Clinical trial results:
An open-label study to evaluate the safety, tolerability and pharmacokinetics of etravirine (ETR) in combination with other antiretrovirals (ARVs) in antiretroviral treatment experienced HIV-1 infected Subjects

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2010-023532-16
Trial protocol	RO
Global end of trial date	11 November 2013

Results information

Result version number	v2 (current)
This version publication date	23 June 2016
First version publication date	26 July 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	TMC125IFD3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01422330
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen R&D Ireland
Sponsor organisation address	Eastgate Village, Eastgate, Little Island, Co. Cork, Ireland,
Public contact	Clinical Registry Group, Janssen Research & Development, +353 21 4673500, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, +353 21 4673500, ClinicalTrialsEU@its.jnj.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	11 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the safety, tolerability and pharmacokinetics of an Etravirine (ETR)-containing regimen without darunavir/ritonavir (DRV/rtv) over 48 weeks.

Protection of trial subjects:

All Events of Special Interest were evaluated in conjunction with other systemic symptoms and laboratory abnormalities: information on time of onset, duration of events, time to resolution, concomitant therapies, and relationship to ETR and background regimen.

Background therapy:

Antiretroviral other than Darunavir/Ritonavir

Evidence for comparator: -

Actual start date of recruitment	26 August 2011
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	Argentina: 4
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Guatemala: 16
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Peru: 10
Country: Number of subjects enrolled	Puerto Rico: 3
Country: Number of subjects enrolled	Romania: 12
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	United States: 35
Country: Number of subjects enrolled	South Africa: 108
Worldwide total number of subjects	211
EEA total number of subjects	15

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)	209
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 26 August 2011 - 11 November 2013.

Pre-assignment

Screening details:

A total of 528 participants were screened, of whom 211 participants were enrolled and treated with Etravirine.

Period 1

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

Arms

Arm title	Etravirine

Arm description:

Participants administered with Etravirine 200 milligram (mg) twice daily in combination with an investigator-selected background regimen consisting of antiretroviral drug except Darunavir/Ritonavir.

Arm type	Experimental
Investigational medicinal product name	Etravirine
Investigational medicinal product code	JNJ-4371315
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Etravirine 200 mg tablet twice daily in combination with an investigator-selected background regimen consisting of antiretroviral drug except Darunavir/Ritonavir.

Number of subjects in period 1	Etravirine
Started	211
Completed	165
Not completed	46
Subject Reached A Virologic Endpoint	11
Sponsor's Decision	2
Adverse Event	9
Withdrawal By Subject	8
Subject Non-Compliant	2
Other	2
Subject Ineligible To Continue The Trial	1
Lost to follow-up	11

Baseline characteristics

Reporting groups	
Reporting group title	Etravirine

Reporting group description:

Participants administered with Etravirine 200 milligram (mg) twice daily in combination with an investigator-selected background regimen consisting of antiretroviral drug except Darunavir/Ritonavir.

Reporting group values	Etravirine	Total	
Number of subjects	211	211	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	209	209	
From 65 to 84 years	2	2	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	40.8		
standard deviation	± 10.06	-	
Title for Gender Units: subjects			
Female	116	116	
Male	95	95	

End points

End points reporting groups

Reporting group title	Etravirine

Reporting group description:

Participants administered with Etravirine 200 milligram (mg) twice daily in combination with an investigator-selected background regimen consisting of antiretroviral drug except Darunavir/Ritonavir.

Subject analysis set title	Baseline Viral Load (copies/mL)<50
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants of ITT population having baseline viral load less than 50 copies/ml.

Subject analysis set title	Baseline Viral Load (copies/mL)>=50
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants of ITT population having baseline viral load greater than or equal to 50 copies/ml.

Subject analysis set title	Intent-to-treat (ITT) population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent-to-treat (ITT) population included all participants who received at least 1 dose of Etravirine.

Primary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

An AE was any untoward medical event that occurs in a participant administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged in-patient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly.

End point type	Primary

End point timeframe:

52 weeks

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Etravirine			
Subject group type	Reporting group			
Number of subjects analysed	211			
Units: Participants				
number (not applicable)				
AEs	144			
SAEs	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Virologic Response (<50 Copies/mL)at Week 48

End point title	Percentage of Participants with Virologic Response (<50 Copies/mL)at Week 48

End point description:

RNA (ribonucleic acid) copies/mL at Week 48 were analyzed as per FDA Snapshot approach. The FDA Snapshot approach is based on the last observed viral load (VL) data within the Week 48 window. Virologic response is defined as a VL<50 copies/milliliter (observed case). Missing VL was considered as non-response. Virologic Failure includes participants who had VL greater than or equal to (>=50) copies/ml in the Week 48 window, participants who discontinued early due to lack or loss of efficacy, participants who discontinued for reasons other than an adverse event, death, or lack or loss of efficacy and at the time of discontinuation had a VL>=50 copies/ml , and participants who had a switch in background regimen that was not permitted by the protocol.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Baseline Viral Load (copies/mL)<50	Baseline Viral Load (copies/mL)>=50	Intent-to-treat (ITT) population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	56	155	211	
Units: Percentage of Participant				
number (not applicable)				
Virologic success HIV RNA <50 copies/mL	75	47.7	55	
Virologic failure	12.5	41.9	34.1	
No viral load data	12.5	10.3	10.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Cluster of Differentiation 4 (CD4+) cell count at Week 48

End point title	Change from Baseline in Cluster of Differentiation 4 (CD4+) cell count at Week 48

End point description:

Change from baseline at Week 48 in CD4 cell count (cells/mm^6) was analyzed.

End point type	Secondary

End point timeframe:

Baseline and week 48

End point values	Baseline Viral Load (copies/mL)<50	Baseline Viral Load (copies/mL)>=50	Intent-to-treat (ITT) population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	56	155	211	
Units: 10^6 cells/Liter				
arithmetic mean (standard error)	32.4 (± 16.96)	64.6 (± 11.4)	56 (± 9.54)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Virologic Response (<400 Copies/mL)at Week 48

End point title	Percentage of Participants with Virologic Response (<400 Copies/mL)at Week 48

End point description:

RNA (ribonucleic acid) copies/mL at Week 48 were analyzed as per FDA Snapshot approach. The FDA Snapshot approach is based on the last observed viral load (VL) data within the Week 48 window. Virologic response is defined as a VL< 400 copies/milliliter (observed case). Missing VL was considered as non-response. Virologic Failure includes participants who had VL greater than or equal to (>=400) copies/ml in the Week 48 window, participants who discontinued early due to lack or loss of efficacy, participants who discontinued for reasons other than an adverse event, death, or lack or loss of efficacy and at the time of discontinuation had a VL>=400 copies/ml, and participants who had a switch in background regimen that was not permitted by the protocol.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Baseline Viral Load (copies/mL)<50	Baseline Viral Load (copies/mL)>=50	Intent-to-treat (ITT) population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	56	155	211	
Units: Percentage of Participants				
number (not applicable)				
Virologic success HIV RNA <400 copies/mL	82.1	54.2	61.6	
Virologic failure	5.4	34.2	26.5	
No viral load data	12.5	11.6	11.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time of

Administration to 12 hours After Dosing (AUC [0-12])

End point title	Area Under the Plasma Concentration-Time Curve From Time of Administration to 12 hours After Dosing (AUC [0-12])

End point description:

The AUC (0-12) is the area under the plasma concentration-time curve from time zero to 12 hours. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Baseline Viral Load (copies/mL)<50	Baseline Viral Load (copies/mL)>=50	Intent-to-treat (ITT) population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	53	146	199	
Units: nanogram*hour per milliliter				
geometric mean (full range (min-max))	5561.1 (366 to 38200)	4637.8 (216 to 29400)	4867.6 (216 to 38200)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Plasma Concentration (C0H)

End point title	Pre-dose Plasma Concentration (C0H)

End point description:

The pre-dose plasma concentration is defined as the plasma concentration obtained before a dose is given.'N' (number of participants analyzed signifies those participants who were evaluable for this measure.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Baseline Viral Load (copies/mL)<50	Baseline Viral Load (copies/mL)>=50	Intent-to-treat (ITT) population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	53	146	199	
Units: Nanogram per milliliter				
geometric mean (full range (min-max))	333.5 (4 to 3080)	279.8 (8 to 2330)	293.2 (4 to 3080)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Virologic Failures With Emerging NNRTI Resistance Associated Mutations at Last Available On-Treatment Genotypic Data after Failure

End point title	Percentage of Virologic Failures With Emerging NNRTI Resistance Associated Mutations at Last Available On-Treatment Genotypic Data after Failure

End point description:

Virologic failure for resistance determination was defined as non-responder(at least 12 weeks on study, and never having had 2 consecutive plasma viral load <50 copies/mL)or rebounder(at least 12 weeks on study, and 2 consecutive plasma viral load >=50 copies/mL or discontinued with a last observed on-treatment plasma viral load >=50 copies/mL after having had 2 consecutive plasma viral load <50 copies/mL). For this study, treatment-emergent mutations from a list of non-nucleoside reverse transcriptase (NNRTI) resistance-associated mutations (RAMs) (i.e. V90I, A98G, L100I, K101E, K101H, K101P,K101Q, K103H, K103N, K103S, K103T, V106A, V106I, V106M, V108I, E138A, E138G, E138K, E138Q, E138R, V179D, V179E, V179F, V179G, V179I, V179L, V179T, Y181C, Y181I, Y181V, Y188C, Y188H, Y188L, V189I, G190A, G190C, G190E, G190Q, G190S, G190T, H221Y, P225H, F227C, F227L, M230I, M230L, P236L, K238N, K238T, and Y318F) occurring in at least 2 virologic failures are presented.

End point type	Secondary

End point timeframe:

48 weeks

End point values	Intent-to-treat (ITT) population			
Subject group type	Subject analysis set			
Number of subjects analysed	49[2]			
Units: Percentage of Participants				
number (not applicable)				
Any NNRTI RAM from list	59.2			
Y181C	36.7			
H221Y	12.2			
E138A	10.2			
M230L	10.2			
E138K	8.2			
V90I	8.2			
E138Q	6.1			
V179I	6.1			
E138G	4.1			
V108I	4.1			
V189I	4.1			

Notes:

[2] - Virologic Failure population

Statistical analyses

No statistical analyses for this end point

Secondary: ETR Fold Change for Virologic Failures at Baseline and Last Available On-Treatment Phenotypic Data after Failure

End point title	ETR Fold Change for Virologic Failures at Baseline and Last Available On-Treatment Phenotypic Data after Failure

End point description:

Virologic failure for resistance determination was defined as non-responder (at least 12 weeks on study, and never having had 2 consecutive plasma viral load <50 copies/mL) or rebounder (at least 12 weeks on study, and 2 consecutive plasma viral load >=50 copies/mL or discontinued with a last observed on-treatment plasma viral load >=50 copies/mL after having had 2 consecutive plasma viral load <50 copies/mL). Fold change represents the phenotypic susceptibility of the participant's HIV-1 virus to ETR as compared to the wild type HIV-1/IIIB virus.

End point type	Secondary

End point timeframe:

48 Weeks

End point values	Intent-to-treat (ITT) population			
Subject group type	Subject analysis set			
Number of subjects analysed	49[3]			
Units: Participants				
median (full range (min-max))				
Baseline	0.84 (0.39 to 39)			
Endpoint	5.76 (0.5 to 276.72)			

Notes:

[3] - Virologic Failure population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 52 weeks	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0
Reporting groups	
Reporting group title	ETR 200 mg bid
Reporting group description:	
ETR 200 mg twice daily (b.i.d.) in combination with an investigator-selected background regimen	

Serious adverse events	ETR 200 mg bid		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 211 (5.21%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Eye injury			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Facial bones fracture			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hand fracture			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			

subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	ETR 200 mg bid		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	144 / 211 (68.25%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Squamous cell carcinoma			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 211 (1.90%)		
occurrences (all)	4		
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	5 / 211 (2.37%)		
occurrences (all)	5		
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	3		
Malaise			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Vaginal discharge			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Vaginal haemorrhage			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Asthma			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Dry throat			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Cough			

subjects affected / exposed	7 / 211 (3.32%)		
occurrences (all)	7		
Nasal polyps			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Pleuritic pain			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Rhinitis allergic			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Rhinitis seasonal			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Yawning			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Tonsillar inflammation			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Somnambulism			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	3		
Investigations			
Blood amylase increased			

subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	3		
Blood phosphorus decreased			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	3		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
International normalised ratio increased			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Weight decreased			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Prothrombin level increased			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Liver function test abnormal			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Excoriation			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Accidental overdose			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Nerve injury			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Humerus fracture			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Joint dislocation			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Joint sprain			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Post-traumatic pain			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Thermal burn			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Soft tissue injury			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Cardiac disorders			
Bradycardia			

subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Nervous system disorders			
Cerebral atrophy			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Cerebral infarction			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	7 / 211 (3.32%)		
occurrences (all)	7		
Neuropathy peripheral			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	9 / 211 (4.27%)		
occurrences (all)	15		
Lethargy			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		

Somnolence			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Anaemia			
subjects affected / exposed	4 / 211 (1.90%)		
occurrences (all)	4		
Macrocytosis			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Pinguecula			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	3		

Abdominal pain				
subjects affected / exposed	3 / 211 (1.42%)			
occurrences (all)	4			
Abnormal faeces				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Breath odour				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	2 / 211 (0.95%)			
occurrences (all)	2			
Dyspepsia				
subjects affected / exposed	7 / 211 (3.32%)			
occurrences (all)	7			
Dry mouth				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Diarrhoea				
subjects affected / exposed	35 / 211 (16.59%)			
occurrences (all)	40			
Dental caries				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Food poisoning				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Tongue ulceration				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Peptic ulcer				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	2 / 211 (0.95%)			
occurrences (all)	2			

Mouth ulceration subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Nausea subjects affected / exposed occurrences (all)	7 / 211 (3.32%) 7		
Vomiting subjects affected / exposed occurrences (all)	2 / 211 (0.95%) 2		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	5 / 211 (2.37%) 9		
Hepatic function abnormal subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Cholelithiasis subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Lipoatrophy subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Dermatitis allergic subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Dermatitis subjects affected / exposed occurrences (all)	6 / 211 (2.84%) 8		
Hyperhidrosis			

subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Macule			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Night sweats			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	7 / 211 (3.32%)		
occurrences (all)	9		
Rash macular			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Lipodystrophy acquired			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Rosacea			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Costochondritis			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Arthralgia			

subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	3		
Muscle spasms			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	2 / 211 (0.95%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	13 / 211 (6.16%)		
occurrences (all)	14		
Acute tonsillitis			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	5 / 211 (2.37%)		
occurrences (all)	5		
Gingival abscess			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		

Fungal infection				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Furuncle				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	4 / 211 (1.90%)			
occurrences (all)	4			
Oral candidiasis				
subjects affected / exposed	2 / 211 (0.95%)			
occurrences (all)	2			
Neurocysticercosis				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	12 / 211 (5.69%)			
occurrences (all)	12			
Mastitis				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Lower respiratory tract infection				
subjects affected / exposed	4 / 211 (1.90%)			
occurrences (all)	4			
Nasopharyngitis				
subjects affected / exposed	11 / 211 (5.21%)			
occurrences (all)	14			
Pseudocroup				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	2 / 211 (0.95%)			
occurrences (all)	3			
Otitis externa				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			

Otitis media				
subjects affected / exposed	2 / 211 (0.95%)			
occurrences (all)	2			
Pharyngitis				
subjects affected / exposed	2 / 211 (0.95%)			
occurrences (all)	2			
Sinusitis				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	9 / 211 (4.27%)			
occurrences (all)	9			
Pyelonephritis				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	2 / 211 (0.95%)			
occurrences (all)	2			
Respiratory tract infection viral				
subjects affected / exposed	3 / 211 (1.42%)			
occurrences (all)	3			
Upper respiratory tract infection				
subjects affected / exposed	17 / 211 (8.06%)			
occurrences (all)	22			
Tonsillitis				
subjects affected / exposed	3 / 211 (1.42%)			
occurrences (all)	3			
Strongyloidiasis				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Syphilis				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			
Subcutaneous abscess				
subjects affected / exposed	1 / 211 (0.47%)			
occurrences (all)	1			

Tinea infection subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Viral rhinitis subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Urinary tract infection subjects affected / exposed occurrences (all)	11 / 211 (5.21%) 12		
Vaginal infection subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Viral diarrhoea subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Vulvitis subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	1 / 211 (0.47%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	5 / 211 (2.37%) 5		
Dehydration subjects affected / exposed occurrences (all)	2 / 211 (0.95%) 3		
Hypercholesterolaemia			

subjects affected / exposed	3 / 211 (1.42%)		
occurrences (all)	5		
Hyperglycaemia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	6 / 211 (2.84%)		
occurrences (all)	7		
Hyperuricaemia			
subjects affected / exposed	4 / 211 (1.90%)		
occurrences (all)	6		
Hypoalbuminaemia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 211 (0.47%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 March 2011	It was created to specify the test used to measure plasma Volume, to add a pharmacokinetic substudy outlined in a separate document, and to add the collection of sparse samples to determine plasma concentrations and pharmacokinetics of the antiretroviral in the background regimen.
02 February 2012	The overall reason for this amendment was: Subjects with a plasma viral volume < 50 HIV-1 RNA copies/mL for which sensitivity to ETR and ARVs in the background regimen cannot be demonstrated, can be enrolled at the discretion of the investigator as guided by historical resistance testing or ARV treatment history. It was created to enhance adherence, by specifying that dispersion of ETR was allowed and that the choice of allowed liquids for ETR intake was broadened. Also, the name of the sponsor of the study changed from Tibotec Pharmaceuticals to Janssen R&D Ireland.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported