# 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 pharmakokinetic 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 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 pharmakokinetic 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:

| Subjects enrolled per age group | |
|---|---|
| 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 (± 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<br>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:<br>PK1 and PK2 all patients | |
| Subject analysis set title | PK2 Lopinavir all patients |
| Subject analysis set type | Per protocol |
| Subject analysis set description:<br>PK2 all patients | |
| Subject analysis set title | PK1 Ritonavir all patients |
| Subject analysis set type | Per protocol |
| Subject analysis set description:<br>Ritonavir PK level at PK1 | |
| Subject analysis set title | PK2 Ritonavir all patients |
| Subject analysis set type | Per protocol |
| Subject analysis set description:<br>Ritonavir PK level at PK2 | |

| Reporting group values | 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 |

| Reporting group values | 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 (± 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 (± 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

| Statistical analysis title | 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[1] |
| 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) | | |

| Attachments (see zip file) | RTV PK1 and PK2/RTV_PK1_PK2_C2T.png |
|---|---|

### Statistical analyses

| Statistical analysis title | 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[2] |
| 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