



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) With an Optimized NRTI Background Therapy, in Human Immunodeficiency Virus (HIV) Infected, Antiretroviral, Naive and Experienced Pediatric Subjects From 3 Months to Less Than 11 Years.(Pediatric Atazanavir International Clinical Evaluation: the PRINCE II Study)

Summary

EudraCT number	2010-024537-23
Trial protocol	GB PL ES Outside EU/EEA
Global end of trial date	22 January 2018

Results information

Result version number	v1 (current)
This version publication date	05 August 2018
First version publication date	05 August 2018

Trial information

Trial identification

Sponsor protocol code	AI424-451
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01335698
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)	EMA-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	22 January 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety of ATV powder formulation boosted with RTV based highly active antiretroviral therapy regimens in pediatric subjects dosed through a minimum of 24 weeks, as measured by the frequency of deaths, serious adverse events (SAEs), and discontinuation due to adverse events (AEs).

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	27 May 2011
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	Argentina: 5
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Chile: 5
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	South Africa: 109
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	160
EEA total number of subjects	6

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)	60
Children (2-11 years)	100
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:

Of 160 subjects enrolled, 99 received treatment.

Period 1

Period 1 title	Treatment Stage 1
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, 80 mg (Weight: 5 to <10 kg)

Arm description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

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

Dosage and administration details:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or 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:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
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Arm description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Arm type	Experimental
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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:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or 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:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
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Arm description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

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:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or 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:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
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Arm description:

Stage 1: HIV-infected pediatric subjects weighing 15 to <25 kg at baseline received atazanir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned

to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

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:

Stage 1: HIV-infected pediatric subjects weighing 15 to <25 kg at baseline received atazanavir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or 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:

Stage 1: HIV-infected pediatric subjects weighing 15 to <25 kg at baseline received atazanavir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)
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Arm description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanavir powder formulation, 300 mg, with ritozinavir capsule/tablets, 100 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

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:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanavir powder formulation, 300 mg, with ritozinavir capsule/tablets, 100 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Number of subjects in period 1^[1]	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
Started	23	12	21
Completed	15	4	16
Not completed	8	8	5

Consent withdrawn by subject	1	2	-
Adverse event, non-fatal	1	2	2
Poor compliance/noncompliance	-	1	-
Not specified	1	-	-
No longer meets study criteria	1	1	-
Lost to follow-up	1	1	-
Lack of efficacy	3	1	3

Number of subjects in period 1^[1]	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)
Started	35	8
Completed	26	6
Not completed	9	2
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	1
Poor compliance/noncompliance	2	-
Not specified	1	-
No longer meets study criteria	1	-
Lost to follow-up	-	-
Lack of efficacy	3	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: The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial as out of 160 subjects who were enrolled only 99 were randomised. 1 subject no longer met study criteria, 5 subjects withdrew consent, 2 Other switched to another formulation, 1 was lost to follow up, 6 did not complete due to poor compliance/noncompliance, 5 experienced an adverse event, and 7 did not complete due to lack of efficacy.

Period 2

Period 2 title	Treatment Stage 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)

Arm description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Arm type	Experimental
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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:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or 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 and solvent for oral solution
Routes of administration	Oral use

Dosage and administration details:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
------------------	---

Arm description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

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:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

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

Dosage and administration details:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
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Arm description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned

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

Dosage and administration details:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanavir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or 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:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanavir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation

Arm title	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
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Arm description:

Stage 1: HIV-infected pediatric subjects weighing 15 to <25 kg at baseline received atazanavir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

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:

Stage 1: HIV-infected pediatric patients weighing 15 to <25 kg at baseline received atazanavir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Patients entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the patient reached 18 years of age or pediatric indication is locally approved and patient 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:

Stage 1: HIV-infected pediatric patients weighing 15 to <25 kg at baseline received atazanavir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Patients entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the patient reached 18 years of age or pediatric indication is locally approved and patient meets requirements to receive appropriate formulation

Arm title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)
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Arm description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 300 mg, with ritozinavir capsule/tablets, 100 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

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:

Stage 1: HIV-infected pediatric patients weighing 10 to <15 kg at baseline received atazanir powder formulation, 300 mg, with ritozinavir capsule/tablets, 100 mg, for 24 to 48 weeks. Patients entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the patient reached 18 years of age or pediatric indication is locally approved and patient meets requirements to receive appropriate formulation

Number of subjects in period 2	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
Started	15	4	16
Completed	4	1	11
Not completed	11	3	5
Consent withdrawn by subject	3	1	1
Adverse event, non-fatal	2	-	-
Poor compliance/noncompliance	1	-	1
Capsules received at state hospital	1	-	-
Lost to follow-up	1	-	-
Subject no longer meets study criteria	-	-	-
Lack of efficacy	2	1	3
Switched to another formulation	1	1	-

Number of subjects in period 2	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)
Started	26	6
Completed	18	5
Not completed	8	1
Consent withdrawn by subject	-	-
Adverse event, non-fatal	3	-
Poor compliance/noncompliance	3	1
Capsules received at state hospital	-	-
Lost to follow-up	-	-

Subject no longer meets study criteria	1	-
Lack of efficacy	1	-
Switched to another formulation	-	-

Baseline characteristics

Reporting groups

Reporting group title	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
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Reporting group title	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 15 to <25 kg at baseline received atazanir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 300 mg, with ritozinavir capsule/tablets, 100 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
Number of subjects	23	12	21
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)	22	11	3
Children (2-11 years)	1	1	18
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
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Age Continuous Units: months arithmetic mean standard deviation	8.4 ± 6.42	10.5 ± 9.21	37.4 ± 12.44
Sex: Female, Male Units: Subjects			
Female	12	6	12
Male	11	6	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	2
Not Hispanic or Latino	1	1	1
Unknown or Not Reported	22	10	18
Race/Ethnicity, Customized Units: Subjects			
White	2	2	12
Black/African American	19	6	7
Other	2	4	2
Region of Enrollment Units: Subjects			
North America	2	1	9
South America	1	1	1
Africa	20	10	8
Europe	0	0	3
Country Units: Subjects			
Argentina	0	1	1
Brazil	0	0	0
Chile	1	0	0
Mexico	1	1	7
Poland	0	0	1
Romania	0	0	0
Russia	0	0	1
South Africa	20	10	8
Spain	0	0	1
United States	1	0	2

Reporting group values	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)	Total
Number of subjects	35	8	99
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	36

Children (2-11 years)	35	8	63
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	67.2	93.4	
standard deviation	± 16.70	± 15.53	-
Sex: Female, Male			
Units: Subjects			
Female	18	3	51
Male	17	5	48
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	4
Not Hispanic or Latino	1	0	4
Unknown or Not Reported	33	8	91
Race/Ethnicity, Customized			
Units: Subjects			
White	13	3	32
Black/African American	20	5	57
Other	2	0	10
Region of Enrollment			
Units: Subjects			
North America	4	2	18
South America	4	1	8
Africa	21	5	64
Europe	6	0	9
Country			
Units: Subjects			
Argentina	2	0	4
Brazil	1	0	1
Chile	1	1	3
Mexico	4	2	15
Poland	0	0	1
Romania	1	0	1
Russia	3	0	4
South Africa	21	5	64
Spain	2	0	3
United States	0	0	3

End points

End points reporting groups

Reporting group title	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 15 to <25 kg at baseline received atazanir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 300 mg, with ritozinavir capsule/tablets, 100 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 5 to <10 kg at baseline received atazanir powder formulation, 150 mg, with ritonavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)
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Reporting group description:

Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanir powder formulation, 200 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Reporting group description:	
Stage 1: HIV-infected pediatric subjects weighing 15 to <25 kg at baseline received atazanavir powder formulation, 250 mg, with ritozinavir oral solution, 80 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.	
Reporting group title	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)
Reporting group description:	
Stage 1: HIV-infected pediatric subjects weighing 10 to <15 kg at baseline received atazanavir powder formulation, 300 mg, with ritozinavir capsule/tablets, 100 mg, for 24 to 48 weeks. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.	

Primary: Number of Participants Who Died and With Adverse Events (AEs) Leading to Discontinuation, Hyperbilirubinemia, Jaundice, First-degree Arterioventricular Block, Tachycardia, and Rash on ATV Powder

End point title	Number of Participants Who Died and With Adverse Events (AEs) Leading to Discontinuation, Hyperbilirubinemia, Jaundice, First-degree Arterioventricular Block, Tachycardia, and Rash on ATV Powder ^[1]
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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.

End point type	Primary
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End point timeframe:

Day one to week 300 (approximately 22-Jan-2018)

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 endpoint

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	21	35
Units: Subjects				
Deaths	0	0	0	0
AEs leading to discontinuation	3	2	2	2
Hyperbilirubinemia-related adverse events	2	0	9	7
Jaundice	0	0	3	3
Atrioventricular block, first degree	0	0	0	1
Tachycardia	0	0	1	0
Rash	3	0	4	5

End point values	Atazanavir, 300 mg +			
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	Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Subjects				
Deaths	0			
AEs leading to discontinuation	1			
Hyperbilirubinemia-related adverse events	0			
Jaundice	0			
Atrioventricular block, first degree	0			
Tachycardia	0			
Rash	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants who experienced a SAE on ATV Powder

End point title	Number of Participants who experienced a SAE on ATV
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End point description:

SAE= any of the the following: is life-threatening (defined as an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe), requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is an important medical event (defined as a medical event(s) that may not be immediately life threatening or result in death or hospitalization but, based upon appropriate medical and scientific judgment, may jeopardize the subject or may require intervention [eg, medical, surgical] to prevent one of the other serious outcomes listed in the definition above.) Examples of such events include, but are not limited to, intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization

End point type	Primary
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End point timeframe:

Day one to week 300 (approximately 22-Jan-2018)

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 provided

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	21	35
Units: Subjects	6	3	8	8

End point values	Atazanavir, 300 mg +			
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	Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With A Center of Disease Control and Prevention (CDC) Class C AIDS Event on ATV Powder

End point title	Number of Participants With A Center of Disease Control and Prevention (CDC) Class C AIDS Event on ATV Powder ^[3]
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End point description:

The CDC disease staging system assesses the severity of HIV disease by CD4 cell counts and by the presence of specific HIV-related conditions. CD4 counts are classified as 1: ≥ 500 cells/ μ L, 2: 200-499 cells/ μ L, and 3: < 200 cells/ μ L. Children with HIV infection are also classified in each of several categories. Category N: Not symptomatic. Category A: Mildly symptomatic. Category B: Moderately symptomatic. Category C: Severely symptomatic.

End point type	Primary
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End point timeframe:

Day one to week 300 (approximately 22-Jan-2018)

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 endpoint

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	21	35
Units: Subjects				
Pulmonary tuberculosis	2	0	1	0
Lymph node tuberculosis	0	0	0	1
Tuberculosis	0	0	0	1
Oropharyngeal Candidiasis	1	0	0	0

End point values	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Subjects				
Pulmonary tuberculosis	0			

Lymph node tuberculosis	0			
Tuberculosis	0			
Oropharyngeal Candidiasis	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Laboratory Test Results Meeting the Criteria for Grade 3-4 Abnormality on ATV powder

End point title	Number of Participants With Laboratory Test Results Meeting the Criteria for Grade 3-4 Abnormality on ATV powder ^[4]
End point description:	
Criteria of the Division of AIDS for grading the severity of adult and pediatric adverse events as follows: Grade (Gr) 1=mild; Gr 2=moderate; Gr 3=severe; Gr 4=potentially life-threatening. Neutrophils (absolute) (adult and infants >7 days): Gr 1=1.000-1300/mm ³ ; Gr 2=750-999 mm ³ ; Gr 3=500-749 mm ³ ; Gr 4= <500 mm ³ . Alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase: Gr 1=1.25-2.5*upper limit of normal (ULN); Gr 2=2.6-5.0*ULN; Gr 3=5.1-10.0*ULN; Gr 4= >10.0*ULN. Bilirubin, total (adults and infants >14 days): Gr 1=1.1-1.5*ULN; Gr 2=1.6-2.5*ULN; Gr 3=2.6-5.0*ULN; Gr 4= >5.0*ULN. Lipase: Gr 1=1.1-1.5*ULN; Gr 2=1.6-3.0*ULN; Gr 3=3.1-5.0*ULN; Gr 4= >5.0*ULN. Bicarbonate, serum low: Gr 1=16.0 mEq/L-<lower limit of normal; Gr 2=11.0-15.9 mEq/L; Gr 3=8.0-10.9 mEq/L; Gr 4= <8 mEq/L. By criteria of the World Health Organization: Amylase: Gr 1=1.0-1.39*ULN; Gr 2=1.40-2.09*ULN; Gr 3.=2.10-5.0*ULN; Gr 4=	
End point type	Primary
End point timeframe:	
Day one to week 300 (approximately 22-Jan-2018)	

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 endpoint

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	21	35
Units: Subjects				
Neutrophils (absolute)(n=23, 11, 21, 34, 8)	0	0	4	6
Alanine aminotransferase (n=23, 12, 21, 34, 8)	4	1	1	2
Aspartate aminotransferase (n=23, 12, 21, 34, 8)	2	0	1	0
Alkaline phosphatase (n=23, 12, 21, 34, 8)	1	2	1	0
Total bilirubin (n=23, 12, 21, 34, 8)	4	1	10	5
Amylase (n=23, 12, 21, 34, 8)	15	7	6	6
Lipase (n=23, 12, 21, 34, 8)	3	2	0	2
Bicarbonate (n=23, 12, 21, 34, 8)	2	0	0	0
Albumin (n=23, 12, 21, 34, 8)	1	1	0	1
Calcium, High (n=23, 12, 21, 34, 8)	0	0	0	1
Chloride, Low (n=23, 12, 21, 34, 8)	0	0	0	1

Total Cholesterol, Fasting (n=23, 12, 21, 34, 8)	0	0	1	0
LDL Cholesterol, Fasting (n=23, 12, 21, 34, 8)	0	0	1	0
Glucose, Fasting, Low (n=23, 12, 21, 34, 8)	0	0	1	0

End point values	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Subjects				
Neutrophils (absolute)(n=23, 11, 21, 34, 8)	0			
Alanine aminotransferase (n=23, 12, 21, 34, 8)	0			
Aspartate aminotransferase (n=23, 12, 21, 34, 8)	0			
Alkaline phosphatase (n=23, 12, 21, 34, 8)	0			
Total bilirubin (n=23, 12, 21, 34, 8)	2			
Amylase (n=23, 12, 21, 34, 8)	1			
Lipase (n=23, 12, 21, 34, 8)	1			
Bicarbonate (n=23, 12, 21, 34, 8)	0			
Albumin (n=23, 12, 21, 34, 8)	0			
Calcium, High (n=23, 12, 21, 34, 8)	0			
Chloride, Low (n=23, 12, 21, 34, 8)	0			
Total Cholesterol, Fasting (n=23, 12, 21, 34, 8)	0			
LDL Cholesterol, Fasting (n=23, 12, 21, 34, 8)	0			
Glucose, Fasting, Low (n=23, 12, 21, 34, 8)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With HIV RNA <50 copies/mL and <400 copies/mL in the Week 24 Atazanavir Powder Cohort and the Eligible Week 48 Atazanavir Powder Cohort

End point title	Number of Subjects With HIV RNA <50 copies/mL and <400 copies/mL in the Week 24 Atazanavir Powder Cohort and the Eligible Week 48 Atazanavir Powder Cohort
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End point description:

Virologic success includes patients with HIV RNA <50 copies/mL. Two cohorts were assessed: The Atazanavir Powder Cohort=patients who received treatment and did not switch to capsule before analysis Week 24 or before their HIV RNA Week 24 assessment, and the Eligible Week 48 Atazanavir Powder Cohort=patients who initiated study treatment at least 48 weeks before last person last visit and did not switch to capsule before analysis Week 48 or before their HIV RNA Week 48 assessment.

End point type	Secondary
End point timeframe:	
Day 1 of treatment to weeks 24 and 48	

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	21	35
Units: Subjects				
Week 24: HIV RNA<50 copies/mL	10	2	10	19
Week 24: HIV RNA<400 copies/mL	15	5	15	24
Week 48: HIV RNA<50 copies/mL (n=23, 1, 20, 34, 2)	11	0	6	18
Week 48:HIV RNA<400 copies/mL (n=23, 1, 20, 34, 2)	14	1	14	22

End point values	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Subjects				
Week 24: HIV RNA<50 copies/mL	5			
Week 24: HIV RNA<400 copies/mL	6			
Week 48: HIV RNA<50 copies/mL (n=23, 1, 20, 34, 2)	1			
Week 48:HIV RNA<400 copies/mL (n=23, 1, 20, 34, 2)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in HIV RNA on ATV powder

End point title	Mean change from baseline in HIV RNA on ATV powder
End point description:	
Human immunodeficiency virus ribonucleic acid (HIV RNA) change from baseline using observed values	
End point type	Secondary
End point timeframe:	
Baseline to Weeks 24 and 48	

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	21	35
Units: Log copies per millileter				
arithmetic mean (standard error)				
Week 24 (n=21, 7, 19, 29, 7)	-2.10 (± 0.2863)	-3.07 (± 0.4780)	-2.69 (± 0.2257)	-2.66 (± 0.1550)
Week 48 (n=16, 2, 15, 25, 1)	-2.31 (± 0.3174)	-4.06 (± 0.1649)	-2.91 (± 0.1883)	-2.70 (± 0.1269)

End point values	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Log copies per millileter				
arithmetic mean (standard error)				
Week 24 (n=21, 7, 19, 29, 7)	-2.24 (± 0.3821)			
Week 48 (n=16, 2, 15, 25, 1)	-3.97 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in CD4 percent on ATV powder

End point title	Mean change from baseline in CD4 percent on ATV powder
End point description:	
Change in CD4 percent using observed values	
End point type	Secondary
End point timeframe:	
Baseline to Weeks 24 and 48	

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	11	15	30
Units: Percent				
arithmetic mean (standard error)				
Week 24 (n=17, 4, 12, 23, 6) Week 48 (n=12, 0, 9, 19, 1)	5.1 (± 1.521) 2.8 (± 3.167)	4.0 (± 1.581) 99999 (± 99999)	5.4 (± 2.448) 8.9 (± 2.182)	6.3 (± 1.280) 7.5 (± 1.825)

End point values	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percent				
arithmetic mean (standard error)				
Week 24 (n=17, 4, 12, 23, 6) Week 48 (n=12, 0, 9, 19, 1)	-0.3 (± 4.349) 1.0 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4 Cell Count Changes From Baseline on ATV powder

End point title	CD4 Cell Count Changes From Baseline on ATV powder
End point description:	CD4 cell count change from baseline using observed values
End point type	Secondary
End point timeframe:	Baseline to Weeks 24 and 48

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	11	13	27
Units: Cells/mm ³				
arithmetic mean (standard error)				
Week 24 (n=15, 4, 9, 19, 6)	218.7 (± 259.102)	67.8 (± 425.659)	247.1 (± 110.739)	246.1 (± 72.044)

Week 48 (n=10, 0, 8, 16. 1)	-409.8 (± 437.686)	99999 (± 99999)	400.0 (± 156.021)	335.4 (± 108.925)
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End point values	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Cells/mm ³				
arithmetic mean (standard error)				
Week 24 (n=15, 4, 9, 19, 6)	145.8 (± 78.443)			
Week 48 (n=10, 0, 8, 16. 1)	213.0 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Emergent Genotypic Substitutions on ATV Powder Through Week 48

End point title	Number of Participants With Emergent Genotypic Substitutions on ATV Powder Through Week 48
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End point description:

Newly emergent substitutions are on-treatment substitutions that were not detected at baseline. Viral rebound in the resistance analysis was defined as: Less than a 1 log₁₀ drop from baseline in plasma HIV RNA level by Week 16, confirmed by a second plasma HIV RNA level redrawn within 2 and 4 weeks from original sample. Or, a plasma HIV RNA level >200 c/mL after Week 24, confirmed by a second plasma HIV RNA level redrawn within 2 and 4 weeks from original sample. Or, repeated plasma HIV RNA level ≥50 c/mL after Week 48. Viral rebound was defined as a plasma HIV RNA level ≥400 c/mL at any time in a patient who had previously achieved a plasma HIV RNA level <50 c/mL. Or, a plasma HIV RNA level ≥50 c/mL and <1,000 c/mL followed by a return to virologic suppression was considered a viral blip and not a viral rebound. NRTI=nucleoside reverse transcriptase inhibitor

End point type	Secondary
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End point timeframe:

Baseline through Week 48

End point values	Atazanavir, 150 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 10 to <15 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	2	10	13
Units: Subjects				
Any PI substitutions	4	0	4	3
Any IAS-USA PI substitutions	1	0	2	0
Any select RT substitutions	2	1	2	1

NRTI	1	1	2	1
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End point values	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
Any PI substitutions	0			
Any IAS-USA PI substitutions	0			
Any select RT substitutions	0			
NRTI	0			

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile of ATV powder formulation with RTV

End point title	PK profile of ATV powder formulation with RTV ^[5]
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End point description:

To describe the PK profile of ATV powder formulation with RTV in pediatric subjects weighing 25 - < 35 kg and/or 6 to < 11 years of age and for the new 5 - < 10 kg cohort (200 mg ATV and 80 mg RTV) in terms of ATV maximum observed plasma concentration (C_{max}), minimum plasma concentration (C_{min}), and area under the concentration-time curve (AUC)

End point type	Secondary
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End point timeframe:

Baseline to Week 2 Baseline to

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only summary statistics were planned for this endpoint

End point values	Atazanavir, 200 mg + Ritonavir, 80 mg (Weight: 5 to <10 kg)	Atazanavir, 250 mg + Ritonavir, 80 mg (Weight: 15 to <25 kg)	Atazanavir, 300 mg + Ritonavir, 100 mg (Weight: 25 to <35 kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	35	8	
Units: subjects				
arithmetic mean (standard deviation)				
C _{max}	5776.70 (± 3417.208)	5644.12 (± 3093.516)	4893.75 (± 2523.959)	
C _{min}	718.90 (± 432.747)	857.06 (± 599.221)	1030.64 (± 1070.932)	
AUC(TAU)	49387.12 (± 26890.782)	59671.80 (± 31706.655)	56356.00 (± 35233.024)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 305 weeks approximately

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Atazanavir 150 mg (Baseline weight: 5 to < 10 kg)
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Reporting group description:

Human immunodeficiency virus (HIV)-infected pediatric subjects having baseline weight between 5 to less than (<) 10 kilogram (kg) received 150 milligram (mg) atazanavir powder formulation, with 80 mg per milliliter (mg/ml) ritonavir oral solution once daily (QD) for 24 to 48 weeks in Stage 1. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to atazanavir capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir 200 mg (Baseline weight: 5 to < 10 kg)
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Reporting group description:

HIV-infected pediatric subjects having baseline weight between 5 to < 10 kg received 200 mg atazanavir powder formulation, with 80 mg/ml ritonavir oral solution QD for 24 to 48 weeks in Stage 1. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to atazanavir capsules. Treatment continued until the patient reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir 200 mg (Baseline weight: 10 to < 15 kg)
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Reporting group description:

HIV-infected pediatric subjects having baseline weight between 10 to < 15 kg received 200 mg atazanavir powder formulation, with 80 mg/ml ritonavir oral solution QD for 24 to 48 weeks in Stage 1. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to atazanavir capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir 250 mg (Baseline weight: 15 to < 25 kg)
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Reporting group description:

HIV-infected pediatric subjects having baseline weight between 15 to < 25 kg received 250 mg atazanavir powder formulation, with 80 mg/ml ritonavir oral solution QD for 24 to 48 weeks in Stage 1. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to atazanavir capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Reporting group title	Atazanavir 300 mg (Baseline weight: 25 to < 35 kg)
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Reporting group description:

HIV-infected pediatric subjects having baseline weight between 25 to < 35 kg received 300 mg atazanavir powder formulation, with ritonavir 100 mg/mL oral solution or 100 mg capsule or tablets QD for 24 to 48 weeks in Stage 1. Subjects entering Stage 2 continued Stage 1 treatment but those aged 12 years or older or weighing at least 35 kg transitioned to atazanavir capsules. Treatment continued until the subject reached 18 years of age or pediatric indication is locally approved and subject meets requirements to receive appropriate formulation.

Serious adverse events	Atazanavir 150 mg (Baseline weight: 5 to < 10 kg)	Atazanavir 200 mg (Baseline weight: 5 to < 10 kg)	Atazanavir 200 mg (Baseline weight: 10 to < 15 kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 23 (26.09%)	3 / 12 (25.00%)	8 / 21 (38.10%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	0 / 21 (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
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental exposure to product			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	0 / 21 (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
Pneumonitis chemical			

subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	0 / 21 (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
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Immune reconstitution inflammatory syndrome			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Varicocele			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
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 / 23 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 23 (4.35%)	1 / 12 (8.33%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysentery			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	0 / 21 (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
Sinusitis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	0 / 21 (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
Infective corneal ulcer			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 23 (4.35%)	0 / 12 (0.00%)	0 / 21 (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
Otitis media			

subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	0 / 21 (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
Pulmonary tuberculosis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 12 (8.33%)	0 / 21 (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
Tonsillitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 23 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Atazanavir 250 mg (Baseline weight: 15 to < 25 kg)	Atazanavir 300 mg (Baseline weight: 25 to < 35 kg)	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 35 (22.86%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	2 / 35 (5.71%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental exposure to product			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis chemical			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Immune reconstitution inflammatory syndrome			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Varicocele			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysentery			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			

subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective corneal ulcer			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			

subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Atazanavir 150 mg (Baseline weight: 5 to < 10 kg)	Atazanavir 200 mg (Baseline weight: 5 to < 10 kg)	Atazanavir 200 mg (Baseline weight: 10 to < 15 kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 23 (95.65%)	10 / 12 (83.33%)	20 / 21 (95.24%)
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	4 / 23 (17.39%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 23 (34.78%)	2 / 12 (16.67%)	0 / 21 (0.00%)
occurrences (all)	10	2	0
Lymphadenopathy			
subjects affected / exposed	1 / 23 (4.35%)	1 / 12 (8.33%)	2 / 21 (9.52%)
occurrences (all)	1	1	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 23 (13.04%)	0 / 12 (0.00%)	7 / 21 (33.33%)
occurrences (all)	3	0	7
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	7 / 23 (30.43%)	1 / 12 (8.33%)	5 / 21 (23.81%)
occurrences (all)	10	9	6
Diarrhoea			

subjects affected / exposed occurrences (all)	6 / 23 (26.09%) 9	0 / 12 (0.00%) 0	3 / 21 (14.29%) 5
Dental caries subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 4	1 / 12 (8.33%) 1	3 / 21 (14.29%) 3
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	3 / 23 (13.04%) 3	2 / 12 (16.67%) 2	0 / 21 (0.00%) 0
Nasal congestion subjects affected / exposed occurrences (all)	5 / 23 (21.74%) 6	4 / 12 (33.33%) 4	0 / 21 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	5 / 23 (21.74%) 6	0 / 12 (0.00%) 0	2 / 21 (9.52%) 2
Asthma subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0	4 / 21 (19.05%) 4
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 12 (8.33%) 2	3 / 21 (14.29%) 7
Hepatobiliary disorders			
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 4	0 / 12 (0.00%) 0	5 / 21 (23.81%) 7
Jaundice subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0	3 / 21 (14.29%) 6
Skin and subcutaneous tissue disorders			
Eczema subjects affected / exposed occurrences (all)	5 / 23 (21.74%) 6	2 / 12 (16.67%) 3	2 / 21 (9.52%) 3
Dermatitis diaper subjects affected / exposed occurrences (all)	5 / 23 (21.74%) 6	3 / 12 (25.00%) 3	0 / 21 (0.00%) 0
Infections and infestations			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	16 / 23 (69.57%) 50	5 / 12 (41.67%) 7	5 / 21 (23.81%) 9
Gastroenteritis subjects affected / exposed occurrences (all)	14 / 23 (60.87%) 27	3 / 12 (25.00%) 6	10 / 21 (47.62%) 17
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 12	0 / 12 (0.00%) 0	8 / 21 (38.10%) 23
Tinea capitis subjects affected / exposed occurrences (all)	7 / 23 (30.43%) 14	1 / 12 (8.33%) 2	3 / 21 (14.29%) 4
Lower respiratory tract infection subjects affected / exposed occurrences (all)	7 / 23 (30.43%) 11	5 / 12 (41.67%) 13	1 / 21 (4.76%) 1
Oral candidiasis subjects affected / exposed occurrences (all)	9 / 23 (39.13%) 11	4 / 12 (33.33%) 7	1 / 21 (4.76%) 1
Otitis media subjects affected / exposed occurrences (all)	6 / 23 (26.09%) 10	3 / 12 (25.00%) 6	0 / 21 (0.00%) 1
Pharyngitis subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 4	0 / 12 (0.00%) 0	5 / 21 (23.81%) 11
Candida nappy rash subjects affected / exposed occurrences (all)	8 / 23 (34.78%) 12	2 / 12 (16.67%) 2	1 / 21 (4.76%) 1
Impetigo subjects affected / exposed occurrences (all)	7 / 23 (30.43%) 7	0 / 12 (0.00%) 0	2 / 21 (9.52%) 3
Acarodermatitis subjects affected / exposed occurrences (all)	6 / 23 (26.09%) 9	0 / 12 (0.00%) 0	1 / 21 (4.76%) 1
Helminthic infection subjects affected / exposed occurrences (all)	7 / 23 (30.43%) 15	2 / 12 (16.67%) 3	0 / 21 (0.00%) 0

Otitis media acute subjects affected / exposed occurrences (all)	7 / 23 (30.43%) 15	0 / 12 (0.00%) 0	0 / 21 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 4	1 / 12 (8.33%) 1	1 / 21 (4.76%) 1
Bronchitis subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	0 / 12 (0.00%) 0	2 / 21 (9.52%) 2
Conjunctivitis subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	0 / 12 (0.00%) 0	1 / 21 (4.76%) 1
Tonsillitis subjects affected / exposed occurrences (all)	3 / 23 (13.04%) 4	1 / 12 (8.33%) 1	1 / 21 (4.76%) 1
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 23 (13.04%) 8	1 / 12 (8.33%) 1	2 / 21 (9.52%) 7
Influenza subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0	2 / 21 (9.52%) 2
Body tinea subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	3 / 12 (25.00%) 3	0 / 21 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 12 (8.33%) 1	1 / 21 (4.76%) 2
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0	5 / 21 (23.81%) 7
Non-serious adverse events	Atazanavir 250 mg (Baseline weight: 15 to < 25 kg)	Atazanavir 300 mg (Baseline weight: 25 to < 35 kg)	
Total subjects affected by non-serious adverse events subjects affected / exposed	32 / 35 (91.43%)	6 / 8 (75.00%)	

Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	0 / 8 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenopathy subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2 4 / 35 (11.43%) 4	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	2 / 8 (25.00%) 2	
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dental caries subjects affected / exposed occurrences (all)	9 / 35 (25.71%) 15 3 / 35 (8.57%) 3 1 / 35 (2.86%) 1	2 / 8 (25.00%) 2 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Asthma	9 / 35 (25.71%) 14 3 / 35 (8.57%) 3 3 / 35 (8.57%) 3	1 / 8 (12.50%) 1 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0	

subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Jaundice			
subjects affected / exposed	3 / 35 (8.57%)	0 / 8 (0.00%)	
occurrences (all)	6	0	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 35 (5.71%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Dermatitis diaper			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	10 / 35 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	16	1	
Gastroenteritis			
subjects affected / exposed	7 / 35 (20.00%)	1 / 8 (12.50%)	
occurrences (all)	8	1	
Nasopharyngitis			
subjects affected / exposed	5 / 35 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	10	0	
Tinea capitis			
subjects affected / exposed	4 / 35 (11.43%)	0 / 8 (0.00%)	
occurrences (all)	5	0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			

subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Otitis media			
subjects affected / exposed	2 / 35 (5.71%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Pharyngitis			
subjects affected / exposed	5 / 35 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	6	0	
Candida nappy rash			
subjects affected / exposed	0 / 35 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Impetigo			
subjects affected / exposed	2 / 35 (5.71%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Acarodermatitis			
subjects affected / exposed	3 / 35 (8.57%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Helminthic infection			
subjects affected / exposed	1 / 35 (2.86%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Otitis media acute			
subjects affected / exposed	3 / 35 (8.57%)	0 / 8 (0.00%)	
occurrences (all)	5	0	
Pneumonia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Bronchitis			
subjects affected / exposed	3 / 35 (8.57%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Conjunctivitis			
subjects affected / exposed	4 / 35 (11.43%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Tonsillitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 7	0 / 8 (0.00%) 0	
Influenza subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 5	1 / 8 (12.50%) 1	
Body tinea subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	0 / 8 (0.00%) 0	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 3	0 / 8 (0.00%) 0	
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	0 / 8 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 April 2011	To allow use of both brand and generic locally approved and available NRTIs by removing statements not intended to have been in protocol section 6.7.1
20 January 2012	1) To allow that also the Ritonavir Trough plasma concentration at each scheduled visit from week 4 through week 48 will be evaluated from the sample tube collected for the ATV trough plasma concentration assessment as ATV/RTV can be assessed simultaneously. 2) Primary Objective: Clarified objective and aligned with the primary objective measurement used in the AI424-397 study. The frequency of AEs and lab abnormalities will be summarized but is not part of the primary objective analysis. 3) Removed an exploratory objective because the subjects duration of study participation in stage 2 is dependent on age (i.e. 18 years old) or by the timing of local pediatric indication. It's expected that a significant proportion of subjects will discontinue from the study before reaching age 18. 4) Added a dosage of reyataz capsules with ritonovir capsules in case the body weight is between 15 and 20 kg. 5) Removed exclusion criterion "children of mothers with known maternal history of HB or HCV infection" has been removed as the HBV and HCV testing will be performed for all subjects regardless of the mother infection status and clarified in exclusion criterion 3c that the HCV and/or HBV testing are to be performed locally. 6) Exclusion criterion: Removed "as defined per protocol" as a 1st degree AV block is exclusionary. 7) Updated the RTV oral solution and RTV tablets storage conditions to be consistent with package insert. 8) Clarified that in the event that the min number of subjects per weight band with required follow up is projected not to be met due to discontinuation, then enrollment will be re-opened. 9) To allow that the timeline to the baseline visit may be extended to 50 days in cases where the test or re-test results are not available after 30 days. 10) Updated Time and Event Schedules to be consistent with the protocol and clarified notes. 11) Updated to be aligned with the Statistical Analysis Plan 12) To address inconsistencies/admin changes in the protocol
03 May 2012	1) To change the whole 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 sister study AI424-397 amendment 05. 2) 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. 3) Table 4.1. Product description: Updated the ATV capsules storage conditions (excursions permitted 15-30°C) to be aligned with the SPC.

16 January 2013	<p>To increase the inclusion upper age limit to < 11 years of age and updated title, research hypothesis and objectives accordingly. Following the AI424-397 intensive PK analysis, add new 5 - < 10kg cohort with higher ATV dose (200 mg ATV and 80 mg RTV).</p> <p>To increase the sample size from 75 to 95 subjects in order to treat approximately 10-15 subjects in the new cohort and have a minimum of 56 subjects with 48 weeks of follow-up on ATV powder overall and minimum number of subjects required per weight band.</p> <p>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.</p> <p>To allow use of RTV capsules or Tablets for subjects enrolled in the 25 - < 35kg weight band or moving into this weight band.</p> <p>Added new assay (Abbott RealTime HIV-1 RNA) to be used when Roche Amplicor HIV RNA is discontinued.</p>
15 April 2014	<p>1) Changes to the protocol were triggered by the outcome of a second Pediatric Investigational Plan request for modification procedure during which the Pediatric Committee (PDCO) in Europe determined that almost all the information needed to adequately assess safety, PK and efficacy data is available. The corresponding changes to the protocol are:</p> <p>To remove the minimum number of 6 subjects required for the 25-<35kg weight band with 48 weeks of ATV powder.</p> <p>To modify primary endpoint study duration from 48 Weeks to a minimum of 24 weeks and key secondary objectives.</p> <p>2) To increase the blood volume collection from 1 up to 2 mL for HIV RNA testing when switching to the new Abbott RealTime HIV-1 assay after the Roche Amplicor assay is discontinued.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported