Clinical trial results:
An Open-Label, Randomized Study Evaluating a Switch from a Regimen of Two Nucleoside Reverse Transcriptase Inhibitors Regimen plus any Third Agent to either a Regimen of Atazanavir/Ritonavir Once Daily and Raltegravir Twice Daily or to a Regimen of Atazanavir/Ritonavir Once Daily and Tenofovir/Emtricitabine Once Daily in Virologically Suppressed HIV-1 Infected subjects With Safety and/or Tolerability Issues on their Present Treatment Regimen.

Summary

EudraCT number	2009-017032-41
Trial protocol	GB DE ES PL IT
Global end of trial date	18 February 2014

Results information

Result version number	v1 (current)
This version publication date	01 April 2016
First version publication date	01 April 2016

Trial information

Trial identification

Sponsor protocol code	AI424-402

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01332227
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to estimate the proportion of subjects with HIV 1 RNA <40 copies/millilitre (c/mL) through 24 weeks, following a switch due to treatment related safety and/or tolerability issues, from a regimen consisting of 2 Nucleoside Reverse Transcriptase Inhibitor + any third agent, to a regimen consisting of Atazanavir/ Heat-Stable Ritonavir 300/100 mg once daily (QD) + Raltegravir 400 mg twice daily or a regimen of Atazanavir/Heat-Stable Ritonavir QD and Tenofovir/Emtricitabine QD.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and incompliance 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 October 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	Poland: 22
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	132
EEA total number of subjects	94

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	127
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 132 subjects were recruited at 29 sites in 7 countries.

Pre-assignment

Screening details:

Of 132 subjects enrolled, 109 were randomized to receive treatment, and 23 subjects were not randomized for the following reasons: 10 did not meet study criteria; 5 withdrew consent; 3 were lost to follow-up, and 5 withdrew for other reasons.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Atazanavir/Ritonavir + Raltegravir

Arm description:

Subjects received atazanavir, 300-mg capsules, and ritonavir, 100-mg tablets, orally once daily and raltegravir, 400-mg tablets, twice daily for 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Atazanavir 300-mg capsule was administered with food once per day in the morning.

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Heat-Stable ritonavir 100-mg tablet was administered with food once per day in the morning.

Investigational medicinal product name	Raltegravir
Investigational medicinal product code	
Other name	Isentress
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Raltegravir 400-mg tablet was administered with or without food twice per day.

Arm title	Atazanavir/Ritonavir + Tenofovir/Emtricitabine

Arm description:

Subjects received atazanavir, 300-mg capsules, plus ritonavir, 100-mg tablets, and tenofovir/emtricitabine, 300/200-mg tablets, orally once daily for 48 weeks.

Arm type	Active comparator

Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	Reyataz
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Atazanavir 300-mg capsule was administered with food once per day in the morning.

Investigational medicinal product name	Tenofovir/Emtricitabine
Investigational medicinal product code	
Other name	Truvada
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tenofovir 300-mg and emtricitabine 200-mg tablets were administered with food once per day in the morning

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	Norvir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Heat-Stable ritonavir 100-mg tablet was administered with food once per day in the morning.

Number of subjects in period 1[1]	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine
Started	72	37
Completed	56	32
Not completed	16	5
Consent withdrawn by subject	4	1
Poor compliance/noncompliance	1	1
Subjects request to discontinue	1	-
Adverse event	4	1
Subjects moved from area	1	-
Lost to follow-up	2	-
Subjects began prohibited medication	-	1
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 in the baseline period are different from the worldwide number enrolled in the trial, as out of 132 subjects only 109 subjects were randomised and treated. 23 subjects discontinued from the study due to various reasons: 10 did not meet study criteria; 5 withdrew consent; 3 were lost to follow-up, and 5 withdrew for other reasons .

Baseline characteristics

Reporting groups	
Reporting group title	Atazanavir/Ritonavir + Raltegravir
Reporting group description:	
Subjects received atazanavir, 300-mg capsules, and ritonavir, 100-mg tablets, orally once daily and raltegravir, 400-mg tablets, twice daily for 48 weeks.	
Reporting group title	Atazanavir/Ritonavir + Tenofovir/Emtricitabine
Reporting group description:	
Subjects received atazanavir, 300-mg capsules, plus ritonavir, 100-mg tablets, and tenofovir/emtricitabine, 300/200-mg tablets, orally once daily for 48 weeks.	

Reporting group values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine	Total
Number of subjects	72	37	109
Age categorical Units: Subjects			
< 65 years	69	36	105
65-85 years	3	1	4
Age continuous			
Mean age			
Units: years			
arithmetic mean	43.1	44	
standard deviation	± 9.26	± 10.38	-
Gender categorical Units: Subjects			
Female	14	6	20
Male	58	31	89
Ethinicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5	1	6
Not Hispanic or Latino	29	13	42
Unknown or Not Reported	38	23	61
Race/Ethnicity, Customized Units: Subjects			
White	54	24	78
Black or African American	8	6	14
Hispanic	2	0	2
Unknown	8	7	15
Age			
Median age			
Units: Years			
median	44	44	
full range (min-max)	25 to 67	25 to 69	-
Mean CD4 count Units: Cells/millimeter^3			
arithmetic mean	587.7	630.9	
standard deviation	± 252.09	± 270.02	-
Median CD4 count			

Units: Cells/millimeter^3			
median	588.5	639.5	
full range (min-max)	10 to 1511	159 to 1359	-

End points

End points reporting groups

Reporting group title	Atazanavir/Ritonavir + Raltegravir
Reporting group description:	
Subjects received atazanavir, 300-mg capsules, and ritonavir, 100-mg tablets, orally once daily and raltegravir, 400-mg tablets, twice daily for 48 weeks.	
Reporting group title	Atazanavir/Ritonavir + Tenofovir/Emtricitabine
Reporting group description:	
Subjects received atazanavir, 300-mg capsules, plus ritonavir, 100-mg tablets, and tenofovir/emtricitabine, 300/200-mg tablets, orally once daily for 48 weeks.	

Primary: Percentage of Subjects with HIV-1 RNA Level <40 c/mL at Week 24

End point title	Percentage of Subjects with HIV-1 RNA Level <40 c/mL at Week 24[1]
End point description:	
HIV-1 RNA level was measured with the Abbott m2000rt® polymerase chain reaction assay. Randomized subjects not meeting the criteria for treatment failure (eg, discontinuation of study therapy or virologic rebound at or before Week 24) were considered responders. Virologic rebound was defined as 2 consecutive on-treatment HIV-1 RNA levels >=40 c/mL or the last on-treatment HIV-1 RNA level >=40 c/mL followed by discontinuation. Subjects who experienced treatment failure or had missing Week 24 HIV-1 RNA levels were considered failures. Analysis was performed in 'Intent-To-Treat'' population: numerator based on subjects meeting the response criteria, and the denominator based on all randomized subjects and Observed population: numerator based on subjects meeting the response criteria at Week 24 and denominator based on treated subjects with on-treatment HIV-1 RNA measurements at or after Week 24.	
End point type	Primary
End point timeframe:	
Day 1 up to Week 24	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: As the outcome was descriptive, no statistical testing or treatment comparison was done.	

End point values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	37		
Units: Percentage of subjects				
number (confidence interval 95%)	80.6 (69.5 to 88.9)	94.6 (81.8 to 99.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HIV-1 RNA Level <40 c/mL at Week 48

End point title	Percentage of Subjects With HIV-1 RNA Level <40 c/mL at

	Week 48

End point description:

Percentages of subjects with HIV-1 RNA levels <40 c/mL were summarized at each scheduled visit. Longitudinal plots were created to display proportion versus visit week through Weeks 24 and 48 with error bars representing 95% confidence intervals. Analysis was performed in ''Intent to treat'' population: numerator based on subjects meeting the response criteria, and the denominator based on all randomized subjects and ''Observed population'': numerator based on subjects meeting the response criteria at Weeks 24 and 48, and denominator based on treated subjects with on-treatment HIV-1 RNA measurements at or after Weeks 24 and 48. Here 'n' signifies number of evaluable subjects in the respective treatment arms.

End point type	Secondary

End point timeframe:

From Day 1 to Week 48

End point values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	37		
Units: Percentage of subjects				
number (confidence interval 95%)				
ITT population (n= 72, 37)	69.4 (57.5 to 79.8)	86.5 (71.2 to 92.5)		
Observed population (n= 56, 32)	89.3 (78.1 to 96)	100 (89.1 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Virologic Rebound at Weeks 24 and 48

End point title	Number of Subjects With Virologic Rebound at Weeks 24 and 48

End point description:

Viral genotypic and phenotypic resistance profiles were assessed for virologic rebound (HIV-1 RNA level >=40 c/mL). Only subjects with HIV-1 RNA levels >=500 c/mL met criteria for resistance testing. Genotypic resistance profile presented subjects with genotypable isolates, those with protease inhibitor substitutions from genotypable isolates, those with integrase substitutions from genotypable isolates, and those with selected reverse transcriptase substitutions from genotypable isolates using International AIDS Society-USA list and Stanford HIV Drug Resistance Database. Analysis was performed in Intent-to-treat population: numerator based on subjects meeting the response criteria, and the denominator based on all randomized subjects and Observed population: numerator based on subjects meeting the response criteria at Weeks 24 and 48, and denominator based on treated subjects with on-treatment measurements at or after Weeks 24 and 48.

End point type	Secondary

End point timeframe:

Day 1 to Weeks 28 and 48

End point values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	37		
Units: subjects				
Week 24:Virologic Rebound	7	1		
Week 48:Virologic Rebound	9	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Genotypable/Phenotypable Isolates, Emergent Genotypic Substitutions in Subjects With Genotypable Isolates, and Phenotypic Resistance in Subjects With Phenotypable Isolates at Week 24

End point title	Number of Subjects with Genotypable/Phenotypable Isolates, Emergent Genotypic Substitutions in Subjects With Genotypable Isolates, and Phenotypic Resistance in Subjects With Phenotypable Isolates at Week 24

End point description:

Viral genotypic and phenotypic resistance profiles were assessed for virologic rebound (HIV-1 RNA level >=40 c/mL). Only subjects with HIV-1 RNA levels >=500 c/mL met criteria for resistance testing. Genotypic resistance profile presented subjects with genotypable isolates, those with protease inhibitor substitutions from genotypable isolates, those with integrase substitutions from genotypable isolates, and those with selected reverse transcriptase substitutions from genotypable isolates using International AIDS Society-USA list and Stanford HIV Drug Resistance Database. Integrase Strand Transfer Inhibitors (INSTI) resistance testing was done for subjects experiencing virologic failure while taking raltegravir. . Analysis was performed in "Intent-to-treat" population: numerator based on subjects meeting the response criteria, and the denominator based on all randomized subjects. Here 'n' signifies number of evaluable subjects in the respective treatment arms.

End point type	Secondary

End point timeframe:

Day 1 to Week 24

End point values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: subjects				
Genotypable(GI)/Phenotypable Isolates (PI) (n=7,1)	4	0		
PI Genotypic resistance (n= 4, 0)	1	0		
INSTI Genotypic resistance(n= 4, 0)	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Genotypable/Phenotypable Isolates, Emergent Genotypic Substitutions in Subjects With Genotypable Isolates, and Phenotypic Resistance in Subjects With Phenotypable Isolates at Week 48

End point title	Number of Subjects with Genotypable/Phenotypable Isolates, Emergent Genotypic Substitutions in Subjects With Genotypable Isolates, and Phenotypic Resistance in Subjects With Phenotypable Isolates at Week 48

