



## Clinical trial results:

### A Phase IIb Randomized, Controlled, Partially-Blinded Trial to Investigate Safety, Efficacy and Dose-response of BMS-663068/GSK3684934 in Treatment-experienced HIV-1 Subjects, Followed by an Open-label Period on the Recommended Dose

#### Summary

EudraCT number	2011-000437-36
Trial protocol	DE ES
Global end of trial date	12 May 2017

#### Results information

Result version number	v2 (current)
This version publication date	01 November 2018
First version publication date	02 September 2018
Version creation reason	

#### Trial information

##### Trial identification

Sponsor protocol code	205889
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Other Identifier: Bristol-Myers Squibb: AI438-011

Notes:

#### Sponsors

Sponsor organisation name	ViiV Healthcare
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	17 April 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 May 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To assess the efficacy of four doses of fostemsavir by determining the proportion of participants with plasma Human Immunodeficiency Virus (HIV-1) Ribonucleic acid (RNA) < 50 copies per milliliter (c/mL) at Week 24.

To assess the safety of four doses of fostemsavir in treatment-experienced HIV-1-infected participants through Week 24 by measuring frequency of Serious Adverse events (SAEs), and AEs leading to discontinuations.

Protection of trial subjects:

Not Applicable

Background therapy:

Participants in the fostemsavir groups and the ritonavir boosted atazanavir reference group received open-label background therapy of 400 mg RAL BID and 300 mg TDF QD

Evidence for comparator: -

Actual start date of recruitment	26 July 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: 18
Country: Number of subjects enrolled	Colombia: 12
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Mexico: 26
Country: Number of subjects enrolled	Peru: 51
Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	South Africa: 66
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 45
Worldwide total number of subjects	254
EEA total number of subjects	18

Notes:

<b>Subjects enrolled per age group</b>	
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)	250
From 65 to 84 years	4
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants with Human Immunodeficiency Virus (HIV-1) were randomized in ratio of 1:1:1:1:1 to 5 treatment arms of the study. Four groups with distinct dose of Fostemsavir (FTR, also referred BMS-663068) with Raltegravir (RAL) Tenofovir Disoproxil Fumarate (TDF). There was a reference group with ritonavir (r) boosted atazanavir (ATV), RAL and TDF.

### Pre-assignment

Screening details:

A total of 581 participants were screened, 254 were enrolled of which 2 participants withdrew consent and 1 was randomized in error. A total 251 participants were randomized and treated of which 32 were in Monotherapy sub-study (only FTR) and continued to Primary study.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Assessor, Subject

Blinding implementation details:

This was a partially-blinded study. All subjects and investigators were partially blinded to the dose of FTR until the last subject completed the Week 48 study visit procedures and an analysis of the Week 24 efficacy and safety data was conducted in order to determine the continuation dose, thereafter all subjects were switched to a continuation dose of FTR (1200 mg once daily), marking the end of the blinded phase of the study.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	FTR 400 mg BID/RAL/TDF

Arm description:

Participants were randomized and administered 400 milligrams (mg) of FTR twice daily (BID) (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF once daily (QD) (open label).

Arm type	Experimental
Investigational medicinal product name	Fostemsavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive oral tablets of 400 and 800 twice daily and 600 and 1200 mg fostemsavir once daily for at least 96 weeks

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

Dosage and administration details:

Participants administered 400 mg raltegravir twice daily for at least 96 weeks

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

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**Dosage and administration details:**

Participants administered 300 mg tenofovir once daily for at least 96 weeks

<b>Arm title</b>	FTR 800 mg BID/RAL/TDF
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**Arm description:**

Participants were randomized and administered 800 mg of FTR BID (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).

Arm type	Experimental
Investigational medicinal product name	Fostemsavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

**Dosage and administration details:**

Participants were randomized to receive oral tablets of 400 and 800 twice daily and 600 and 1200 mg fostemsavir once daily for at least 96 weeks

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

**Dosage and administration details:**

Participants administered 300 mg tenofovir once daily for at least 96 weeks

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

**Dosage and administration details:**

Participants administered 400 mg raltegravir twice daily for at least 96 weeks

<b>Arm title</b>	FTR 600 mg QD/RAL/TDF
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**Arm description:**

Participants were randomized and administered 600 mg of FTR QD (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).

Arm type	Experimental
Investigational medicinal product name	Fostemsavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

**Dosage and administration details:**

Participants were randomized to receive oral tablets of 400 and 800 twice daily and 600 and 1200 mg fostemsavir once daily for at least 96 weeks

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

**Dosage and administration details:**

Participants administered 400 mg raltegravir twice daily for at least 96 weeks

Investigational medicinal product name	Tenofovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Participants administered 300 mg tenofovir once daily for at least 96 weeks	
<b>Arm title</b>	FTR 1200 mg QD/RAL/TDF
Arm description:	
Participants were randomized and administered 1200 mg of FTR QD along (double-blind) with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).	
Arm type	Experimental
Investigational medicinal product name	Fostemsavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Participants were randomized to receive oral tablets of 400 and 800 twice daily and 600 and 1200 mg fostemsavir once daily for at least 96 weeks	
Investigational medicinal product name	Raltegravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Participants administered 400 mg raltegravir twice daily for at least 96 weeks	
Investigational medicinal product name	Tenofovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
Participants administered 300 mg tenofovir once daily for at least 96 weeks	
<b>Arm title</b>	ATV/r/RAL/TDF
Arm description:	
Participants were randomized to Reference group (open label) and administered ATV/r 300/100 mg once daily along with 400 mg RAL BID and 300 mg TDF QD.	
Arm type	Active comparator
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Participants randomized to reference group administered 300 mg atazanavir once daily for at least 96 weeks	
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered 100 mg ritonavir once daily for at least 96 weeks

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

Dosage and administration details:

Participants administered 400 mg raltegravir twice daily for at least 96 weeks

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

Dosage and administration details:

Participants administered 300 mg tenofovir once daily for at least 96 weeks

<b>Number of subjects in period 1<sup>[1]</sup></b>	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF
Started	50	49	51
Completed	33	25	28
Not completed	17	24	23
Physician decision	1	-	-
Prison	-	-	1
Continuation criteria not met	-	-	1
Sponsor terminated	-	-	-
As per Exclusion criteria	-	1	-
Consent withdrawn by subject	5	5	6
Unable to come back for visit	1	-	1
Adverse event, non-fatal	-	3	-
Death	1	-	1
Pregnancy	-	1	-
Non-compliance with study drug	1	2	6
Missed End of treatment visit	-	-	-
Adhesion problem	-	-	-
Lost to follow-up	5	3	3
Investigator relocating	-	2	-
Early termination	-	-	-
Lack of efficacy	3	7	4

<b>Number of subjects in period 1<sup>[1]</sup></b>	FTR 1200 mg QD/RAL/TDF	ATV/r/RAL/TDF
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Started	50	51
Completed	22	22
Not completed	28	29
Physician decision	-	-
Prison	-	-
Continuation criteria not met	1	-
Sponsor terminated	-	1
As per Exclusion criteria	-	-
Consent withdrawn by subject	7	9
Unable to come back for visit	1	-
Adverse event, non-fatal	2	7
Death	-	-
Pregnancy	-	1
Non-compliance with study drug	-	2
Missed End of treatment visit	1	-
Adhesion problem	1	-
Lost to follow-up	8	5
Investigator relocating	3	1
Early termination	-	1
Lack of efficacy	4	2

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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: Total 254 were randomized of which 251 participants were treated in Stage 1 Primary study, 2 participants withdrew consent and 1 was randomized in error.



## Baseline characteristics

### Reporting groups

Reporting group title	FTR 400 mg BID/RAL/TDF
Reporting group description:	
Participants were randomized and administered 400 milligrams (mg) of FTR twice daily (BID) (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF once daily (QD) (open label).	
Reporting group title	FTR 800 mg BID/RAL/TDF
Reporting group description:	
Participants were randomized and administered 800 mg of FTR BID (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).	
Reporting group title	FTR 600 mg QD/RAL/TDF
Reporting group description:	
Participants were randomized and administered 600 mg of FTR QD (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).	
Reporting group title	FTR 1200 mg QD/RAL/TDF
Reporting group description:	
Participants were randomized and administered 1200 mg of FTR QD along (double-blind) with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).	
Reporting group title	ATV/r/RAL/TDF
Reporting group description:	
Participants were randomized to Reference group (open label) and administered ATV/r 300/100 mg once daily along with 400 mg RAL BID and 300 mg TDF QD.	

Reporting group values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF
Number of subjects	50	49	51
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	38.1	38.4	40.1
standard deviation	± 8.17	± 9.49	± 9.45
Gender categorical			
Units: Subjects			
Female	19	21	22
Male	31	28	29
Race/Ethnicity, Customized			
Units: Subjects			
African American/African Heritage	14	15	16
American Indian Or Alaska Native	0	0	1
Asian	0	2	0
White	20	19	17
Other/Mixed	16	13	17

Reporting group values	FTR 1200 mg QD/RAL/TDF	ATV/r/RAL/TDF	Total
Number of subjects	50	51	251

Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	39.2 ± 11.41	39.7 ± 10.63	-
Gender categorical Units: Subjects			
Female	16	22	100
Male	34	29	151
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	18	13	76
American Indian Or Alaska Native	1	1	3
Asian	0	0	2
White	16	23	95
Other/Mixed	15	14	75

## End points

### End points reporting groups

Reporting group title	FTR 400 mg BID/RAL/TDF
Reporting group description: Participants were randomized and administered 400 milligrams (mg) of FTR twice daily (BID) (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF once daily (QD) (open label).	
Reporting group title	FTR 800 mg BID/RAL/TDF
Reporting group description: Participants were randomized and administered 800 mg of FTR BID (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).	
Reporting group title	FTR 600 mg QD/RAL/TDF
Reporting group description: Participants were randomized and administered 600 mg of FTR QD (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).	
Reporting group title	FTR 1200 mg QD/RAL/TDF
Reporting group description: Participants were randomized and administered 1200 mg of FTR QD along (double-blind) with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).	
Reporting group title	ATV/r/RAL/TDF
Reporting group description: Participants were randomized to Reference group (open label) and administered ATV/r 300/100 mg once daily along with 400 mg RAL BID and 300 mg TDF QD.	

### Primary: Percentage of participants with plasma HIV-1 Ribonucleic acid (RNA) < 50 Copies per milliliter (c/mL) at Week 24

End point title	Percentage of participants with plasma HIV-1 Ribonucleic acid (RNA) < 50 Copies per milliliter (c/mL) at Week 24 <sup>[1]</sup>
End point description: Percentage of participants with plasma HIV 1 RNA < 50 c/mL at Week 24 using the Food and Drug Administration (FDA) snapshot algorithm was assessed to evaluate the antiviral activity. Treatment comparisons were not performed as this was an estimation study. Response rates were tabulated by treatment arm with exact Clopper-Pearson binomial 95 percentage confidence intervals (CI). Virologic success or failure was determined by the last available HIV-1 RNA assessment while the participant was on-treatment within the snapshot window of the visit of interest. Intent-To-Treat-Exposed (ITT-E) Population includes all randomized participants who received at least one dose of study treatment.	
End point type	Primary
End point timeframe: 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: There are no statistical data to report.

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50 <sup>[2]</sup>	49 <sup>[3]</sup>	51 <sup>[4]</sup>	50 <sup>[5]</sup>
Units: Percentage of Participants				
number (confidence interval 95%)				
Percentage of Participants	80 (66.3 to 90.0)	69 (54.6 to 81.7)	76 (62.5 to 87.2)	72 (57.5 to 83.8)

Notes:

- [2] - ITT-E Population
- [3] - ITT-E Population
- [4] - ITT-E Population
- [5] - ITT-E Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	51 <sup>[6]</sup>			
Units: Percentage of Participants				
number (confidence interval 95%)				
Percentage of Participants	75 (60.4 to 85.7)			

Notes:

- [6] - ITT-E Population

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with serious adverse events (SAE) and discontinuation due to AEs up to Week 24

End point title	Number of participants with serious adverse events (SAE) and discontinuation due to AEs up to Week 24 <sup>[7]</sup>
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End point description:

Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or suspected transmission of an infectious agent via the study drug were categorized as SAE. AEs leading to discontinuation of study therapy were also reported as safety assessment. Safety population included all participants who received at least one dose of study treatment. Summaries of SAEs and AEs leading to discontinuation or withdrawal through Week 24 included AEs with onset on or after the start of study treatment (i.e. study date of first study treatment intake) up to and including the end of the Week 24 visit snapshot window.

End point type	Primary
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End point timeframe:

Up to Week 24

Notes:

- [7] - 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: There are no statistical data to report.

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50 <sup>[8]</sup>	49 <sup>[9]</sup>	51 <sup>[10]</sup>	50 <sup>[11]</sup>
Units: Participants				
SAE	3	4	4	2
AEs leading to discontinuation	1	2	0	1

Notes:

- [8] - Safety Population
- [9] - Safety Population
- [10] - Safety Population
- [11] - Safety Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	51 <sup>[12]</sup>			
Units: Participants				
SAE	5			
AEs leading to discontinuation	2			

Notes:

[12] - Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from monotherapy Baseline in log10 HIV RNA

End point title	Change from monotherapy Baseline in log10 HIV RNA <sup>[13]</sup>
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End point description:

Change from monotherapy Baseline in log10 HIV RNA to assess the antiviral activity of temsavir following administration of selected doses of FTR administered orally to HIV-1-infected participants for 7 days. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment. Change from Baseline was calculated as value at indicated time point minus Baseline value. ITT-E Monotherapy Population comprised of participants that were randomized and participated in the monotherapy sub-study and received at least one dose of FTR Monotherapy. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline and up to Day 8 of the monotherapy period

Notes:

[13] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7 <sup>[14]</sup>	5 <sup>[15]</sup>	10 <sup>[16]</sup>	10 <sup>[17]</sup>
Units: log10 c/mL				
arithmetic mean (standard deviation)				
Day 2, n=7, 5, 10, 9	0.220 (± 0.1630)	0.149 (± 0.1820)	0.126 (± 0.1811)	0.126 (± 0.4216)
Day 5, n=7, 4, 10, 10	-0.340 (± 0.3185)	-0.811 (± 0.3455)	-0.593 (± 0.2429)	-0.767 (± 0.6388)
Day 6, n=7, 5, 10, 10	-0.530 (± 0.3170)	-1.082 (± 0.3388)	-0.822 (± 0.3076)	-1.053 (± 0.7491)
Day 7, n=6, 5, 10, 10	-0.556 (± 0.4264)	-1.443 (± 0.4484)	-1.086 (± 0.4216)	-1.198 (± 0.6863)
Day 8, n=6, 4, 9, 9	-0.691 (± 0.5380)	-1.372 (± 0.3208)	-1.218 (± 0.3902)	-1.470 (± 0.6570)

Notes:

[14] - ITT-E Monotherapy Population

[15] - ITT-E Monotherapy Population

[16] - ITT-E Monotherapy Population

[17] - ITT-E Monotherapy Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum decrease from monotherapy Baseline in log10 plasma HIV-1 RNA

End point title	Maximum decrease from monotherapy Baseline in log10 plasma HIV-1 RNA <sup>[18]</sup>
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End point description:

Maximum decrease from monotherapy Baseline in log10 plasma HIV-1 RNA during monotherapy to assess the antiviral activity of temsavir following administration of selected doses of FTR administered orally to HIV-1-infected participants for 7 days. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment. Change from Baseline was calculated as value at indicated time point minus Baseline value. The data for monotherapy nadir has been presented where nadir represents the maximum decrease from Baseline.

End point type	Secondary
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End point timeframe:

Baseline and up to Day 8 of the monotherapy period

Notes:

[18] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7 <sup>[19]</sup>	5 <sup>[20]</sup>	10 <sup>[21]</sup>	10 <sup>[22]</sup>
Units: log10 c/mL				
arithmetic mean (standard deviation)				
log10 c/mL	-0.770 (± 0.4487)	-1.524 (± 0.3898)	-1.250 (± 0.3818)	-1.399 (± 0.6688)

Notes:

[19] - ITT-E Monotherapy Population

[20] - ITT-E Monotherapy Population

[21] - ITT-E Monotherapy Population

[22] - ITT-E Monotherapy Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with plasma HIV-1 RNA < 50 c/mL at Day 8 of the monotherapy period

End point title	Percentage of participants with plasma HIV-1 RNA < 50 c/mL at Day 8 of the monotherapy period <sup>[23]</sup>
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End point description:

Percentage of participants with plasma HIV 1 RNA < 50 c/mL at Baseline of combination therapy was assessed to evaluate the antiviral activity of four doses of FTR. Baseline of combination therapy was the Day 1 of the combination therapy. Virologic success or failure was determined using the non-missing viral load value at Baseline of combination therapy. The assessment closest to the window target Study Day was used for the analysis. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Up to Day 8 of the monotherapy period

Notes:

[23] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6 <sup>[24]</sup>	4 <sup>[25]</sup>	9 <sup>[26]</sup>	9 <sup>[27]</sup>
Units: Percentage of Participants				
number (confidence interval 95%)				
Percentage of Participants	0 (0.0 to 45.9)	0 (0.0 to 60.2)	0 (0.0 to 33.6)	11 (0.3 to 48.2)

Notes:

[24] - ITT-E Monotherapy Population

[25] - ITT-E Monotherapy Population

[26] - ITT-E Monotherapy Population

[27] - ITT-E Monotherapy Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with SAE and discontinuation due to AEs during monotherapy period

End point title	Number of participants with SAE and discontinuation due to AEs during monotherapy period <sup>[28]</sup>
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End point description:

Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or suspected transmission of an infectious agent via the study drug were categorized as SAE. AEs leading to discontinuation of study therapy were also reported as safety assessment.

End point type	Secondary
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End point timeframe:

Up to Day 8 of the monotherapy period

Notes:

[28] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7 <sup>[29]</sup>	5 <sup>[30]</sup>	10 <sup>[31]</sup>	10 <sup>[32]</sup>
Units: Participants				
SAE	0	0	0	0
AEs leading to discontinuation	0	0	0	0

Notes:

[29] - ITT-E Monotherapy Population

[30] - ITT-E Monotherapy Population

[31] - ITT-E Monotherapy Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from monotherapy Baseline in Cluster of Differentiation (CD)4+ and CD8+ T-cell counts during monotherapy**

End point title	Change from monotherapy Baseline in Cluster of Differentiation (CD)4+ and CD8+ T-cell counts during monotherapy <sup>[33]</sup>
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End point description:

Blood was collected and CD4+ and CD8+ cell count assessment was done by flow cytometry and was carried out at Baseline (Day 1) to evaluate the immunological activity of multiple doses of FTR. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment and the values are absolute values. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Baseline and Day 8

Notes:

[33] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 <sup>[34]</sup>	4 <sup>[35]</sup>	8 <sup>[36]</sup>	8 <sup>[37]</sup>
Units: Cells per cubic millimeter				
arithmetic mean (standard deviation)				
CD4+	58.4 (± 81.60)	134.8 (± 25.70)	71.8 (± 117.68)	63.4 (± 100.86)
CD8+	134.2 (± 180.64)	216.3 (± 215.57)	188.0 (± 363.58)	67.6 (± 236.55)

Notes:

[34] - ITT-E Monotherapy Population

[35] - ITT-E Monotherapy Population

[36] - ITT-E Monotherapy Population

[37] - ITT-E Monotherapy Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from monotherapy Baseline in CD4+ and CD8+ T-cell proportion during monotherapy**

End point title	Change from monotherapy Baseline in CD4+ and CD8+ T-cell proportion during monotherapy <sup>[38]</sup>
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**End point description:**

Blood was collected and CD4+ and CD8+ proportion assessment was done by flow cytometry and was carried out at Baseline (Day 1) to evaluate the immunological activity of multiple doses of FTR. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment and the values are absolute values. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary
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**End point timeframe:**

Baseline and Day 8

**Notes:**

[38] - 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

<b>End point values</b>	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6 <sup>[39]</sup>	4 <sup>[40]</sup>	9 <sup>[41]</sup>	8 <sup>[42]</sup>
Units: cells per cubic millimeter				
arithmetic mean (standard deviation)				
CD4+	-0.005 (± 0.0084)	0.023 (± 0.0299)	0.008 (± 0.0335)	0.014 (± 0.0320)
CD8+	-0.003 (± 0.0273)	-0.040 (± 0.0245)	-0.009 (± 0.0465)	-0.021 (± 0.0364)

**Notes:**

[39] - ITT-E Monotherapy Population

[40] - ITT-E Monotherapy Population

[41] - ITT-E Monotherapy Population

[42] - ITT-E Monotherapy Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of participants with plasma HIV-1 RNA < 50 c/mL at primary study**

End point title	Percentage of participants with plasma HIV-1 RNA < 50 c/mL at primary study
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**End point description:**

Percentage of participants with plasma HIV 1 RNA < 50 c/mL at Weeks 48 and 96 using the FDA snapshot algorithm was assessed to evaluate the antiviral activity. Treatment comparisons were not performed as this was an estimation study. Response rates were tabulated by treatment arm with exact Clopper-Pearson binomial 95 percentage CI. Virologic success or failure was determined by the last available HIV-1 RNA assessment while the participant was on-treatment within the snapshot window of the visit of interest.

End point type	Secondary
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**End point timeframe:**

Weeks 48 and 96

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50 <sup>[43]</sup>	49 <sup>[44]</sup>	51 <sup>[45]</sup>	50 <sup>[46]</sup>
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 48	82 (68.6 to 91.4)	61 (46.2 to 74.8)	69 (54.1 to 80.9)	68 (53.3 to 80.5)
Week 96	78 (64.0 to 88.5)	49 (34.4 to 63.7)	63 (48.1 to 75.9)	58 (43.2 to 71.8)

Notes:

[43] - ITT-E Population

[44] - ITT-E Population

[45] - ITT-E Population

[46] - ITT-E Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	51 <sup>[47]</sup>			
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 48	71 (56.2 to 82.5)			
Week 96	57 (42.2 to 70.7)			

Notes:

[47] - ITT-E Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with SAE and discontinuation due to AEs during primary study

End point title	Number of participants with SAE and discontinuation due to AEs during primary study
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End point description:

Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or suspected transmission of an infectious agent via the study drug were categorized as SAE. AEs leading to discontinuation of study therapy were also reported as safety assessment. Safety Population comprised of participants who received at least one dose of study treatment. Summaries of SAEs and AEs leading to discontinuation or withdrawal through Week X (where X = 48 or 96) included AEs with onset on or after the start of study treatment (i.e. study date of first study treatment intake) up to and including the end of the Week 48 and 96 visit snapshot window.

End point type	Secondary
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End point timeframe:

Weeks 48 and 96

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50 <sup>[48]</sup>	49 <sup>[49]</sup>	51 <sup>[50]</sup>	50 <sup>[51]</sup>
Units: Participants				
SAE, Week 48	3	5	4	2
SAE, Week 96	5	7	6	4
AEs leading to discontinuation, Week 48	1	2	0	1
AEs leading to discontinuation, Week 96	1	2	0	2

Notes:

[48] - Safety Population

[49] - Safety Population

[50] - Safety Population

[51] - Safety Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	51 <sup>[52]</sup>			
Units: Participants				
SAE, Week 48	5			
SAE, Week 96	7			
AEs leading to discontinuation, Week 48	3			
AEs leading to discontinuation, Week 96	5			

Notes:

[52] - Safety Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in CD4+ T-cell count

End point title	Change from Baseline in CD4+ T-cell count
End point description:	
Blood was collected and CD4+ cell count assessment by flow cytometry was carried out at Baseline (Day 1), Weeks 24, 48 and 96 to evaluate the immunological activity of multiple doses of BMS-663068/GSK3684934. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment and those values are absolute values. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 24, 48 and 96	

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50 <sup>[53]</sup>	49 <sup>[54]</sup>	51 <sup>[55]</sup>	50 <sup>[56]</sup>
Units: Cells per cubic millimeter				
arithmetic mean (standard deviation)				

Week 24, n=41, 38, 48, 42, 40	134.3 (± 84.63)	111.0 (± 123.75)	109.5 (± 87.20)	124.5 (± 111.04)
Week 48, n=43, 34, 43, 41, 41	199.1 (± 124.24)	158.7 (± 118.70)	140.5 (± 97.16)	155.4 (± 107.06)
Week 96, n=42, 28, 35, 28, 31	264.6 (± 147.83)	210.8 (± 158.03)	175.7 (± 98.28)	211.7 (± 151.03)

Notes:

[53] - ITT-E Population

[54] - ITT-E Population

[55] - ITT-E Population

[56] - ITT-E Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	51 <sup>[57]</sup>			
Units: Cells per cubic millimeter				
arithmetic mean (standard deviation)				
Week 24, n=41, 38, 48, 42, 40	119.4 (± 142.85)			
Week 48, n=43, 34, 43, 41, 41	178.7 (± 133.90)			
Week 96, n=42, 28, 35, 28, 31	250.1 (± 217.54)			

Notes:

[57] - ITT-E Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with newly-emergent genotypic substitutions at Week 24

End point title	Number of participants with newly-emergent genotypic substitutions at Week 24
-----------------	---

End point description:

Participants who administered antiretroviral (ARV) with virologic failure (VF) were assessed. Genotypic substitution included assessment of Reverse Transcriptase (RT) substitution, Protease Inhibitor (PI) substitution and Integrase RAL substitution as per International Acquired Immune Deficiency Syndrome (AIDS) Society-USA (IAS-USA) list. ITT-E Resistance Tested through Week 24 population included participants who met the criteria for Resistance testing, and the confirmatory value or value at discontinuation occurred at or before the end of the Week 24 Snapshot analysis window. The criteria for resistance tested was participant who had virologic failure or met the following criteria a) Participants who achieved viral suppression (plasma HIV-1 RNA < 50 c/mL) and have confirmed plasma HIV-1 RNA ≥ 400 c/mL at any time during the study. b) Participants who were discontinued before achieving viral suppression (plasma HIV-1 RNA < 50 c/mL) after Week 8 with last plasma HIV-1 RNA ≥ 400 c/mL.

End point type	Secondary
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End point timeframe:

Up to Week 24

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 <sup>[58]</sup>	7 <sup>[59]</sup>	11 <sup>[60]</sup>	3 <sup>[61]</sup>
Units: Participants				
PI substitution	0	0	0	0
RT substitution	0	0	0	1
Integrase substitution	0	0	1	1

Notes:

[58] - ITT-E Resistance Tested through Week 24 Population

[59] - ITT-E Resistance Tested through Week 24 Population

[60] - ITT-E Resistance Tested through Week 24 Population

[61] - ITT-E Resistance Tested through Week 24 Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	5 <sup>[62]</sup>			
Units: Participants				
PI substitution	0			
RT substitution	0			
Integrase substitution	0			

Notes:

[62] - ITT-E Resistance Tested through Week 24 Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with newly-emergent genotypic substitutions at Week 48

End point title	Number of participants with newly-emergent genotypic substitutions at Week 48
-----------------	---

End point description:

Participants who administered ARV with VF were assessed. Genotypic substitution included assessment of RT substitution, PI substitution and Integrase RAL substitution as per IAS-USA list. ITT-E Resistance Tested through Week 48 population included participants who met the criteria for Resistance testing, and the confirmatory value or value at discontinuation occurred at or before the end of the Week 48 Snapshot analysis window. The criteria for resistance tested was participant who had virologic failure or the following criteria a) Participants who achieved viral suppression (plasma HIV-1 RNA < 50 c/mL) and have confirmed plasma HIV-1 RNA ≥ 400 c/mL at any time during the study. b) Participants who were discontinued before achieving viral suppression (plasma HIV-1 RNA < 50 c/mL) after Week 8 with last plasma HIV-1 RNA ≥ 400 c/mL.

End point type	Secondary
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End point timeframe:

Up to Week 48

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9 <sup>[63]</sup>	10 <sup>[64]</sup>	16 <sup>[65]</sup>	9 <sup>[66]</sup>
Units: Participants				
PI substitution	1	0	0	1
RT substitution	0	0	0	2
Integrase substitution	1	1	1	2

Notes:

[63] - ITT-E Resistance Tested through Week 48 Population

[64] - ITT-E Resistance Tested through Week 48 Population

[65] - ITT-E Resistance Tested through Week 48 Population

[66] - ITT-E Resistance Tested through Week 48 Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	6 <sup>[67]</sup>			
Units: Participants				
PI substitution	0			
RT substitution	0			
Integrase substitution	0			

Notes:

[67] - ITT-E Resistance Tested through Week 48 Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with newly-emergent genotypic substitutions at Week 96

End point title	Number of participants with newly-emergent genotypic substitutions at Week 96
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End point description:

Participants who administered ARV with VF were assessed. Genotypic substitution included assessment of RT substitution, PI substitution and Integrase RAL substitution as per IAS-USA list. ITT-E Resistance Tested through Week 96 population included participants who met the criteria for Resistance testing, and the confirmatory value or value at discontinuation occurred at or before the end of the Week 96 Snapshot analysis window. The criteria for resistance tested was participants with virologic failure or the following criteria a) Participants who achieved viral suppression (plasma HIV-1 RNA < 50 c/mL) and have confirmed plasma HIV-1 RNA  $\geq$  400 c/mL at any time during the study. b) Participants who were discontinued before achieving viral suppression (plasma HIV-1 RNA < 50 c/mL) after Week 8 with last plasma HIV-1 RNA  $\geq$  400 c/mL.

End point type	Secondary
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End point timeframe:

Up to Week 96

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20 <sup>[68]</sup>	18 <sup>[69]</sup>	23 <sup>[70]</sup>	13 <sup>[71]</sup>
Units: Participants				
PI substitution	3	1	2	2
RT substitution	2	1	2	2
Integrase RAL substitution	2	2	1	3

Notes:

[68] - ITT-E Resistance Tested through Week 96 Population

[69] - ITT-E Resistance Tested through Week 96 Population

[70] - ITT-E Resistance Tested through Week 96 Population

[71] - ITT-E Resistance Tested through Week 96 Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	11 <sup>[72]</sup>			
Units: Participants				
PI substitution	0			
RT substitution	1			
Integrase RAL substitution	0			

Notes:

[72] - ITT-E Resistance Tested through Week 96 Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum change from Baseline in Inhibitory Concentration at 50% (IC50) fold change among participants with VF at Week 24

End point title	Maximum change from Baseline in Inhibitory Concentration at 50% (IC50) fold change among participants with VF at Week 24
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End point description:

Virologic failure is defined clinically as confirmed plasma HIV-1 RNA  $\geq$  50 copies/mL at Week 24 or later or virologic rebound defined as confirmed HIV-1 RNA  $\geq$  50 copies/mL at any time after prior confirmed suppression to  $<$  50 copies/mL OR confirmed  $>$  1 log<sub>10</sub> copies/mL increase in HIV-1 RNA at any time above nadir level where nadir was  $\geq$  50 copies/mL. The phenotypic resistance to a drug is defined as a fold change (i.e, ratio of the IC<sub>50</sub> of the clinical isolate to the IC<sub>50</sub> of the reference strain) greater than the cut-off for reduced susceptibility. Maximum change from Baseline in Tenofovir IC<sub>50</sub> fold change based on all on-treatment values has been presented. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment and those values are absolute values. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Baseline and up to Week 24

End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 <sup>[73]</sup>	4 <sup>[74]</sup>	6 <sup>[75]</sup>	2 <sup>[76]</sup>
Units: IC50 Fold Change				
arithmetic mean (standard deviation)				
IC50 Fold Change	-2.350 (± 3.4536)	1014.748 (± 2015.5876)	101.627 (± 190.4849)	39.030 (± 55.1119)

Notes:

[73] - ITT-E Resistance Tested through Week 24 Population

[74] - ITT-E Resistance Tested through Week 24 Population

[75] - ITT-E Resistance Tested through Week 24 Population

[76] - ITT-E Resistance Tested through Week 24 Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	2 <sup>[77]</sup>			
Units: IC50 Fold Change				
arithmetic mean (standard deviation)				
IC50 Fold Change	-0.030 (± 0.6364)			

Notes:

[77] - ITT-E Resistance Tested through Week 24 Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in IC50 fold change among participants with VF at Week 48

End point title	Change from Baseline in IC50 fold change among participants with VF at Week 48
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End point description:

Virologic failure is defined clinically as confirmed plasma HIV-1 RNA  $\geq$  50 copies/mL at Week 24 or later or later or virologic rebound defined as confirmed HIV-1 RNA  $\geq$  50 copies/mL at any time after prior confirmed suppression to  $<$  50 copies/mL OR confirmed  $>$  1 log<sub>10</sub> copies/mL increase in HIV-1 RNA at any time above nadir level where nadir was  $\geq$  50 copies/mL. The phenotypic resistance to a drug is defined as a fold change (i.e, ratio of the IC<sub>50</sub> of the clinical isolate to the IC<sub>50</sub> of the reference strain) greater than the cut-off for reduced susceptibility. Maximum change from Baseline in Tenofovir IC<sub>50</sub> fold change based on all on-treatment values has been presented. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment and those values are absolute values. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Baseline and up to Week 48



End point values	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 <sup>[78]</sup>	7 <sup>[79]</sup>	8 <sup>[80]</sup>	5 <sup>[81]</sup>
Units: IC50 Fold Change				
arithmetic mean (standard deviation)				
IC50 Fold Change	-2.624 (± 3.2819)	586.776 (± 1521.9126)	81.729 (± 165.4931)	449.092 (± 647.9828)

Notes:

[78] - ITT-E Resistance Tested through Week 48 Population

[79] - ITT-E Resistance Tested through Week 48 Population

[80] - ITT-E Resistance Tested through Week 48 Population

[81] - ITT-E Resistance Tested through Week 48 Population

End point values	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	4 <sup>[82]</sup>			
Units: IC50 Fold Change				
arithmetic mean (standard deviation)				
IC50 Fold Change	1.020 (± 1.4770)			

Notes:

[82] - ITT-E Resistance Tested through Week 48 Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in IC50 fold change among participants with VF at Week 96

End point title	Change from Baseline in IC50 fold change among participants with VF at Week 96
-----------------	--

End point description:

Virologic failure is defined clinically as confirmed plasma HIV-1 RNA  $\geq$  50 copies/mL at Week 24 or later or virologic rebound defined as confirmed HIV-1 RNA  $\geq$  50 copies/mL at any time after prior confirmed suppression to  $<$  50 copies/mL OR confirmed  $>$  1 log<sub>10</sub> copies/mL increase in HIV-1 RNA at any time above nadir level where nadir was  $\geq$  50 copies/mL. The phenotypic resistance to a drug is defined as a fold change (i.e, ratio of the IC<sub>50</sub> of the clinical isolate to the IC<sub>50</sub> of the reference strain) greater than the cut-off for reduced susceptibility. Maximum change from Baseline in Tenofovir IC<sub>50</sub> fold change based on all on-treatment values has been presented. Baseline is defined as the last non-missing value on or before the date of first dose of study treatment and those values are absolute values. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Baseline and up to Week 96

<b>End point values</b>	FTR 400 mg BID/RAL/TDF	FTR 800 mg BID/RAL/TDF	FTR 600 mg QD/RAL/TDF	FTR 1200 mg QD/RAL/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6 <sup>[83]</sup>	14 <sup>[84]</sup>	11 <sup>[85]</sup>	9 <sup>[86]</sup>
Units: IC50 Fold Change				
arithmetic mean (standard deviation)				
IC50 Fold Change	25.480 (± 68.9030)	419.901 (± 1092.5929)	46.351 (± 157.9219)	777.818 (± 1550.8887)

Notes:

[83] - ITT-E Resistance Tested through Week 96 Population

[84] - ITT-E Resistance Tested through Week 96 Population

[85] - ITT-E Resistance Tested through Week 96 Population

[86] - ITT-E Resistance Tested through Week 96 Population

<b>End point values</b>	ATV/r/RAL/TDF			
Subject group type	Reporting group			
Number of subjects analysed	4 <sup>[87]</sup>			
Units: IC50 Fold Change				
arithmetic mean (standard deviation)				
IC50 Fold Change	1.090 (± 1.5444)			

Notes:

[87] - ITT-E Resistance Tested through Week 96 Population

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from start of study treatment (Day 1) until 2117 days

Adverse event reporting additional description:

The analysis was based on the Safety Population. Adverse events data were not reported cumulatively for all intervention concentrations, and were only reported cumulatively per FTR or ATV/r interventions.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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### Reporting groups

Reporting group title	FTR/RAL/TDF Total
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Reporting group description:

All participants who were randomized to receive either of FTR 400mg BID, 800 mg BID, 600mg QD or 1200 mg QD (double-blind) along with 400 mg RAL BID (open label) and 300 mg TDF QD (open label).

Reporting group title	ATV/r/RAL/TDF
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Reporting group description:

Participants were randomized to Reference group (open label) and administered ATV/r 300/100 mg once daily along with 400 mg RAL BID and 300 mg TDF QD.

Serious adverse events	FTR/RAL/TDF Total	ATV/r/RAL/TDF	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 200 (17.50%)	8 / 51 (15.69%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of salivary gland			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian neoplasm			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hysterectomy			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Obstructive airways disorder			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Depression			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			

subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	3 / 200 (1.50%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 5	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	2 / 200 (1.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 200 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 200 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post herpetic neuralgia			

subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 200 (1.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 200 (0.50%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 200 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bone tuberculosis			

subjects affected / exposed	2 / 200 (1.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis staphylococcal			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated tuberculosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 200 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis herpetic			



subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 200 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 200 (0.50%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	FTR/RAL/TDF Total	ATV/r/RAL/TDF	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	163 / 200 (81.50%)	46 / 51 (90.20%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	9 / 200 (4.50%)	3 / 51 (5.88%)	
occurrences (all)	16	5	

Alanine aminotransferase increased subjects affected / exposed occurrences (all)	6 / 200 (3.00%) 6	4 / 51 (7.84%) 6	
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	4 / 51 (7.84%) 9	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	15 / 200 (7.50%) 16	3 / 51 (5.88%) 3	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	38 / 200 (19.00%) 64	6 / 51 (11.76%) 18	
Dizziness subjects affected / exposed occurrences (all)	9 / 200 (4.50%) 9	4 / 51 (7.84%) 6	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	11 / 200 (5.50%) 14	4 / 51 (7.84%) 4	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	37 / 200 (18.50%) 48	10 / 51 (19.61%) 16	
Nausea subjects affected / exposed occurrences (all)	19 / 200 (9.50%) 22	6 / 51 (11.76%) 18	
Vomiting subjects affected / exposed occurrences (all)	16 / 200 (8.00%) 18	6 / 51 (11.76%) 8	
Abdominal pain subjects affected / exposed occurrences (all)	13 / 200 (6.50%) 13	4 / 51 (7.84%) 6	
Dyspepsia			

subjects affected / exposed	12 / 200 (6.00%)	2 / 51 (3.92%)	
occurrences (all)	13	2	
Constipation			
subjects affected / exposed	11 / 200 (5.50%)	0 / 51 (0.00%)	
occurrences (all)	12	0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 200 (0.00%)	11 / 51 (21.57%)	
occurrences (all)	0	35	
Jaundice			
subjects affected / exposed	0 / 200 (0.00%)	8 / 51 (15.69%)	
occurrences (all)	0	9	
Ocular icterus			
subjects affected / exposed	1 / 200 (0.50%)	7 / 51 (13.73%)	
occurrences (all)	1	8	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	17 / 200 (8.50%)	2 / 51 (3.92%)	
occurrences (all)	21	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	15 / 200 (7.50%)	0 / 51 (0.00%)	
occurrences (all)	21	0	
Alopecia			
subjects affected / exposed	0 / 200 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	13 / 200 (6.50%)	2 / 51 (3.92%)	
occurrences (all)	16	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	20 / 200 (10.00%)	3 / 51 (5.88%)	
occurrences (all)	25	3	
Arthralgia			

subjects affected / exposed	18 / 200 (9.00%)	1 / 51 (1.96%)	
occurrences (all)	22	1	
Pain in extremity			
subjects affected / exposed	14 / 200 (7.00%)	1 / 51 (1.96%)	
occurrences (all)	17	1	
Myalgia			
subjects affected / exposed	10 / 200 (5.00%)	0 / 51 (0.00%)	
occurrences (all)	10	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	32 / 200 (16.00%)	5 / 51 (9.80%)	
occurrences (all)	52	10	
Upper respiratory tract infection			
subjects affected / exposed	27 / 200 (13.50%)	7 / 51 (13.73%)	
occurrences (all)	47	7	
Urinary tract infection			
subjects affected / exposed	28 / 200 (14.00%)	6 / 51 (11.76%)	
occurrences (all)	62	19	
Influenza			
subjects affected / exposed	22 / 200 (11.00%)	7 / 51 (13.73%)	
occurrences (all)	43	8	
Bronchitis			
subjects affected / exposed	22 / 200 (11.00%)	4 / 51 (7.84%)	
occurrences (all)	34	4	
Pharyngitis			
subjects affected / exposed	17 / 200 (8.50%)	5 / 51 (9.80%)	
occurrences (all)	19	5	
Herpes zoster			
subjects affected / exposed	17 / 200 (8.50%)	2 / 51 (3.92%)	
occurrences (all)	20	2	
Gastroenteritis			
subjects affected / exposed	11 / 200 (5.50%)	6 / 51 (11.76%)	
occurrences (all)	11	6	
Lower respiratory tract infection			
subjects affected / exposed	10 / 200 (5.00%)	1 / 51 (1.96%)	
occurrences (all)	12	1	

Onychomycosis			
subjects affected / exposed	8 / 200 (4.00%)	3 / 51 (5.88%)	
occurrences (all)	8	3	
Sinusitis			
subjects affected / exposed	5 / 200 (2.50%)	4 / 51 (7.84%)	
occurrences (all)	12	12	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2011	Amendment 01: Permit the collection and storage of blood samples for use in future exploratory pharmacogenetic research. The sponsor may use deoxyribonucleic acid (DNA) obtained from the blood sample and health information collected from the main clinical study to study the association between genetic variation and drug response. The sponsor could also use the DNA to study the causes and further progression of HIV-1 infections. Samples from this study could also be used in conjunction with pharmacogenetic research results from other clinical studies to accomplish this objective.
05 February 2013	Amendment 02: 1. Remove all 4 of the required visits in the 24 weeks of the post-dosing follow-up period. 2. Add an optional visit at post-dosing Week 2, intended primarily for the collection of a blood sample for the assessment of Neutralizing Antibody Potency, for those participants who meet the criteria for participation. 3. Modify the description of the Neutralizing Antibody Potency analysis. 4. Table numbering has been modified in accordance with new sponsor Core Template standards.
08 December 2014	Amendment 03: 1. Add Pregnancy Testing for WOCBP every 4 weeks during Stage 2. 2. Add Telephone Contact Visits (and supporting text) between Stage 2 visits for adherence assessments. 3. Indicated adherence issues of < 90 percentage will be assessed closely. 4. Clarified that participants with a confirmed viral load that requires study discontinuation may remain on study therapies until resistance results are available. 5. Corrected references to other sections in the protocol: In Section 3.5, the reference in the 8th bullet to Section 6.6.1.5 was corrected to 6.7.1.5. In Table 5.1-3, the reference in the Intensive PK and Sparse PK rows to Section 5.5.3 was corrected to 5.5.2. In Section 5.3, the reference to 6.6.1 was corrected to 6.7.1.
04 February 2016	Amendment 04: Section 4.1, Study Treatments - Table 4-1.1, Added: first row to table showing the details of the new formulation Updated: Storage conditions for Raltegravir tablet and Tenofovir tablet.
25 October 2016	Amendment 05: 1. Identify ViiV Healthcare Company (ViiV Healthcare) as the Sponsor and removed references to Bristol-Myers Squibb (BMS). 2. Acknowledge that GlaxoSmithKline (GSK) and ICON plc are supporting ViiV Healthcare in the conduct of the study. 3. Include the GSK study number (205889). 4. Include the GSK compound number (GSK3684934) and metabolite number (GSK2616713). 5. Indicate that molecular analysis will occur at ViiV Healthcare Discovery (Wallingford, CT, USA) instead of at BMS. 6. Updated Sponsor Information and included ICON Medical Monitor Emergency Contact information. 7. Other minor edits were made to improve the readability of the document.

Notes:

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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported