (2004)" was used to assess adverse events.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	DAIDS Grading Scale
-----------------	---------------------

Dictionary version	2004
--------------------	------

### Reporting groups

Reporting group title	all patients
-----------------------	--------------

Reporting group description:

All study patients at PK2

Serious adverse events	all patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	all patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 15 (46.67%)		
Blood and lymphatic system disorders			
lymph node swelling			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

respiratory infection			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
suspicion fracture Aitken I	Additional description: Initial suspicion of Aitken I fracture. Exclusion of fracture after x-ray.		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

---

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28591025>