Clinical trial results:
Supersaturation and precipitation of ritonavir in the gastrointestinal tract of healthy volunteers

Summary

EudraCT number	2016-002700-78
Trial protocol	BE
Global end of trial date	27 August 2018

Results information

Result version number	v1 (current)
This version publication date	28 April 2021
First version publication date	28 April 2021

Trial information

Trial identification

Sponsor protocol code	DDD16RITONAVIR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Clinical Trial Center UZ Leuven: S59578

Notes:

Sponsors

Sponsor organisation name	Drug Delivery and Disposition
Sponsor organisation address	Herestraat 49, Leuven, Belgium,
Public contact	Drug Delivery and Disposition, KU Leuven, +32 16379105, jens.vandenabeele@kuleuven.be
Scientific contact	Drug Delivery and Disposition, KU Leuven, +32 16379105, jens.vandenabeele@kuleuven.be

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	25 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2018
Global end of trial reached?	Yes
Global end of trial date	27 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the gastrointestinal behaviour of a weakly basic drug (ritonavir) in healthy volunteers and its implications for systemic drug exposure

Protection of trial subjects:

Identification of trial subjects was replaced by study participant numbers

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2017
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	Belgium: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Candidate volunteers were excluded from participation in case of he-patitis B/C and/or HIV infection, illness at the time of the trial, medi-cation use, a history of acute/chronic gastrointestinal disease(s), (pos-sible) pregnancy, and/or frequent exposure to radiation during theprevious year.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	No
Arm title	Ritonavir

Arm description:

Oral intake of one Norvir®tablet (100 mg ritonavir) with 240 mL oftap water under fasted state conditions

Arm type	Active comparator
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral intake of one Norvir®tablet (100 mg ritonavir) with 240 mL oftap water under fasted state conditions

Arm title	Ritonavir + PPI

Arm description:

Oral intake of one Norvir®tablet (100 mg ritonavir) with 240 mL oftap water under fasted state conditions after intake of a proton-pump inhibitor (PPI) once-daily, starting 48 hours before the start ofthe study (Nexium®, 40 mg esomeprazole)

Arm type	Experimental
Investigational medicinal product name	Ritonavir + esomeprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ral intake of one Norvir®tablet (100 mg ritonavir) with 240 mL oftap water under fasted state conditions after intake of a proton-pump inhibitor (PPI) once-daily, starting 48 hours before the start ofthe study (Nexium®, 40 mg esomeprazole)

Number of subjects in period 1	Ritonavir	Ritonavir + PPI
Started	5	5
Completed	5	5

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	5	5	
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)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	27		
full range (min-max)	25 to 31	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	3	3	

End points

End points reporting groups

Reporting group title	Ritonavir
Reporting group description:	
Oral intake of one Norvir®tablet (100 mg ritonavir) with 240 mL oftap water under fasted state conditions	
Reporting group title	Ritonavir + PPI
Reporting group description:	
Oral intake of one Norvir®tablet (100 mg ritonavir) with 240 mL oftap water under fasted state conditions after intake of a proton-pump inhibitor (PPI) once-daily, starting 48 hours before the start ofthe study (Nexium®, 40 mg esomeprazole)	

Primary: Solubility in the stomach

End point title	Solubility in the stomach[1]
End point description:	
End point type	Primary
End point timeframe:	
Visit 1 - visit 2	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No p values mentioned only description of the measured values.

End point values	Ritonavir	Ritonavir + PPI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: µM				
arithmetic mean (full range (min-max))	135.1 (15.6 to 793.3)	13.5 (10.4 to 25.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Visit 1 - visit 2	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse events reported in the 5 HV

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