End point description:

Viral genotypic and phenotypic resistance profiles were assessed for virologic rebound (HIV-1 RNA level >=40 c/mL). Only subjects with HIV-1 RNA levels >=500 c/mL met the criteria for resistance testing. The genotypic resistance profile presented subjects with genotypable isolates, those with protease inhibitor substitutions from genotypable isolates, those with integrase substitutions from genotypable isolates, and those with selected reverse transcriptase substitutions from genotypable isolates using International AIDS Society-USA list and Stanford HIV Drug Resistance Database. Integrase Strand Transfer Inhibitors (INSTI) resistance testing was done for subjects experiencing virologic failure while taking raltegravir. Analysis was performed in ''Intent-To-Treat'' population: numerator based on subjects meeting the response criteria, and the denominator based on all randomized subjects. Here 'n' signifies number of evaluable subjects in the respective treatment arms.

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: subjects				
Genotypable (GI)/phenotypable isolates (PI)	5	0		
PI Genotypic resistance (n= 5, 0)	1	0		
INSTI Genotypic resistance(n=5, 0)	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Death as Outcome, Serious Adverse Events (SAEs), Treatment-related SAEs, Treatment-emergent Adverse Events (AEs) Leading to Discontinuation, and Treatment-emergent AEs

End point title	Number of Subjects With Death as Outcome, Serious Adverse Events (SAEs), Treatment-related SAEs, Treatment-emergent Adverse Events (AEs) Leading to Discontinuation, and Treatment-emergent AEs

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Related=having certain, probable, possible, or unknown relationship to study drug. Analysis was

performed in all the subjects who were randomized and received at least 1 dose of the study drug.

End point type	Secondary

End point timeframe:

Day 1 to Week 48

End point values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	37		
Units: subjects				
Deaths	0	0		
SAEs	4	1		
Treatment-related SAEs	1	0		
Treatment-emergent AEs leading to discontinuation	4	1		
Treatment-emergent AEs	51	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Lipid Levels at Week 48

End point title	Change From Baseline in Fasting Lipid Levels at Week 48

End point description:

Changes from baseline in fasting lipids parameters (total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol and triglycerides) were summarized at each scheduled visit through Weeks 24 and 48. Safety analysis was performed on ''Intent-To-Treat'' population defined as subjects who were randomized and received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

From Baseline to Week 48

End point values	Atazanavir/Ritonavir + Raltegravir	Atazanavir/Ritonavir + Tenofovir/Emtricitabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	37		
Units: mg/dL				
arithmetic mean (standard error)				
Fasting total cholesterol	11.7 (± 5.239)	-10.2 (± 4.769)		
Fasting LDL cholesterol	7.7 (± 3.986)	-5.4 (± 4.691)		
Fasting HDL cholesterol	2.7 (± 2.055)	-0.3 (± 1.915)		

Fasting non-HDL cholesterol	9 (± 4.983)	-9.8 (± 4.43)		
Fasting triglycerides	14.7 (± 16.667)	-17.6 (± 16.994)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the signature of informed consent form up to 30 days after last administration of study drug (Week 48).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Atazanavir/Ritonavir + Tenofovir/Emtricitabine

Reporting group description:

subjects received atazanavir, 300-mg capsules, plus ritonavir, 100-mg tablets, and tenofovir 300-mg/emtricitabine 200-mg tablets, orally once daily for 48 weeks.

Reporting group title	Atazanavir/Ritonavir + Raltegravir

Reporting group description:

subjects received atazanavir, 300-mg capsules, and ritonavir, 100-mg tablets, orally once daily and raltegravir, 400-mg tablets, twice daily for 48 weeks.

Serious adverse events	Atazanavir/Ritonavir + Tenofovir/Emtricitabine	Atazanavir/Ritonavir + Raltegravir	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 37 (2.70%)	4 / 72 (5.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Atazanavir/Ritonavir + Tenofovir/Emtricitabine	Atazanavir/Ritonavir + Raltegravir	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 37 (62.16%)	27 / 72 (37.50%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	2 / 37 (5.41%)	0 / 72 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 37 (5.41%)	4 / 72 (5.56%)	
occurrences (all)	2	4	
Eye disorders			
Ocular icterus			
subjects affected / exposed	3 / 37 (8.11%)	6 / 72 (8.33%)	
occurrences (all)	3	6	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 37 (5.41%)	1 / 72 (1.39%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	4 / 37 (10.81%)	3 / 72 (4.17%)	
occurrences (all)	4	3	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	4 / 37 (10.81%)	4 / 72 (5.56%)	
occurrences (all)	4	4	
Hyperbilirubinaemia			
subjects affected / exposed	4 / 37 (10.81%)	6 / 72 (8.33%)	
occurrences (all)	4	6	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 37 (5.41%)	1 / 72 (1.39%)	
occurrences (all)	2	1	
Rash			
subjects affected / exposed	2 / 37 (5.41%)	0 / 72 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 37 (0.00%)	4 / 72 (5.56%)	
occurrences (all)	0	4	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	3 / 37 (8.11%)	1 / 72 (1.39%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			

Musculoskeletal pain			
subjects affected / exposed	2 / 37 (5.41%)	0 / 72 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Gonorrhoea			
subjects affected / exposed	2 / 37 (5.41%)	1 / 72 (1.39%)	
occurrences (all)	2	1	
Nasopharyngitis			
subjects affected / exposed	2 / 37 (5.41%)	4 / 72 (5.56%)	
occurrences (all)	3	4	
Bronchitis			
subjects affected / exposed	1 / 37 (2.70%)	4 / 72 (5.56%)	
occurrences (all)	2	4	
Metabolism and nutrition disorders			
Hyperlactacidaemia			
subjects affected / exposed	2 / 37 (5.41%)	0 / 72 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2012	1) Changed exclusion criterion to require a history of 2 or more Highly Active Antiretroviral Therapy (HAART) regimens. 2) Deleted exclusion criteria: Subjects with no genotypic resistance test prior to starting HAART for the first time and Lactate >=5 mmol/L. 3) Modified exclusion criterion to read as "Positive Hepatitis C Virus (HCV) RNA test for HCV or subjects who are currently receiving treatment for HCV or are planning to receive treatment for HCV in the next 6 months. 4) Modified exclusion criterion to read as "Platelets <50*10^9/L". 5) Updated the description of the use of oral contraceptives. 6) To add information about EU and US approvals of the BMS study NCT00326716 (ClinicalTrials.gov Identifier number) pregnancy study data.
09 July 2012	1) Reduced the sample size of the protocol considering the current enrollment and the screening failure rate. In order to recruit the original sample size of 120 treated subjects, the enrollment period would have to be extended by 1 additional year. Therefore, the sample size was reduced to a minimum of 90 and maximum of 120 treated subjects. This planned reduction in sample size was thought to be enough to provide sufficient robust descriptive data in this population. With the reduction of the total sample size, the sample size for the first interim analysis was also reduced from 60 randomized subjects to 45 randomized subjects who were treated for 12 weeks. 2) Removed exclusion criterion: 2 or more HAART regimens prior to current treatment regimen. Subjects with a history of previous HAART switch due to virological failure were still to be excluded from the trial. 3) Modified exclusion criterion 2g to allow the inclusion of subjects with positive HCV RNA test for HCV, provided it was not an acute HCV infection and the subject was currently not receiving or not planning to receive treatment for HCV. Efficacy and safety profiles of both atazanavir/ritonavir and raltegravir-based regimens in subjects with chronic HCV and HIV co-infection are well characterized. 4) Changed the schedule of lactate measurements to be consistent with current standards of care of lactate assessment in subjects taking antiretroviral agents. Serum lactate was not to be measured in a routine basis at each study visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported