Clinical trial results:
A Prospective Single Arm, Open-label, International, Multicenter Study to Evaluate the Safety, Efficacy and Pharmacokinetics of Atazanavir (ATV) Powder Boosted with Ritonavir (RTV) Liquid with an Optimized NRTI Background Therapy, in HIV Infected Pediatric Patients Greater Than or Equal to 3 Months to Less Than 6 Years. (Pediatric Atazanavir International Clinical Evaluation: the PRINCE I study)

Summary

EudraCT number	2009-016361-28
Trial protocol	PL IT Outside EU/EEA
Global end of trial date	11 September 2017

Results information

Result version number	v1 (current)
This version publication date	25 March 2018
First version publication date	25 March 2018

Trial information

Trial identification

Sponsor protocol code	AI424-397

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01099579
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	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, 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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000804-PIP01-09
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Study AI424397 was to describe the safety of ATV powder formulation boosted with RTV liquid-based highly active antiretroviral therapy regimens in pediatric subjects dosed through 48 weeks (or a minimum of 24 weeks for subjects who were 5.5 years of age at the time of study start)

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: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	Peru: 3
Country: Number of subjects enrolled	South Africa: 56
Country: Number of subjects enrolled	Thailand: 2
Worldwide total number of subjects	82
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)	41
Children (2-11 years)	41
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 82 pediatric subjects were enrolled, and 56 received treatment. Reasons for not receiving treatment treated were: no longer met study criteria (23 subjects), other reason (2 subjects), and withdrew consent (1 subjects).

Period 1

Period 1 title	Stage 1 (ATV powder formulation)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg

Arm description:

Subjects weighing 5 to <10 kg received atazanavir (ATV), 150-mg powder dosed in 50-mg sachet packets, and ritonavir (RTV) oral solution, 80 mg. Stage 1: Initial dose was determined by subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight of 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Arm type	Experimental
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz BMS-232632
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Powder, oral, dosed by weight. Subjects who weighed 5 to <10 kg received atazanavir (ATV), 150 mg, and ritonavir (RTV), 80 mg once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral solution, 80 mg/mL, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg

Arm description:

Subjects weighing 10 to <15 kg received ATV powder, 200 mg, dosed in 50-mg sachet packets and RTV oral solution, 80 mg. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. All of the mixture must have been consumed to obtain the full dose. The RTV oral solution was taken immediately before or after the ATV powder preparation. Stage

2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Arm type	Experimental
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral solution, 80 mg/mL, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz BMS-232632
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Powder, oral, dosed by weight. Subjects who weighed 5 to <10 kg received atazanavir (ATV), 150 mg, and ritonavir (RTV), 80 mg; those who weighed 10 to <15 kg received ATV, 200 mg, and RTV, 80 mg; and those who weighed 15 to <25 kg received ATV, 250 mg, and RTV, 80 mg, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg

Arm description:

Subjects weighing 15 to <25 kg received 250 mg of ATV powder dosed in 50-mg sachet packets, with 80 mg of RTV solution. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Arm type	Experimental
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral solution, 80 mg/mL, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz BMS-232632
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Powder, oral, dosed by weight. Subjects who weighed 15 to <25 kg received ATV, 250 mg, and RTV, 80 mg, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Number of subjects in period 1[1]	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg
Started	21	19	16
Completed	17	14	15
Not completed	4	5	1
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	4	1	-
Poor compliance/noncompliance	-	2	-
Lack of efficacy	-	2	-

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: A total of 82 pediatric subjects were enrolled, and 56 received treatment. Reasons for not receiving treatment treated were: no longer met study criteria (23 subjects), other reason (2 subjects), and withdrew consent (1 subjects).

Period 2

Period 2 title	Stage 2 (ATV capsules)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg

Arm description:

Subjects weighing 5 to <10 kg received atazanavir (ATV), 150-mg powder dosed in 50-mg sachet packets, and ritonavir (RTV) oral solution, 80 mg. Stage 1: Initial dose was determined by subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight of 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Arm type	Experimental
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral solution, 80 mg/mL, once per day for 48 weeks or until pediatric indication is locally approved and subjects meets requirements to receive appropriate formulation

Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz BMS-232632
Pharmaceutical forms	Powder for oral solution, Capsule
Routes of administration	Oral use

Dosage and administration details:

Powder, oral, dosed by weight. Subjects who weighed 5 to <10 kg received atazanavir (ATV), 150 mg, and ritonavir (RTV), 80 mg once per day for 48 weeks or until pediatric indication is locally

approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg

Arm description:

Subjects weighing 10 to <15 kg received ATV powder, 200 mg, dosed in 50-mg sachet packets and RTV oral solution, 80 mg. Stage 1: Initial dose was determined by the patient's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. All of the mixture must have been consumed to obtain the full dose. The RTV oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Arm type	Experimental
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral solution, 80 mg/mL, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz BMS-232632
Pharmaceutical forms	Powder for oral solution, Capsule
Routes of administration	Oral use

Dosage and administration details:

Powder, oral, dosed by weight. Subjects who weighed10 to <15 kg received ATV, 200 mg, and RTV, 80 mg once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg

Arm description:

Subjects weighing 15 to <25 kg received 250 mg of ATV powder dosed in 50-mg sachet packets, with 80 mg of RTV solution. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Arm type	Experimental
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz BMS-232632
Pharmaceutical forms	Powder for oral solution, Capsule
Routes of administration	Oral use

Dosage and administration details:

Powder, oral, dosed by weight. Subjects who weighed 15 to <25 kg received ATV, 250 mg, and RTV, 80 mg, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral solution, 80 mg/mL, once per day for 48 weeks or until pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Number of subjects in period 2[2]	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg
Started	16	14	15
Completed	10	9	9
Not completed	6	5	6
No longer met study criteria	2	2	1
Consent withdrawn by subject	1	1	1
Poor/Non-Compliance	2	-	1
Adverse event, non-fatal	-	1	-
Lost to follow-up	1	1	1
Lack of efficacy	-	-	2

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all subjects continued to stage 2.

Baseline characteristics

Reporting groups

Reporting group title	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 5 to <10 kg received atazanavir (ATV), 150-mg powder dosed in 50-mg sachet packets, and ritonavir (RTV) oral solution, 80 mg. Stage 1: Initial dose was determined by subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight of 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group title	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 10 to <15 kg received ATV powder, 200 mg, dosed in 50-mg sachet packets and RTV oral solution, 80 mg. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. All of the mixture must have been consumed to obtain the full dose. The RTV oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group title	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 15 to <25 kg received 250 mg of ATV powder dosed in 50-mg sachet packets, with 80 mg of RTV solution. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg
Number of subjects	21	19	16
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)	21	6	0
Children (2-11 years)	0	13	16
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

Age Continuous			
Units: months			
arithmetic mean	7.3	35.4	52.1
standard deviation	± 4.05	± 11.63	± 10.49
Gender, Male/Female			
Units: Subjects			
Female	10	12	6
Male	11	7	10
Race/Ethnicity, Customized			
Units: Subjects			
Not Hispanic or Latino|	0	0	1
Not reported|	21	19	15
Race/Ethnicity, Customized			
Units: Subjects			
White|	2	3	6
Black/African American|	13	12	7
Asian|	0	1	0
Other|	6	3	3
Country			
Units: Subjects			
Chile|	1	2	3
Mexico|	2	3	4
Peru|	1	0	1
South Africa|	17	13	8
Thailand|	0	1	0
HIV RNA Categories			
Units: Subjects			
<30,000 c/mL	3	2	9
30,000 to 100,000 c/mL	0	7	3
>100,000 c/mL	18	10	4
CD4 Percent Categories			
Units: Subjects			
<15|	2	2	1
15 to <25|	7	6	4
>=25|	7	6	6
Not reported|	5	5	5
Prior Antiretroviral (ARV) Treatment Use			
ATV naive is defined as without prior exposure to ARV treatment; ARV experienced is defined as previous exposure to ARV drugs through prior treatment for HIV infection or through postnatal treatment with ≥1 ARVs for the prevention of mother-to-child-transmission in accordance with multiple international guidelines. Subjects exposed to ARVs in utero or intrapartum were permitted in the study but were considered treatment naive.			
Units: Subjects			
ARV-experienced	14	9	11
ARV-naive	7	10	5
HIV RNA			
Units: Log10 c/mL			
arithmetic mean	4.77	4.83	4.18
standard deviation	± 0.602	± 0.268	± 0.727
CD4 Count			
Units: Cells/mm^3			
arithmetic mean	1594.1	1107.4	661.1

standard deviation	± 897.19	± 643.25	± 302.60
CD4 Percent			
Units: Percentage			
arithmetic mean	25.4	22.0	27.5
standard deviation	± 12.11	± 9.35	± 9.85

Reporting group values	Total		
Number of subjects	56		
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)	27		
Children (2-11 years)	29		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Gender, Male/Female			
Units: Subjects			
Female	28		
Male	28		
Race/Ethnicity, Customized			
Units: Subjects			
Not Hispanic or Latino|	1		
Not reported|	55		
Race/Ethnicity, Customized			
Units: Subjects			
White|	11		
Black/African American|	32		
Asian|	1		
Other|	12		
Country			
Units: Subjects			
Chile|	6		
Mexico|	9		
Peru|	2		
South Africa|	38		
Thailand|	1		
HIV RNA Categories			
Units: Subjects			
<30,000 c/mL	14		
30,000 to 100,000 c/mL	10		
>100,000 c/mL	32		
CD4 Percent Categories			

Units: Subjects			
<15|	5		
15 to <25|	17		
>=25|	19		
Not reported|	15		
Prior Antiretroviral (ARV) Treatment Use			
ATV naive is defined as without prior exposure to ARV treatment; ARV experienced is defined as previous exposure to ARV drugs through prior treatment for HIV infection or through postnatal treatment with ≥1 ARVs for the prevention of mother-to-child-transmission in accordance with multiple international guidelines. Subjects exposed to ARVs in utero or intrapartum were permitted in the study but were considered treatment naive.			
Units: Subjects			
ARV-experienced	34		
ARV-naive	22		
HIV RNA			
Units: Log10 c/mL			
arithmetic mean			
standard deviation	-		
CD4 Count			
Units: Cells/mm^3			
arithmetic mean			
standard deviation	-		
CD4 Percent			
Units: Percentage			
arithmetic mean			
standard deviation	-		

End points reporting groups

Reporting group title	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 5 to <10 kg received atazanavir (ATV), 150-mg powder dosed in 50-mg sachet packets, and ritonavir (RTV) oral solution, 80 mg. Stage 1: Initial dose was determined by subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight of 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group title	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 10 to <15 kg received ATV powder, 200 mg, dosed in 50-mg sachet packets and RTV oral solution, 80 mg. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. All of the mixture must have been consumed to obtain the full dose. The RTV oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group title	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 15 to <25 kg received 250 mg of ATV powder dosed in 50-mg sachet packets, with 80 mg of RTV solution. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group title	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 5 to <10 kg received atazanavir (ATV), 150-mg powder dosed in 50-mg sachet packets, and ritonavir (RTV) oral solution, 80 mg. Stage 1: Initial dose was determined by subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight of 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group title	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 10 to <15 kg received ATV powder, 200 mg, dosed in 50-mg sachet packets and RTV oral solution, 80 mg. Stage 1: Initial dose was determined by the patient's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. All of the mixture must have been consumed to obtain the full dose. The RTV oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Reporting group title	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg

Reporting group description:

Subjects weighing 15 to <25 kg received 250 mg of ATV powder dosed in 50-mg sachet packets, with 80 mg of RTV solution. Stage 1: Initial dose was determined by the subject's weight on the day of the first on-treatment study visit (Day 1). ATV dispersible powder was mixed with a small amount of food or beverage (water, milk, chocolate milk, liquid infant formula, applesauce, or yogurt). If water was used, mixture must have been taken with food. The entire contents of the mixture must have been consumed to obtain the full dose. The ritonavir oral solution was taken immediately before or after the ATV powder preparation. Stage 2: Subjects who reached the age of 6 years or a weight 25 kg were transitioned to the capsule formulation of ATV. Those who weighed 15 to <20 kg received ATV, 150 mg, with RTV, 100 mg; those who weighed 20 to <40 mg received ATV, 200, with RTV, 100 mg; and those who weighed at least 40 mg received ATV, 300 mg, with RTV, 100 mg.

Subject analysis set title	ARV-experienced
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Antiretroviral (ARV) treatment-experienced subjects were those with previous exposure to ARV drugs through prior treatment for HIV infection or through postnatal treatment with ≥1 ARVs for the prevention of mother-to-child-transmission in accordance with multiple international guidelines.

Subject analysis set title	ARV-naive
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ARV treatment-naive subjects were those with no prior exposure to ARV treatment. Subjects exposed to ARVs in utero or intrapartum were also considered treatment naive.

Primary: Number of Subjects With Death as Outcome, Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Discontinuation

End point title	Number of Subjects With Death as Outcome, Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Discontinuation[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.

End point type	Primary

End point timeframe:

From Day 1 to Week 48

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 summary statistics were planned for this outcome measure.

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	16	
Units: Subjects				
Deaths|	0	0	0	
SAEs|	5	2	4	
AEs leading to discontinuation|	4	1	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Results With Worst Toxicity of Grade 3-4

End point title	Number of Subjects With Laboratory Test Results With Worst Toxicity of Grade 3-4[2]

End point description:

ALT=alanine aminotransferase; SGPT=serum glutamic-pyruvic transaminase; AST=aspartate aminotransferase; SGOT=serum glutamic-oxaloacetic transaminase; ULN=upper limit of normal. Grading by the National Institute of Health Division of AIDs and World Health Organization criteria. Hemoglobin (g/dL): Grade (Gr)1=9.5-11.0; Gr 2=8.0-9.4; Gr 3=6.5-7.9; Gr 4=<6.5. Neutrophils, absolute (/mm^3): Gr 1=>=1000-<1500; Gr 2= >=750-<1000; Gr 3=>=500-<750; Gr 4=<500. ALT/SGPT (*ULN): Gr 1=1.25-2.5; Gr 2=2.6–5; Gr 3=5.1-10; Gr 4=>10. AST/SGOT (*ULN): Gr 1=1.25-2.5; Gr 2=2.6-5; Gr 3=5.1-10; Gr 4=>10. Alkaline phosphatase(*ULN): Gr 1=1.25-2.5; Gr 2=2.6–5: Gr 3=5.1-10; Gr 4=>10. Total bilirubin (*ULN): Gr 1=1.1-1; Gr 2=1.6-2.5; Gr 3=2.6-5; Gr 4=>5. Amylase (*ULN): Gr 1=1.10-39; Gr 2=1.40-2; Gr 3=2.10-5.0; Gr 4=>5.0. Lipase (*ULN): Gr 1=1.10-1.39: Gr 2=1.40-2; Gr 3=2.10-5.0; Gr 4=>5.0. Uric acid (mg/dL): Gr 1=7.5-10.0; Gr 2=10.1-12.0; Gr 3=12.1-15.0; Gr 4=>15.

End point type	Primary

End point timeframe:

After Day 1 to Week 48

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 summary statistics were planned for this outcome measure.

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	16	
Units: Subjects				
Hemoglobin (n=20, 17, 15)|	2	3	0	
Neutrophils, absolute (n=20, 17, 15)|	3	2	0	
ALT/SGPT (n=20, 18, 15)|	5	0	1	
AST/SGOT (n=20, 18, 15)|	1	0	0	
Alkaline phosphatase (n=20, 18, 15)|	0	1	0	
Total bilirubin (n=20, 18, 15)|	2	0	3	
Amylase (n=20, 18, 15)|	8	5	1	
Lipase (n=20, 18, 15)|	0	1	1	
Uric acid n=20, 18, 15)|	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Electrocardiogram Changes From Baseline in PR Interval, QTC Bazett (QTcB), and QTC Fridericia (QTcF) at Week 48

End point title	Electrocardiogram Changes From Baseline in PR Interval, QTC Bazett (QTcB), and QTC Fridericia (QTcF) at Week 48[3]

End point description:

Electrocardiogram parameters were measured at baseline for QTcB, QTcF, and PR interval. The mean

change from baseline at week 48 is reported by arm in milliseconds.

End point type	Primary

End point timeframe:

From Baseline to Week 48

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 summary statistics were planned for this outcome measure.

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	15	13	
Units: Milliseconds				
arithmetic mean (standard deviation)				
PR Interval|	4.9 (± 21.80)	12.0 (± 8.04)	6.2 (± 8.54)	
QTC Bazett|	1.7 (± 17.73)	-3.2 (± 21.78)	-4.2 (± 13.02)	
QTC Fridericia|	7.9 (± 18.36)	13.2 (± 18.92)	4.8 (± 11.49)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Centers for Disease Control (CDC) Class C AIDS Events

End point title	Number of Subjects With Centers for Disease Control (CDC) Class C AIDS Events[4]

End point description:

CDC Class C events are AIDS-defining events that include recurrent bacterial pneumonia (>=2 episodes in 12 months); candidiasis of the bronchi, trachea, lungs, or esophagus; invasive cervical carcinoma; disseminated or extrapulmonary coccidioidomycosis; extrapulmonary cryptococcosis; chronic intestinal cryptosporidiosis (>1 month); cytomegalovirus disease; HIV-related encephalopathy; herpes simplex: chronic ulcers, or bronchitis, pneumonitis, or esophagitis; disseminated or extrapulmonary histoplasmosis; chronic intestinal isosporiasis; Kaposi sarcoma; immunoblastic or primary brain Burkitt lymphoma; mycobacterium avium complex, kansasii, or tuberculosis; mycobacterium, other species; Pneumocystis carinii pneumonia; progressive multifocal leukoencephalopathy; Salmonella septicemia; recurrent toxoplasmosis of brain; HIV wasting syndrome (involuntary weight loss >10% of baseline body weight) with chronic diarrhea or chronic weakness and documented fever for ≥1 month.

End point type	Primary

End point timeframe:

From Day 1 to Week 48

Notes:

[4] - 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 summary statistics were planned for this outcome measure.

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	16	
Units: Subjects	1	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HIV RNA Levels <50 c/mL and <400 c/mL at Week 48 by Treatment/Weight

End point title	Percentage of Subjects With HIV RNA Levels <50 c/mL and <400 c/mL at Week 48 by Treatment/Weight

End point description:

The definition of virologic success included HIV RNA levels <50 c/mL or 400 c/mL at the Week 48 analysis window.

End point type	Secondary

End point timeframe:

At Week 48

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	14	
Units: Percentage of subjects				
number (not applicable)				
HIV RNA levels <50 c/mL|	47.6	68.4	71.4	
HIV RNA levels <400 c/mL|	66.7	73.7	85.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HIV RNA Levels <50 c/mL and <400 c/mL at Week 48 by Prior Antiretroviral (ARV) Treatment Status

End point title	Percentage of Subjects With HIV RNA Levels <50 c/mL and <400 c/mL at Week 48 by Prior Antiretroviral (ARV) Treatment Status

End point description:

The definition of virologic success included HIV RNA levels <50 c/mL or <400 c/mL at the Week 48 analysis.

End point type	Secondary

End point timeframe:

From Day 1 to Week 48

End point values	ARV-experienced	ARV-naive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	22		
Units: Percentage of subjects				
number (not applicable)				
HIV RNA levels <50 c/mL|	56.3	68.2		
HIV RNA levels <400 c/mL|	65.6	86.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in HIV RNA Levels at Week 48 by Treatment/Weight

End point title	Mean Change From Baseline in HIV RNA Levels at Week 48 by Treatment/Weight

End point description:

Subjects who received at least 1 dose of atazanavir (ATV) and had an HIV RNA measurement on ATV powder at did not switch to the capsule formulation before Week 48

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	15	13	
Units: Log10 c/mL				
arithmetic mean (standard error)	-2.61 (± 0.3111)	-2.93 (± 0.1678)	-2.40 (± 0.2412)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in HIV RNA Levels at Week 48 by Prior

Antiretroviral (ARV) Treatment Status

End point title	Mean Change from Baseline in HIV RNA Levels at Week 48 by Prior Antiretroviral (ARV) Treatment Status

End point description:

The mean change from baseline in HIV RNA levels was reported by arm at week 48 for all treated subjects.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	ARV-experienced	ARV-naive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	22		
Units: Log10 c/mL				
arithmetic mean (standard error)	-2.53 (± 0.2452)	-2.81 (± 0.1296)		

Statistical analyses

No statistical analyses for this end point

Secondary: CD4 Cell Count Changes From Baseline at Week 48 by Treatment/Weight

End point title	CD4 Cell Count Changes From Baseline at Week 48 by Treatment/Weight

End point description:

The mean change from baseline in CD4 cell count at week 48 was reported by treatment/weight for all treated subjects.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	11	5	
Units: Cells/mm^3				
arithmetic mean (standard error)	550.1 (± 285.24)	225.3 (± 198.34)	373.8 (± 68.83)	

Statistical analyses

No statistical analyses for this end point

Secondary: CD4 Cell Count Changes From Baseline at week 48 by Prior Antiretroviral (ARV) Treatment Status

End point title	CD4 Cell Count Changes From Baseline at week 48 by Prior Antiretroviral (ARV) Treatment Status

End point description:

The mean change from baseline in CD4 cell count at week 48 was reported for prior ARV treatment status.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	ARV-experienced	ARV-naive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	22		
Units: Cells/mm^3				
arithmetic mean (standard error)	437.9 (± 253.123)	352.1 (± 152.600)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percent Change of CD4% From Baseline at Week 48 by Treatment/Weight

End point title	Mean Percent Change of CD4% From Baseline at Week 48 by Treatment/Weight

End point description:

The mean percent of change from baseline in CD4% is reported by arm for all treated subjects at week 48.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	12	6	
Units: Percentage of lymphocytes				
arithmetic mean (standard error)	6.1 (± 1.56)	7.3 (± 2.26)	8.8 (± 1.14)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean CD4 Percent Changes From Baseline at Week 48 by Antiretroviral (ARV) Treatment Status

End point title	Mean CD4 Percent Changes From Baseline at Week 48 by Antiretroviral (ARV) Treatment Status

End point description:

The mean change from baseline in CD4 % at week 48 was reported by prior ARV treatment status.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	ARV-experienced	ARV-naive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	22		
Units: Percentage of lymphocytes				
arithmetic mean (standard error)	4.3 (± 1.316)	9.8 (± 1.496)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Acquired Phenotypic Resistance to Atazanavir or Atazanovir/Ritonavir

End point title	Number of Subjects Who Acquired Phenotypic Resistance to Atazanavir or Atazanovir/Ritonavir

End point description:

Criteria for resistance testing= meeting at least 1 of the following: <1 log10 drop from baseline in HIV RNA level by Week 16 and confirmed by a second HIV RNA level; an HIV RNA level >200 copies/mL after Week 24, confirmed by a second HIV RNA level; repeated HIV RNA levels ≥50 copies/mL after Week 48; an HIV RNA level ≥400 copies/mL confirmed by a second HIV RNA level of ≥400 copies/mL at any time in a subject who had previously achieved a plasma HIV RNA level <50 copies/mL; or discontinued due to lack of efficacy. Virologic failure was defined as an incomplete virologic response to therapy or as a viral rebound after the achievement of virologic suppression. The phenotypic resistance to a drug is defined as a fold change (ie, ratio of the 50% inhibitory concentration [IC50] of the clinical isolate to the IC50 of the reference strain) greater than the cut-off for reduced susceptibility.

End point type	Secondary

End point timeframe:

After Day 1 to through Week 48

End point values	ARV-experienced	ARV-naive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	8		
Units: Subjects				
Atazanavir|	0	0		
Ritonavir|	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) and Minimum Observed Concentration (Cmin) of Atazanavir and Ritonavir

End point title	Maximum Observed Concentration (Cmax) and Minimum Observed Concentration (Cmin) of Atazanavir and Ritonavir

End point description:

Serial plasma concentrations will be collected over a 24-hour period at Week 2 in order to assess the steady state PK of ATV and RTV. Pharmacokinetic parameters of ATV and RTV will be derived from plasma concentration versus time data by a non-compartmental method using a validated pharmacokinetic program.

End point type	Secondary

End point timeframe:

At Week 2 at Hour 0 predose and at Hours 1.5, 2.5, 4, 6, 8, 12, and 24 postdose

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	15	
Units: ng/mL				
geometric mean (full range (min-max))				
Atazanavir Cmax|	4131 (1110 to 9660)	5197 (390 to 15000)	6172 (3560 to 10400)	
Atazanavir Cmin|	336 (11.4 to 1330)	572 (11.2 to 4870)	698 (238 to 2410)	
Ritonavir Cmax (n=19, 18, 15)|	2919 (188 to 9160)	2634 (163 to 17700)	1838 (582 to 4960)	
Ritonavir Cmin (n=18, 16, 15)|	41.8 (12.7 to 311)	143 (14.2 to 1610)	51.0 (9.0 to 468)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Curve (in 1 Dosing Interval From Time 0 to 24 Hours Post Observed Dose) (AUC[TAU])of Atazanavir and Ritonavir

End point title	Area Under the Concentration Curve (in 1 Dosing Interval From Time 0 to 24 Hours Post Observed Dose) (AUC[TAU])of Atazanavir and Ritonavir

End point description:

Serial plasma concentrations will be collected over a 24-hour period at Week 2 in order to assess the steady state PK of ATV and RTV. Pharmacokinetic parameters of ATV and RTV will be derived from plasma concentration versus time data by a non-compartmental method using a validated pharmacokinetic program.

End point type	Secondary

End point timeframe:

At Week 2 at Hour 0 predose and at Hours 1.5, 2.5, 4, 6, 8, 12, and 24 postdose

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	15	
Units: ng*h/mL				
geometric mean (full range (min-max))				
AUC(TAU) Atazanavir|	32503 (10441 to 94352)	50305 (6697 to 189971)	61485 (31599 to 117171)	
AUC(TAU) Ritonavir (n=19, 18, 15)|	17439 (1322 to 56864)	20510 (971 to 229777)	13640 (3376 to 40806)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Observed Concentration (Tmax) of Atazanavir and Ritonavir

End point title	Time to Maximum Observed Concentration (Tmax) of Atazanavir and Ritonavir

End point description:

Serial plasma concentrations will be collected over a 24-hour period at Week 2 in order to assess the steady state PK of ATV and RTV. Pharmacokinetic parameters of ATV and RTV will be derived from plasma concentration versus time data by a non-compartmental method using a validated pharmacokinetic program.

End point type	Secondary

End point timeframe:

At Week 2 at Hour 0 predose and at Hours 1.5, 2.5, 4, 6, 8, 12, and 24 postdose

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	15	
Units: Hours				
median (full range (min-max))				
Tmax Atazanavir|	1.58 (1.40 to 12.0)	1.97 (1.00 to 6.00)	4.0 (1.5 to 6.0)	
Tmax Ritonavir (n=19, 18, 50)|	1.8 (1.3 to 11.9)	2.9 (1.0 to 8.0)	4.0 (1.5 to 6.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Total Body Clearance (CLT/F) of Atazanavir and Ritonavir

End point title	Apparent Total Body Clearance (CLT/F) of Atazanavir and Ritonavir

End point description:

Calculated as dose divided by AUC(TAU). AUC(TAU)=area under the concentration-time curve in 1 dosing interval from time 0 to 24 hours post observed dose.

End point type	Secondary

End point timeframe:

At Week 2

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	15	
Units: L/h				
geometric mean (full range (min-max))				
CLT/F Atazanavir|	4.61 (1.6 to 14.4)	3.98 (1.1 to 29.9)	4.07 (2.1 to 7.9)	
CLT/F Ritonavir (n=19, 18, 15|	4.59 (1.4 to 60.5)	3.90 (0.3 to 82.4)	5.87 (2.0 to 23.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Total Body Clearance per Body Weight (CLT/F) per Kilogram of Atazanavir and Ritonavir

End point title	Apparent Total Body Clearance per Body Weight (CLT/F) per Kilogram of Atazanavir and Ritonavir

End point description:

Calculated as CLT/F divided by body weight

End point type	Secondary

End point timeframe:

At Week 2

End point values	Atazanavir powder, 150 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 200 mg/Ritonavir oral solution, 80 mg	Atazanavir powder, 250 mg/Ritonavir oral solution, 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	15	
Units: L/h per kilogram				
geometric mean (full range (min-max))				
CLT/F per kilogram Atazanavir|	0.65 (0.2 to 1.8)	0.32 (0.1 to 2.6)	0.24 (0.1 to 0.5)	
CLT/F per kilogram Ritonavir (n=19, 18, 15)|	0.65 (0.2 to 7.5)	0.32 (0.04 to 5.9)	0.35 (0.1 to 1.4)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Events were reported from start of treatment up to 30 days following discontinuation of treatment (ATV powder or capsule, through Stages 1 and 2 combined).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Body Weight 5 Kilogram (kg) to less than 10 kg

Reporting group description:

Subjects received 150 milligram (mg) Atazanvir (ATV) as powder (Initially contained 10 percent (%) aspartame, after protocol amendment quantity of aspartame reduced to 4.2%) and 100 mg Ritonavir (RTV) as oral solution once a day in combination of an optimized nucleoside backbone therapy. When participant reached to 6 years of age or had a body weight at least 25 Kilogram (kg) they transitioned to the capsule formulations of ATV and RTV.

Reporting group title	Body Weight 10 kg to less than 15 kg

Reporting group description:

Subjects received 200 mg ATV as powder (Initially contained 10% aspartame, after protocol amendment quantity of aspartame reduced to 4.2%) with 80 mg RTV as oral solution once a day in combination of an optimized nucleoside backbone therapy. When participant reached to 6 years of age or had a body weight at least 25 kg they transitioned to the capsule formulations of ATV and RTV.

Reporting group title	Body Weight 15 kg to less than 25 kg

Reporting group description:

Subjects received 250 mg ATV as powder (Initially contained 10% aspartame, after protocol amendment quantity of aspartame reduced to 4.2%) with 80 mg RTV as oral solution once a day in combination of an optimized nucleoside backbone therapy. When participant reached to 6 years of age or had a body weight at least 25 kg they transitioned to the capsule formulations of ATV.

Serious adverse events	Body Weight 5 Kilogram (kg) to less than 10 kg	Body Weight 10 kg to less than 15 kg	Body Weight 15 kg to less than 25 kg
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 21 (33.33%)	5 / 19 (26.32%)	6 / 16 (37.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Electrocardiogram qt prolonged			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			

subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (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
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
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			
Drug-Induced liver injury			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (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
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
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			
Dengue fever			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (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
Gastroenteritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis bacterial			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			

subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
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	Body Weight 5 Kilogram (kg) to less than 10 kg	Body Weight 10 kg to less than 15 kg	Body Weight 15 kg to less than 25 kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)	18 / 19 (94.74%)	15 / 16 (93.75%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	3
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Local swelling			

subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	3 / 21 (14.29%)	7 / 19 (36.84%)	5 / 16 (31.25%)
occurrences (all)	3	7	6
Social circumstances			
Physical assault			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	1	3	2
Bronchospasm			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Cough			
subjects affected / exposed	7 / 21 (33.33%)	6 / 19 (31.58%)	7 / 16 (43.75%)
occurrences (all)	13	19	21
Epistaxis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Lung disorder			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	4 / 21 (19.05%)	3 / 19 (15.79%)	0 / 16 (0.00%)
occurrences (all)	4	4	0
Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinitis allergic			

subjects affected / exposed	4 / 21 (19.05%)	3 / 19 (15.79%)	1 / 16 (6.25%)
occurrences (all)	6	5	4
Rhinorrhoea			
subjects affected / exposed	5 / 21 (23.81%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	5	3	3
Sneezing			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Psychiatric disorders			
Enuresis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Blood bilirubin increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	2
Blood sodium increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Cardiac murmur			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Crystal urine present			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Electrocardiogram abnormal			

subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Urinary sediment present			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	4 / 21 (19.05%)	3 / 19 (15.79%)	1 / 16 (6.25%)
occurrences (all)	5	3	1
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	5 / 21 (23.81%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	10	0	1
Burns first degree			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Foreign body			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Overdose			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Scar			

subjects affected / exposed	1 / 21 (4.76%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Skin abrasion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Upper limb fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	6
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	1	4	0
Basophilia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	1	2	2
Basophilopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Eosinophilia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 19 (10.53%)	2 / 16 (12.50%)
occurrences (all)	1	2	2
Leukopenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Lymphadenitis			

subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Lymphadenopathy			
subjects affected / exposed	4 / 21 (19.05%)	4 / 19 (21.05%)	0 / 16 (0.00%)
occurrences (all)	5	4	0
Lymphocytosis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	2	2	4
Lymphopenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Monocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Monocytosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	2	3	1
Splenomegaly			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	3
Ear pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	3 / 16 (18.75%)
occurrences (all)	0	1	4
Excessive cerumen production			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Otorrhoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2

Tympanic membrane perforation			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Conjunctivitis allergic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	2 / 16 (12.50%)
occurrences (all)	0	1	3
Abdominal pain upper			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Anal pruritus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dental caries			
subjects affected / exposed	4 / 21 (19.05%)	3 / 19 (15.79%)	3 / 16 (18.75%)
occurrences (all)	4	5	5
Diarrhoea			
subjects affected / exposed	11 / 21 (52.38%)	6 / 19 (31.58%)	7 / 16 (43.75%)
occurrences (all)	22	9	7
Gastritis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Oral mucosal blistering			

subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tongue geographic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 21 (4.76%)	2 / 19 (10.53%)	2 / 16 (12.50%)
occurrences (all)	1	2	2
Vomiting			
subjects affected / exposed	9 / 21 (42.86%)	8 / 19 (42.11%)	4 / 16 (25.00%)
occurrences (all)	13	18	8
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	4 / 21 (19.05%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	4	1	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 19 (10.53%)	4 / 16 (25.00%)
occurrences (all)	3	4	7
Jaundice			
subjects affected / exposed	1 / 21 (4.76%)	3 / 19 (15.79%)	2 / 16 (12.50%)
occurrences (all)	1	5	2
Ocular icterus			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	2	3	2
Skin and subcutaneous tissue disorders			
Dandruff			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Dermatitis allergic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Dermatitis diaper			

subjects affected / exposed	6 / 21 (28.57%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	7	2	0
Dry skin			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Ecchymosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	7 / 21 (33.33%)	4 / 19 (21.05%)	1 / 16 (6.25%)
occurrences (all)	8	5	3
Lipodystrophy acquired			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Macule			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Onychomadesis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pityriasis alba			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Prurigo			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	2	2
Pruritus			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	2 / 21 (9.52%)	2 / 19 (10.53%)	2 / 16 (12.50%)
occurrences (all)	2	3	3
Rash papular			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Seborrhoeic dermatitis			

subjects affected / exposed	3 / 21 (14.29%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	4	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin ulcer			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urticaria papular			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Leukocyturia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Proteinuria			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Joint swelling			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tendonitis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	6 / 21 (28.57%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	10	0	2
Bacteriuria			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	1	3	1
Bronchitis			
subjects affected / exposed	2 / 21 (9.52%)	4 / 19 (21.05%)	2 / 16 (12.50%)
occurrences (all)	2	10	6
Candida nappy rash			
subjects affected / exposed	5 / 21 (23.81%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	9	0	0
Conjunctivitis			
subjects affected / exposed	2 / 21 (9.52%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	2	2	1
Ear infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	6	2	0
Enterobiasis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Fungal infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Fungal skin infection			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Gastroenteritis			
subjects affected / exposed	9 / 21 (42.86%)	5 / 19 (26.32%)	2 / 16 (12.50%)
occurrences (all)	18	6	2

Helminthic infection			
subjects affected / exposed	5 / 21 (23.81%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	8	2	1
Herpes simplex			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	4 / 21 (19.05%)	2 / 19 (10.53%)	2 / 16 (12.50%)
occurrences (all)	7	3	3
Influenza			
subjects affected / exposed	3 / 21 (14.29%)	1 / 19 (5.26%)	2 / 16 (12.50%)
occurrences (all)	3	1	2
Lice infestation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	2 / 21 (9.52%)	3 / 19 (15.79%)	1 / 16 (6.25%)
occurrences (all)	3	7	1
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Molluscum contagiosum			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	3 / 21 (14.29%)	1 / 19 (5.26%)	5 / 16 (31.25%)
occurrences (all)	12	2	14
Oral candidiasis			
subjects affected / exposed	9 / 21 (42.86%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	10	0	0
Oral herpes			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	2 / 16 (12.50%)
occurrences (all)	0	1	3

Otitis externa			
subjects affected / exposed	3 / 21 (14.29%)	3 / 19 (15.79%)	1 / 16 (6.25%)
occurrences (all)	3	3	1
Otitis media			
subjects affected / exposed	8 / 21 (38.10%)	4 / 19 (21.05%)	4 / 16 (25.00%)
occurrences (all)	17	9	10
Otitis media acute			
subjects affected / exposed	3 / 21 (14.29%)	2 / 19 (10.53%)	2 / 16 (12.50%)
occurrences (all)	4	4	2
Otitis media chronic			
subjects affected / exposed	3 / 21 (14.29%)	1 / 19 (5.26%)	2 / 16 (12.50%)
occurrences (all)	3	2	2
Parasitic gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	5 / 21 (23.81%)	4 / 19 (21.05%)	4 / 16 (25.00%)
occurrences (all)	6	4	4
Pharyngotonsillitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	4
Pneumonia			
subjects affected / exposed	3 / 21 (14.29%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	3	2	0
Pulmonary tuberculosis			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	2 / 16 (12.50%)
occurrences (all)	1	1	3
Rhinitis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	2 / 16 (12.50%)
occurrences (all)	1	1	3
Sinusitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	3

Skin infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tinea capitis			
subjects affected / exposed	4 / 21 (19.05%)	2 / 19 (10.53%)	2 / 16 (12.50%)
occurrences (all)	6	3	6
Tinea faciei			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tinea infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	3 / 16 (18.75%)
occurrences (all)	1	1	4
Tonsillitis			
subjects affected / exposed	7 / 21 (33.33%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	11	2	1
Tooth abscess			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	11 / 21 (52.38%)	6 / 19 (31.58%)	5 / 16 (31.25%)
occurrences (all)	55	15	8
Urinary tract infection			
subjects affected / exposed	6 / 21 (28.57%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	8	2	0
Varicella			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	2	2	1
Viral rash			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 21 (19.05%)	8 / 19 (42.11%)	4 / 16 (25.00%)
occurrences (all)	8	12	5
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	1	3	0

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 21 (23.81%)	3 / 19 (15.79%)	2 / 16 (12.50%)
occurrences (all)	7	4	5
Hyperamylasaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	3
Hypercholesterolaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	3	0	1
Hyperlipasaemia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2010	The primary purpose of this amendment is as follows: 1) To clarify subjects' age range at time of first treatment, which will be 3 months to 5 years and 6 months of age. This change is to allow subjects who are nearly 6 years of age to have a minimum of 24 weeks of treatment with the powder formulation. 2) Additional visits are included in Stage 2 of the study. Subjects who switch to the capsule formulation will have 2 additional visits after the day of the switch. The new visits will be added at Weeks 4 and 8 following Day 0 of Stage 2 (day of switch to capsule). There will be a visit at Week 12 and every 12 weeks thereafter (ie, every 3 months). A transition period of 8 weeks is allowed to enable subjects to switch from the powder to the capsule. Subjects who are not able to swallow the capsule by the Stage 2 Week 8 week visit will be discontinued from the study. 3) Supplementary trough PK (ATV/RTV only) testing will be added as part of the clinical evaluation of a subject, for whom an investigator has a clinical concern (eg: a subject who has virologic rebound or is failing to suppress at a rate expected by the investigator).
18 April 2011	The purpose of this amendment is to clarify the intent to allow the use of both brand and generic locally approved and available NRTIs by removing statements not intended to have been in the protocol.
24 October 2011	1) To allow switch of NRTIs during the study in case of confirmed viral rebound >= 400 copies virologic rebound > = 400 copies/mL and < 10,000 copies/mL associated with a genotypic and / or phenotypic resistance to one or more assigned NRTI study drugs without genotypic and/or phenotypic resistance (including reduced sensitivity) to ATV or due to treatment-limiting NRTI toxicity 2) To add section on identification and reporting of events occurring in study participants which meet protocol-defined criteria of Drug Induced Liver Injury (DILI). 3) To allow RTV tablets in stage 2 of the study 4) To define treatment experienced subjects in Section 1.1 and Section 3.3.1. 5) To clarify the definition and management of virologic rebound and failure (Section 4.5.2) and discontinuation of subjects from treatment (Section 3.5). 6) To clarify that the age limit should be achieved at the time of first treatment. 7) Table 4.1 Product description: Added ritonavir tablet product information and updated the RTV oral solution storage conditions.
27 April 2012	1) To change the whole treatment regimen, including ATV, in patients with confirmed virologic failure or virologic rebound above 1000 copies/mL based on the resistance profile at failure in accordance with the recommendations from guidelines as per FDA comments on amendment 05 in Section 1.1. 2) Table 3.1.1B: Removed table note b as it is inconsistent with other protocol sections. Clarified in table title that ritonavir tablets or capsules should be used for pediatric patients (8 to less than 18 years of age). 3) To modify the definition of virologic failure in accordance with the updated 2011 DHHS pediatric guidelines in section 4.5.2 and clarify the virologic failure criteria to discontinue a subject in the study in Sections 3.5 and 4.5.2. 4) Table 4.1. Product description: Updated the ATV capsules storage conditions (excursions permitted 15-30°C) to be aligned with the

29 January 2013	1) To switch all subjects in Stage 2, who are still on the current atazanavir oral powder formulation (10% aspartame), to the new 4.2% aspartame atazanavir oral powder formulation and to collect palatability/acceptability data at the time of switch and after the switch in Sections 3.1.1 and 4.1. 2) Added background information on ATV 4.2% aspartame powder formulation in Section 1.4. 3) Added that subject diaries should be used for subjects switching to the new 4.2% aspartame ATV powder formulation in stage 2 and as long as the subject is on the new ATV powder or maximum duration of one year, whichever comes first in Section 4.5. 4) Added Adherence/Tolerability assessment procedures and added note that the assessments only apply to subjects remaining on ATV powder in Stage 2 in Time and Event Table 5.1C. 5) Throughout the protocol, the numbering and lay-out of Tables and Figures is changed and hyperlinks are inserted. 6) Cover page: BMS Research & Development Belgium address has been changed
15 April 2014	1) To increase the blood volume collection from 1 up to 2 mL for HIV RNA testing in Stage 2 when switching to the new Abbott RealTime HIV-1 assay after the Roche Amplicor assay is discontinued. 2) To address inconsistencies and administrative changes in Appendices 1 and 4.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported