Clinical trial results:
A Prospective Single Arm, Open-label, International, Multicenter Study to Evaluate the Safety of Atazanavir (ATV) Capsule Boosted with Ritonavir (RTV) with an Optimized NRTI Background Therapy, in HIV Infected, Antiretroviral Naive and Experienced Pediatric Subjects Greater Than or Equal to 6 Years to Less Than 18 Years

Summary

EudraCT number	2011-003300-21
Trial protocol	Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	27 April 2016

Trial information

Trial identification

Sponsor protocol code	AI424-452

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01691794
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com
Scientific contact	Bristol Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

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	Interim
Date of interim/final analysis	05 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 December 2014
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess the safety and tolerability of atazanavir capsule boosted with ritonavir based regimens in pediatric subjects ages >=6 years to <18 years dosed for 24 weeks.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy:

2 Nucleoside reverse-transcriptase inhibitors (NRTI) were used as a background therapy in this study. NRTIs like zidovudine, stavudine, lamivudine, ritonavir, nelfinavir, nevirapine, lopinavir, indinavir, and efavirenz were prescribed based on viral resistance results, the local guidelines for antiretroviral treatment, and subject's treatment history.

Evidence for comparator: -

Actual start date of recruitment	29 November 2012
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	Peru: 14
Country: Number of subjects enrolled	Brazil: 14
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	South Africa: 59
Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Chile: 3
Worldwide total number of subjects	108
EEA total number of subjects	0

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)	50
Adolescents (12-17 years)	58
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 22 study centers in 8 countries.

Pre-assignment

Screening details:

Overall, 108 subjects were enrolled, and 59 received treatment. Reasons for not entering the treatment period: 1 subject withdrew consent, 1 lost to follow-up, 46 subjects no longer meets study criteria, 1 other reasons.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)

Arm description:

Subjects with baseline weight of 15 to <20 kg received 150 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 nucleoside reverse transcriptase inhibitors (NRTIs) for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Arm type	Experimental
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	BMS-232632
Other name	Reyataz™
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Atazanavir capsule 150-mg were administered orally once daily with food.

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Ritonavir 100-mg capsule or tablet were administered orally once daily with food.

Arm title	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)

Arm description:

Subjects with baseline weight of 20 to <40 kg received 200 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Arm type	Experimental
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	BMS-232632
Other name	Reyataz™
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:	
Atazanavir capsule 200-mg were administered orally once daily with food.	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use
Dosage and administration details:	
Ritonavir 100-mg capsule or tablet were administered orally once daily with food.	
Arm title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)
Arm description:	
Subjects with baseline weight >=40 kg received 300 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.	
Arm type	Experimental
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	BMS-232632
Other name	Reyataz™
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Atazanavir capsule 300-mg were administered orally once daily with food.	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ritonavir 100-mg capsule or tablet were administered orally once daily with food.	

Number of subjects in period 1[1]	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)
Started	3	33	23
Completed	3	30	20
Not completed	0	3	3
Adverse event, non-fatal	-	-	1
Subject no longer meets study criteria	-	2	-
Poor/non-compliance	-	-	1
Lack of efficacy	-	1	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 108 subjects who were enrolled, only 59 entered treatment period. Reason for not entering treatment period were: Subject no longer meets study criteria - 46, subject withdrew consent - 1, lost to follow-up - 1, other reason - 1.

Baseline characteristics

Reporting groups	
Reporting group title	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)

Reporting group description:

Subjects with baseline weight of 15 to <20 kg received 150 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 nucleoside reverse transcriptase inhibitors (NRTIs) for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)

Reporting group description:

Subjects with baseline weight of 20 to <40 kg received 200 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Reporting group title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)

Reporting group description:

Subjects with baseline weight >=40 kg received 300 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Reporting group values	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)
Number of subjects	3	33	23
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	6	10.7	14.7
standard deviation	± 0	± 2.67	± 1.72
Gender categorical Units: Subjects			
Female	2	17	11
Male	1	16	12
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	2
Not Hispanic or Latino	1	2	2
Unknown or Not Reported	2	30	19
Race/Ethnicity, Customized Units: Subjects			
White	1	5	4
Black/African American	2	24	9
Other	0	4	10
Region of Enrollment Units: Subjects			
Africa	2	24	8

Europe	0	1	0
North America	1	0	3
South America	0	8	12
Country Units: Subjects			
Argentina	0	3	0
Brazil	0	3	4
Chile	0	1	2
Mexico	1	0	1
Peru	0	1	6
Russia	0	1	0
South Africa	2	24	8
United States	0	0	2

Reporting group values	Total		
Number of subjects	59		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	30		
Male	29		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	5		
Unknown or Not Reported	51		
Race/Ethnicity, Customized Units: Subjects			
White	10		
Black/African American	35		
Other	14		
Region of Enrollment Units: Subjects			
Africa	34		
Europe	1		
North America	4		
South America	20		
Country Units: Subjects			
Argentina	3		
Brazil	7		
Chile	3		
Mexico	2		
Peru	7		
Russia	1		

South Africa	34		
United States	2		

End points

End points reporting groups

Reporting group title	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)

Reporting group description:

Subjects with baseline weight of 15 to <20 kg received 150 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 nucleoside reverse transcriptase inhibitors (NRTIs) for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)

Reporting group description:

Subjects with baseline weight of 20 to <40 kg received 200 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Reporting group title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)

Reporting group description:

Subjects with baseline weight >=40 kg received 300 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Primary: Number of Subjects Who Died and With Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Discontinuation, Grade 2-4 Related AEs, Grade 3-4 AEs, Cardiac Abnormalities, and Centers for Disease Control (CDC) Class C AIDS Events

End point title	Number of Subjects Who Died and With Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Discontinuation, Grade 2-4 Related AEs, Grade 3-4 AEs, Cardiac Abnormalities, and Centers for Disease Control (CDC) Class C AIDS Events[1]

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Related=having certain, probable, possible, or unknown relationship to study drug. Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4=Life-threatening or disabling, Grade 5=Death. The analysis was performed in all the subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Day 1 of treatment through Week 24

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: Only descriptive summary statistics were planned for this outcome measure.

End point values	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	33	23	
Units: Subjects				

Death	0	0	0	
SAEs	0	1	3	
AEs leading to discontinuation	0	1	1	
Grade 2-4 related AEs	0	22	7	
Grade 3-4 AEs	0	3	5	
CDC Class C AIDS events	0	1	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Results Meeting the Criteria for Abnormal, Grades 1-4

End point title	Number of Subjects With Laboratory Test Results Meeting the Criteria for Abnormal, Grades 1-4[2]

End point description:

Hematocrit (%): Grade (Gr) 1= ≥28.5- <31.5; Gr 2= ≥24- <28.5; Gr 3= ≥19.5- <24; Gr 4= <19.5. Hemoglobin (g/dL): Grade (Gr) 1=8.5-10.0; Gr 2=7.5-8.4; Gr 3=6.50-7.4; Gr 4= <6.5. Platelets (/mm^3): Gr 1=100,000-124,999; Gr 2=50,000-99,999; Gr 3=25,000-49,999; Gr 4= <25,000. White blood cells (/mm^3): Gr 1=2000-2500; Gr 2=1500-1999; Gr 3=1000-1499; Gr 4= <1000. Neutrophils (/mm^3): Gr 1=1000-1500; Gr 2= >=750-1000; Gr 3= >=500-750; Gr 4= <500. Alanine transaminase (ALT), alkaline phosphatase (ALP), aspartate transaminase (AST) (*upper limit of normal [ULN]): Gr 1=1.5-2.5; Gr 2=2.6-5.0; Gr 3=5.1-10.0; Gr 4= >10.0. Total bilirubin (adult and pediatric >14 days) (*ULN): Gr 1=1.1-1.5; Gr 2=1.6-2.5; Gr 3=2.6-5.0; Gr 4= >5.0. Albumin (g/dL): Gr 1= 3.1-<LLN; Gr 2=2.0-2.9; Gr 3= <2.0; Gr 4=NA. Amylase (*ULN): Gr 1=1.10-1.39; Gr 2=1.40-2.09; Gr 3=2.10-5.0; Gr 4= >5. Lipase (*ULN): Gr 1=1.1-1.5; Gr 2=1.6-3.0; Gr 3=3.1-5.0; Gr 4= >5.0. Analysis was performed in all subjects treated with study drug.

End point type	Primary

End point timeframe:

Day 1 of treatment to Week 24

Notes:

[2] - 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: Only descriptive summary statistics were planned for this outcome measure.

End point values	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	33	23	
Units: Subjects				
Hematocrit	0	3	0	
Hemoglobin	0	5	0	
Platelets	0	0	1	
White blood cells	0	2	0	
Neutrophils+bands (absolute)	0	11	3	
ALT	1	3	7	
AST	0	2	4	
ALP	0	6	10	
Total bilirubin	2	20	15	
Albumin	0	1	0	
Amylase	2	27	14	

Lipase	0	11	7	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Results Meeting the Criteria for Abnormal, Grades 1-4 (Continued)

End point title	Number of Subjects With Laboratory Test Results Meeting the Criteria for Abnormal, Grades 1-4 (Continued)[3]

End point description:

Blood urea nitrogen (*upper limit of normal [ULN]): Grade (Gr) 1=1.25-2.5; Gr 2=2.6-5.0; Gr 3=5.1-10; Gr 4= >10. Uric acid (mg/dL): Gr 1=7.5-10.0; Gr 2=10.1-12; Gr 3=12.1-15.0; Gr 4= >15.0. Bicarbonate (mEqL): Gr 1= 19.0-21.0; Gr 2=15.0-18.0; Gr 3=41-45; Gr 4= >45. Calcium, low (mg/dL): Gr 1=7.8-8.4; Gr 2=7.0-7.7; Gr 3=6.1-6.9; Gr 4= <6.1.Potassium (mEq/L), high: Gr 1=5.6-6.0; Gr 2=6.1-6.5; Gr 3=6.6-7.0; Gr 4= >7.0. Potassium (mEq/L), low: Gr 1=3.1-3.4; Gr 2=2.5-2.9; Gr 3=2.0-2.4; Gr 4= <2.0. Sodium (mEq/L), low: Gr 1=130-135; Gr 2=125-129; Gr 3=121-124; Gr 4= <1. Total cholesterol, fasting (mg/dL): Gr 1=200-239; Gr 2=240-300; Gr 3= >300; Gr 4=Not applicable (NA). Low-density lipoprotein (LDL) cholesterol, fasting (mg/dL): Gr 1=130-159; Gr 2=160-190; Gr 3= >190; Gr 4= NA. Glucose, low (mg/dL): Gr 1= 55-64; Gr 2=40-54; Gr 3=30-39; Gr 4= <30. Glucose, fasting (mg/dL): Gr 1=110-125; Gr 2=126-250; Gr 3=251-500; Gr 4 >500.The analysis was performed in all subjects treated with study drug.

End point type	Primary

End point timeframe:

Day 1 of treatment through Week 24

Notes:

[3] - 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: Only descriptive summary statistics were planned for this outcome measure.

End point values	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	33	23	
Units: Subjects				
Blood urea nitrogen	0	1	0	
Uric acid	0	0	3	
Bicarbonate, low	3	26	13	
Calcium, low	0	2	0	
Potassium, high	0	1	0	
Potassium, low	0	1	0	
Total cholesterol, fasting (n=3, 31, 21)	0	4	3	
Sodium, low	1	11	0	
LDL cholesterol, fasting (n=3, 31, 21)	0	2	1	
Glucose, low (n=1, 11, 9)	0	3	0	
Glucose, fasting, high (3, 31, 22)	0	2	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 30 days after the last dose of the study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)

Reporting group description:

Subjects with baseline weight of 15 to <20 kg received 150 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 nucleoside reverse transcriptase inhibitors (NRTIs) for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)

Reporting group description:

Subjects with baseline weight of 20 to <40 kg received 200 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Reporting group title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)

Reporting group description:

Subjects with baseline weight >=40 kg received 300 mg of atazanavir plus 100 mg of ritonavir once daily with an optimized background therapy of 2 NRTIs for 24 weeks. In countries without locally approved pediatric indication for atazanavir, subjects may continue to receive study treatment, with regular 12-week visits, until the age of 18 years.

Serious adverse events	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	1 / 33 (3.03%)	3 / 23 (13.04%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 3 (0.00%)	1 / 33 (3.03%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 33 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 33 (3.03%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 3 (0.00%)	0 / 33 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 33 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Atazanavir, 150 mg + Ritonavir, 100 mg (Weight: 15 to <20 kg)	Atazanavir, 200 mg + Ritonavir, 100 mg (Weight: 20 to <40 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: >=40 kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	26 / 33 (78.79%)	19 / 23 (82.61%)
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 3 (33.33%)	0 / 33 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Sinus arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Sinus bradycardia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 33 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Atrioventricular block first degree			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	3 / 33 (9.09%)	2 / 23 (8.70%)
occurrences (all)	0	3	3
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Ocular icterus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 33 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	7 / 33 (21.21%)	3 / 23 (13.04%)
occurrences (all)	0	9	3
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 33 (3.03%)	5 / 23 (21.74%)
occurrences (all)	0	1	5
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	4 / 23 (17.39%)
occurrences (all)	0	2	5
Diarrhoea			

subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	5 / 23 (21.74%)
occurrences (all)	0	2	6
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	1 / 33 (3.03%)	6 / 23 (26.09%)
occurrences (all)	0	1	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	8 / 33 (24.24%)	2 / 23 (8.70%)
occurrences (all)	0	9	2
Oropharyngeal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 33 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 3 (0.00%)	4 / 33 (12.12%)	2 / 23 (8.70%)
occurrences (all)	0	4	2
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 3 (66.67%)	9 / 33 (27.27%)	2 / 23 (8.70%)
occurrences (all)	3	13	2
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	3 / 33 (9.09%)	6 / 23 (26.09%)
occurrences (all)	1	6	7

Influenza			
subjects affected / exposed	1 / 3 (33.33%)	3 / 33 (9.09%)	2 / 23 (8.70%)
occurrences (all)	2	3	3
Otitis media			
subjects affected / exposed	1 / 3 (33.33%)	2 / 33 (6.06%)	1 / 23 (4.35%)
occurrences (all)	1	2	1
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 33 (6.06%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Impetigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 33 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Pharyngotonsillitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 33 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 33 (3.03%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 33 (3.03%)	0 / 23 (0.00%)
occurrences (all)	1	1	0

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