Clinical trial results:
A Phase II, Multicenter, Open-Label, Noncomparative Study of Raltegravir (MK-0518) in Two Oral Formulations in Combination with Other Antiretroviral Agents to Evaluate the Safety, Tolerability, and Antiretroviral Activity in HIV-1 Infected Russian Children and Adolescents

Summary

EudraCT number	2017-000050-18
Trial protocol	Outside EU/EEA
Global end of trial date	11 December 2013

Results information

Result version number	v1 (current)
This version publication date	24 February 2017
First version publication date	24 February 2017

Trial information

Trial identification

Sponsor protocol code	MK-0518-248

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01717287
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2013
Global end of trial reached?	Yes
Global end of trial date	11 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This multicenter, open-label, noncomparative study evaluates two oral formulations of raltegravir (MK-0518, film-coated tablet and chewable tablet) in combination with other antiretroviral therapy (ART) for safety, tolerability, and antiretroviral activity in treatment-naïve or treatment-experienced Russian children and adolescents infected with human immunodeficiency virus-1 (HIV-1).

As raltegravir is indicated in combination with other antiretroviral therapies (ARTs) for the treatment of HIV-1 infection in pediatric patients in the United States (US), this study is designed to gain local treatment experience on the use of raltegravir in the pediatric HIV-infected population in Russia.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 32
Worldwide total number of subjects	32
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	30
Adolescents (12-17 years)	2

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Pediatric (2 to 18 years of age) male and female participants infected with human immunodeficiency virus (HIV) were recruited in the Russian Federation.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Raltegravir Film-coated Tablet

Arm description:

Raltegravir film-coated tablet 400 mg administered by mouth twice per day (b.i.d.) in combination with other anti-retroviral therapy (ART) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Raltegravir 400 mg film-coated tablet
Investigational medicinal product code	MK-0518
Other name	ISENTRESS®, MK-0518
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Single 400 mg tablet taken twice daily by mouth.

Arm title	Raltegravir Chewable Tablet

Arm description:

Raltegravir chewable tablet weight-based dose up to 300 mg administered by mouth b.i.d. in combination with other ART for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Raltegravir chewable tablet
Investigational medicinal product code	MK-0518
Other name	ISENTRESS®, MK-0518
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

Weight-based dosing up to 300 mg twice daily via 25 mg or 100 mg chewable tablets taken twice daily by mouth.

Number of subjects in period 1	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet
Started	4	28
Completed	4	25
Not completed	0	3
Lost to follow-up	-	2
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Raltegravir Film-coated Tablet
Reporting group description:	
Raltegravir film-coated tablet 400 mg administered by mouth twice per day (b.i.d.) in combination with other anti-retroviral therapy (ART) for 24 weeks.	
Reporting group title	Raltegravir Chewable Tablet
Reporting group description:	
Raltegravir chewable tablet weight-based dose up to 300 mg administered by mouth b.i.d. in combination with other ART for 24 weeks.	

Reporting group values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet	Total
Number of subjects	4	28	32
Age Categorical Units: Subjects			
Children (2-11 years)	2	28	30
Adolescents (12-17 years)	2	0	2
Age Continuous Units: years			
arithmetic mean	11.8	6.4	
standard deviation	± 3.77	± 2.64	-
Gender Categorical Units: Subjects			
Female	1	16	17
Male	3	12	15

End points

End points reporting groups

Reporting group title	Raltegravir Film-coated Tablet
Reporting group description:	
Raltegravir film-coated tablet 400 mg administered by mouth twice per day (b.i.d.) in combination with other anti-retroviral therapy (ART) for 24 weeks.	
Reporting group title	Raltegravir Chewable Tablet
Reporting group description:	
Raltegravir chewable tablet weight-based dose up to 300 mg administered by mouth b.i.d. in combination with other ART for 24 weeks.	

Primary: Percentage of Participants Experiencing a Clinical Adverse Event (AE)

End point title	Percentage of Participants Experiencing a Clinical Adverse Event (AE)[1]
End point description:	
A clinical AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE. The all participants as treated population included all enrolled participants who received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
Up to Week 26	

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: The Sponsor made a business decision to terminate the trial early due to poor enrollment; the decision was not related to any findings regarding the efficacy or safety profile of odanacatib.

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	28		
Units: Percentage of Participants				
number (not applicable)	0	42.9		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Discontinuing Study Therapy Due to a Clinical AE

End point title	Percentage of Participants Discontinuing Study Therapy Due to a Clinical AE[2]
End point description:	
A clinical AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE. The all participants as treated population	

included all enrolled participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to Week 24

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The Sponsor made a business decision to terminate the trial early due to poor enrollment; the decision was not related to any findings regarding the efficacy or safety profile of odanacatib.

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	28		
Units: Percentage of Participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing a Laboratory AE

End point title	Percentage of Participants Experiencing a Laboratory AE[3]

End point description:

A laboratory AE is defined as any unfavorable and unintended change in the chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE. The all participants as treated population included all enrolled participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to Week 26

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The Sponsor made a business decision to terminate the trial early due to poor enrollment; the decision was not related to any findings regarding the efficacy or safety profile of odanacatib.

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	28		
Units: Percentage of Participants				
number (not applicable)	0	3.6		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Discontinuing Study Therapy Due to a Laboratory AE

End point title	Percentage of Participants Discontinuing Study Therapy Due to a Laboratory AE[4]

End point description:

A laboratory AE is defined as any unfavorable and unintended change in the chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE. The all participants as treated population included all enrolled participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Up to Week 24

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The Sponsor made a business decision to terminate the trial early due to poor enrollment; the decision was not related to any findings regarding the efficacy or safety profile of odanacatib.

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	28		
Units: Percentage of Participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Cluster of Differentiation 4 (CD4) Cell Counts

End point title	Change from Baseline in Cluster of Differentiation 4 (CD4) Cell Counts

End point description:

This outcome is a measure of immunological response to treatment. The population analyzed included all participants who received at least one dose of study drug and had baseline evaluation.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	24		
Units: Cells/mm^3				
arithmetic mean (confidence interval 95%)	30.3 (-178.6 to 239.2)	296.3 (133.6 to 458.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4 Cell Percentage

End point title	Change from Baseline in CD4 Cell Percentage

End point description:

This outcome is a measure of immunological response to treatment. The population analyzed included all participants who received at least one dose of study drug and had baseline evaluation.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	24		
Units: Percentage change				
arithmetic mean (confidence interval 95%)	4 (-5 to 13)	6 (3.8 to 8.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ≥1 log10 Reduction From Baseline in HIV Ribonucleic Acid (RNA) or Had an HIV RNA Assessment of <200 Copies/mL

End point title	Percentage of Participants Achieving ≥1 log10 Reduction From Baseline in HIV Ribonucleic Acid (RNA) or Had an HIV RNA Assessment of <200 Copies/mL

End point description:

This outcome is a measure of virological (anti-retroviral) response to treatment. Plasma HIV RNA was measured using the Abbott RealTime HIV-1 assay, which has a linear range of 40 HIV RNA copies/mL to 10 million HIV RNA copies/mL. The full analysis set included all participants who received at least one dose of study drug, had baseline evaluation for those analyses that required baseline data, and had at least one post-baseline evaluation.

End point type	Secondary

End point timeframe:

Week 24

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	25		
Units: Percentage of Participants				
number (confidence interval 95%)	75 (19.4 to 99.4)	88 (68.8 to 97.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving HIV RNA <40 Copies/mL

End point title	Percentage of Participants Achieving HIV RNA <40 Copies/mL

End point description:

This outcome is a measure of virological (anti-retroviral) response to treatment. Plasma HIV RNA was measured using the Abbott RealTime HIV-1 assay, which has a linear range of 40 HIV RNA copies/mL to 10 million HIV RNA copies/mL. The full analysis set included all participants who received at least one dose of study drug, had baseline evaluation for those analyses that required baseline data, and had at least one post-baseline evaluation.

End point type	Secondary

End point timeframe:

Week 24

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	25		
Units: Percentage of Participants				
number (confidence interval 95%)	50 (6.8 to 93.2)	44 (24.4 to 65.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving HIV RNA <200 Copies/mL

End point title	Percentage of Participants Achieving HIV RNA <200 Copies/mL

End point description:

This outcome is a measure of virological (anti-retroviral) response to treatment. Plasma HIV RNA was measured using the Abbott RealTime HIV-1 assay, which has a linear range of 40 HIV RNA copies/mL to

10 million HIV RNA copies/mL. The full analysis set included all participants who received at least one dose of study drug, had baseline evaluation for those analyses that required baseline data, and had at least one post-baseline evaluation.

End point type	Secondary

End point timeframe:

Week 24

End point values	Raltegravir Film-coated Tablet	Raltegravir Chewable Tablet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	25		
Units: Percentage of Participants				
number (confidence interval 95%)	50 (6.8 to 93.2)	76 (54.9 to 90.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 26	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Raltegravir Chewable Tablet
Reporting group description:	
Raltegravir chewable tablet weight-based dose up to 300 mg administered by mouth twice daily in combination with other ART for 24 weeks.	
Reporting group title	Raltegravir Film-coated Tablet
Reporting group description:	
Raltegravir film-coated tablet 400 mg administered by mouth twice daily in combination with other ART for 24 weeks.	

Serious adverse events	Raltegravir Chewable Tablet	Raltegravir Film-coated Tablet	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Raltegravir Chewable Tablet	Raltegravir Film-coated Tablet	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 28 (28.57%)	0 / 4 (0.00%)	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 28 (10.71%)	0 / 4 (0.00%)	
occurrences (all)	6	0	
Infections and infestations			
Otitis media			
subjects affected / exposed	2 / 28 (7.14%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection			

subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 4	0 / 4 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported