



## Clinical trial results:

### A Phase I, Open-Label Trial to Investigate Pharmacokinetics, Safety and Tolerability of TMC125 at Steady-State in Treatment-Experienced HIV-1 Infected Children

#### Summary

EudraCT number	2006-002183-26
Trial protocol	DE GB
Global end of trial date	27 February 2008

#### Results information

Result version number	v1
This version publication date	06 July 2016
First version publication date	12 June 2015

#### Trial information

##### Trial identification

Sponsor protocol code	TMC125-C126
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Tibotec Pharmaceuticals Ltd
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, 2340
Public contact	Clinical Registry Group, Tibotec Pharmaceuticals Ltd, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Tibotec Pharmaceuticals Ltd, 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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 February 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2008
Global end of trial reached?	Yes
Global end of trial date	27 February 2008
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to obtain steady-state pharmacokinetics of TMC125 in treatment-experienced human immunodeficiency virus - type 1 (HIV-1) infected children and dose recommendations of TMC125 per body weight in treatment-experienced HIV-1 infected children greater than or equal to ( $\geq$ ) 6 years old and weighing  $\geq$  20 kilogram (kg).

Protection of trial subjects:

An interim analysis of the pharmacokinetic and safety data of Stage 1 was performed in order to decide whether or not to proceed to Stage 2 of the trial. The safety assessments included laboratory measurements (for example biochemistry, blood coagulation, hematology, and urinalysis), cardiovascular safety, vital sign measurements and electrocardiograms (ECGs). Adverse events and vital signs were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 September 2006
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	Germany: 20
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	42
EEA total number of subjects	41

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)	22
Adolescents (12-17 years)	20
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:

A total of 42 participants were enrolled and treated with etravirine also known as TMC125 and included in the intent-to-treat (ITT) population.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Stage I: 6-11 Years Old

Arm description:

Participants of 6-11 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

Arm type	Experimental
Investigational medicinal product name	TMC125
Investigational medicinal product code	TMC125 (Formulation - F060 and F066)
Other name	R165335, Lab code 094268
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants of 6-11 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

<b>Arm title</b>	Stage I: 12-17 Years Old
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Arm description:

Participants of 12-17 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

Arm type	Experimental
Investigational medicinal product name	TMC125
Investigational medicinal product code	TMC125 (Formulation - F060 and F066)
Other name	R165335, Lab code 094268
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants of 12-17 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

<b>Arm title</b>	Stage II: 6-11 Years Old
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Arm description:

Participants of 6-11 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

Arm type	Experimental
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Investigational medicinal product name	TMC125
Investigational medicinal product code	TMC125 (Formulation - F060 and F066)
Other name	R165335, Lab code 094268
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants of 6-11 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

<b>Arm title</b>	Stage II: 12-17 Years Old
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Arm description:

Participants of 12-17 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

Arm type	Experimental
Investigational medicinal product name	TMC125
Investigational medicinal product code	TMC125 (Formulation - F060 and F066)
Other name	R165335, Lab code 094268
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants of 12-17 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.

<b>Number of subjects in period 1</b>	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old
Started	10	11	12
Completed	10	10	12
Not completed	0	1	0
Adverse Event	-	1	-

<b>Number of subjects in period 1</b>	Stage II: 12-17 Years Old
Started	9
Completed	9
Not completed	0
Adverse Event	-

## Baseline characteristics

### Reporting groups

Reporting group title	Stage I: 6-11 Years Old
Reporting group description: Participants of 6-11 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	
Reporting group title	Stage I: 12-17 Years Old
Reporting group description: Participants of 12-17 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	
Reporting group title	Stage II: 6-11 Years Old
Reporting group description: Participants of 6-11 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	
Reporting group title	Stage II: 12-17 Years Old
Reporting group description: Participants of 12-17 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	

Reporting group values	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old
Number of subjects	10	11	12
Title for AgeCategorical Units: subjects			
Children (2-11 years)	10	0	12
Adolescents (12-17 years)	0	11	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	8.6	13.7	14.4
standard deviation	± 1.35	± 1.49	± 1.74
Title for Gender Units: subjects			
Female	4	4	8
Male	6	7	4

Reporting group values	Stage II: 12-17 Years Old	Total	
Number of subjects	9	42	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	22	
Adolescents (12-17 years)	9	20	
Adults (18-64 years)	0	0	
From 65 to 84 years	0	0	
85 years and over	0	0	

Title for AgeContinuous Units: years arithmetic mean standard deviation	9.2 ± 1.27	-	
Title for Gender Units: subjects			
Female	5	21	
Male	4	21	

## End points

### End points reporting groups

Reporting group title	Stage I: 6-11 Years Old
Reporting group description: Participants of 6-11 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	
Reporting group title	Stage I: 12-17 Years Old
Reporting group description: Participants of 12-17 years old received 4 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	
Reporting group title	Stage II: 6-11 Years Old
Reporting group description: Participants of 6-11 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	
Reporting group title	Stage II: 12-17 Years Old
Reporting group description: Participants of 12-17 years old received 5.2 milligram per kilogram (mg/kg) twice daily for 7 days with an additional morning dose on Day 8.	
Subject analysis set title	Intent-to-treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: The intent-to-treat (ITT) population include those participants who had received at least 1 dose of study medication.	

### Primary: Minimum Plasma Concentration (Cmin) of TMC125

End point title	Minimum Plasma Concentration (Cmin) of TMC125 <sup>[1]</sup>
End point description: The Cmin is the minimum observed plasma concentration of TMC125.	
End point type	Primary
End point timeframe: Pre-dose; 0, 1, 2, 3, 4, 6, 8, 10 and 12 hours post-dose on Day 8	
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	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old	Stage II: 12-17 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	11	9
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	208.6 (± 210.1)	160.8 (± 70.16)	362.8 (± 351.7)	210.5 (± 119.8)

### Statistical analyses

No statistical analyses for this end point

### Primary: Area Under the Plasma Concentration-Time Curve From 0 to 12 Hours (AUC[0-12]) Post Dose of TMC125



End point title	Area Under the Plasma Concentration-Time Curve From 0 to 12 Hours (AUC[0-12]) Post Dose of TMC125 <sup>[2]</sup>
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End point description:

The AUC (0-12hrs) is the area under the plasma TMC125 concentration-time curve from 0 to 12 hours post dosing.

End point type	Primary
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End point timeframe:

Pre-dose; 0, 1, 2, 3, 4, 6, 8, 10 and 12 hours post-dose on Day 8

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

End point values	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old	Stage II: 12-17 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	10	11	9
Units: ng.h/mL				
arithmetic mean (standard deviation)	4989 (± 5189)	3299 (± 1468)	7713 (± 7160)	4219 (± 1575)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Predose Plasma Concentration (C0h) of TMC125

End point title	Predose Plasma Concentration (C0h) of TMC125
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End point description:

The C0h is the predose plasma observed concentration of TMC125.

End point type	Secondary
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End point timeframe:

Predose on Day 8

End point values	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old	Stage II: 12-17 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	11	9
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	238.1 (± 202.4)	178 (± 63.23)	453.3 (± 441.6)	246.7 (± 154.6)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Plasma Concentration (Cmax) of TMC125

End point title	Maximum Plasma Concentration (Cmax) of TMC125
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End point description:

The C<sub>max</sub> is the maximum observed plasma concentration of TMC125.

End point type	Secondary
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End point timeframe:

Pre-dose; 0, 1, 2, 3, 4, 6, 8, 10 and 12 hours post-dose on Day 8

End point values	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old	Stage II: 12-17 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	11	9
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	597.9 (± 634.8)	402.9 (± 180.5)	971.1 (± 866.4)	494.3 (± 144)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Reach the Maximum Plasma Concentration (T<sub>max</sub>) of TMC125

End point title	Time to Reach the Maximum Plasma Concentration (T <sub>max</sub> ) of TMC125
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End point description:

The T<sub>max</sub> is the time to reach the maximum observed plasma concentration of TMC125.

End point type	Secondary
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End point timeframe:

Pre-dose; 0, 1, 2, 3, 4, 6, 8, 10 and 12 hours post-dose on Day 8

End point values	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old	Stage II: 12-17 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	11	9
Units: Hour (h)				
median (full range (min-max))	4.02 (2.83 to 8)	4 (2 to 6.02)	4 (2 to 6.07)	3.92 (2.98 to 6)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Average Steady-State Plasma Concentration (C<sub>ss,av</sub>) of TMC125

End point title	Average Steady-State Plasma Concentration (C <sub>ss,av</sub> ) of TMC125
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End point description:

The  $C_{ss,av}$  is calculated by area under the plasma concentration-time curve (AUC) x dosing interval/dosing interval at steady-state ( $AUC_{\tau} / \tau$ ), where  $\tau$  = dosing interval.

End point type	Secondary
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End point timeframe:

Pre-dose; 0, 1, 2, 3, 4, 6, 8, 10 and 12 hours post-dose on Day 8

End point values	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old	Stage II: 12-17 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	10	11	9
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	416.3 (± 431.3)	275.8 (± 121.8)	644.3 (± 595.7)	352.6 (± 132.6)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Fluctuation Index (FI Ind) of TMC125

End point title	Fluctuation Index (FI Ind) of TMC125
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End point description:

The FI Ind is defined as percentage fluctuation is variation between maximum and minimum plasma concentration at steady-state, calculated as  $100 \times ([C_{max} - C_{min}] / C_{ss,av})$ .

End point type	Secondary
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End point timeframe:

Pre-dose; 0, 1, 2, 3, 4, 6, 8, 10 and 12 hours post-dose on Day 8

End point values	Stage I: 6-11 Years Old	Stage I: 12-17 Years Old	Stage II: 6-11 Years Old	Stage II: 12-17 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	10	11	9
Units: Percentage (%)				
arithmetic mean (standard deviation)	107.9 (± 44.09)	87.97 (± 13.23)	102.9 (± 24.98)	86.79 (± 26.75)

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Screening up to Follow-up (1 month after last dose administration)

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.1
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### Reporting groups

Reporting group title	Stage I: 6-11 years old
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Reporting group description:

Stage I Subjects 6-11 years old received 4 mg/kg BID for 7 days with an additional morning dose on Day 8

Reporting group title	Stage I: 12-17 years old
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Reporting group description: -

Reporting group title	Stage II: 6-11 years old
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Reporting group description:

Stage II Subjects 6-11 years old received 5.2 mg/kg BID for 7 days with an additional morning dose on Day 8

Reporting group title	Stage II: 12-17 years old
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Reporting group description: -

Serious adverse events	Stage I: 6-11 years old	Stage I: 12-17 years old	Stage II: 6-11 years old
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Stage II: 12-17 years old		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

<b>Non-serious adverse events</b>	Stage I: 6-11 years old	Stage I: 12-17 years old	Stage II: 6-11 years old
Total subjects affected by non-serious adverse events subjects affected / exposed	7 / 10 (70.00%)	7 / 11 (63.64%)	3 / 12 (25.00%)
Investigations			
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
Injury, poisoning and procedural complications			
Excoriation subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Traumatic haematoma subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	2 / 11 (18.18%) 2	0 / 12 (0.00%) 0
Syncope vasovagal subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
Blood and lymphatic system disorders			
Lymphadenitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
Diarrhoea			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1
Vomiting subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Pharyngeal erythema subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
Rash subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0

Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
Pharyngotonsillitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1

<b>Non-serious adverse events</b>	Stage II: 12-17 years old		
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 9 (66.67%)		
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Injury, poisoning and procedural complications Excoriation subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Traumatic haematoma subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Headache			

subjects affected / exposed occurrences (all)  Syncope vasovagal subjects affected / exposed occurrences (all)	3 / 9 (33.33%)  4  0 / 9 (0.00%)  0		
Blood and lymphatic system disorders Lymphadenitis subjects affected / exposed occurrences (all)	0 / 9 (0.00%)  0		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)	0 / 9 (0.00%)  0  1 / 9 (11.11%)  1  0 / 9 (0.00%)  0  0 / 9 (0.00%)  0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)  Pharyngeal erythema subjects affected / exposed occurrences (all)  Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	0 / 9 (0.00%)  0  0 / 9 (0.00%)  0  0 / 9 (0.00%)  0		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	0 / 9 (0.00%)  0		



Rash			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pharyngotonsillitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2006	The overall reason for the amendment was to delete baseline urine alcohol and drug test and to remove the requirement for automated device for blood pressure and pulse rate measurements.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported