Clinical trial results:
A Comparative Single-Dose Pharmacokinetic and Safety Study of TAK-491 Between Infants, Children, and Adolescents with Hypertension and Healthy Adults

Summary

EudraCT number	2009-013165-25
Trial protocol	GB Outside EU/EEA
Global end of trial date	10 July 2013

Results information

Result version number	v1 (current)
This version publication date	04 March 2016
First version publication date	26 July 2015

Trial information

Trial identification

Sponsor protocol code	TAK-491_109

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01078376
WHO universal trial number (UTN)	U1111-1113-4416

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	One Takeda Parkway, Deerfield, IL, United States, 60015
Public contact	Medical Director, Clinical Science, Takeda , +1 877-825-3327, trialdisclosures@takeda.com
Scientific contact	Medical Director, Clinical Science, Takeda , +1 877-825-3327, trialdisclosures@takeda.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000237-PIP01-08
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	12 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2013
Global end of trial reached?	Yes
Global end of trial date	10 July 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to determine the pharmacokinetic parameters, safety, and tolerability of a single dose of TAK-491 in pediatric subjects with hypertension, who are between the ages of 1 to 16 years (including those up to their 17th birthday) and gender matched healthy adult subjects aged 18 to 45 years, inclusive.

Takeda decided to close Cohort 3 (participants between 1 and 6 years of age with hypertension) enrollment early and end this study with the agreement of both the US Food and Drug Administration (FDA) and the Pediatric Committee (PDCO) at the European Medicines Agency. Requests to the FDA and PDCO were submitted to close the study without completion of enrollment in Cohort 3 due to difficulty enrolling this particular patient population. Takeda proposed an alternative option to collect PK data in this age subset by utilizing PK modeling to determine the appropriate doses in children 1-5 years of age in lieu of completing Cohort 3.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 May 2010
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	United Kingdom: 5
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	29
EEA total number of subjects	5

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)	11
Adolescents (12-17 years)	9
Adults (18-64 years)	9
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 6 sites in the United States and 3 sites in the United Kingdom from 10 May 2010 to 10 July 2013.

Pre-assignment

Screening details:

Children between the ages of 1 to 16 years (including up to their 17th birthday) with hypertension and gender-matched healthy adults aged 18 to 45 years, inclusive, were enrolled in 1 of 3 cohorts.

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
Arm title	Cohort 1: Healthy Adults

Arm description:

Azilsartan medoxomil 80 mg, tablets, orally, one day only

Arm type	Experimental
Investigational medicinal product name	Azilsartan medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Azilsartan medoxomil tablets

Arm title	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg

Arm description:

Azilsartan medoxomil 40-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.

Arm type	Experimental
Investigational medicinal product name	Azilsartan medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Azilsartan medoxomil tablets

Arm title	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg

Arm description:

Azilsartan medoxomil 20-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 20 to < 40 kg received a 20 mg dose, participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.

Arm type	Experimental

Investigational medicinal product name	Azilsartan medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Azilsartan medoxomil tablets

Arm title	Cohort 3: Children (≥1 to <6 Years Old)

Arm description:

Azilsartan medoxomil 0.66 mg/kg participant body weight, granules, reconstituted orally, one day only.

Arm type	Experimental
Investigational medicinal product name	Azilsartan medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Azilsartan medoxomil granules for oral suspension

Number of subjects in period 1	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg
Started	9	9	8
Completed	9	9	8

Number of subjects in period 1	Cohort 3: Children (≥1 to <6 Years Old)
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Healthy Adults
Reporting group description:	
Azilsartan medoxomil 80 mg, tablets, orally, one day only	
Reporting group title	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg
Reporting group description:	
Azilsartan medoxomil 40-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.	
Reporting group title	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg
Reporting group description:	
Azilsartan medoxomil 20-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 20 to < 40 kg received a 20 mg dose, participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.	
Reporting group title	Cohort 3: Children (≥1 to <6 Years Old)
Reporting group description:	
Azilsartan medoxomil 0.66 mg/kg participant body weight, granules, reconstituted orally, one day only.	

Reporting group values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg
Number of subjects	9	9	8
Age categorical Units: Subjects			
Children (2-11 years)	0	0	8
Adolescents (12-17 years)	0	9	0
Adults (18-64 years)	9	0	0
Age continuous Units: years			
arithmetic mean	28.3	14.2	9.1
standard deviation	± 7.78	± 1.64	± 2.1
Gender categorical Units: Subjects			
Female	2	2	5
Male	7	7	3
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	4	0	1
Not Hispanic or Latino	5	7	5
Not Reported	0	2	2
Race/Ethnicity, Customized Units: Subjects			
Asian	0	0	1
Black or African American	1	2	2
White	8	7	5
Height Units: cm			
arithmetic mean	172.6	163.1	138.6
standard deviation	± 9.7	± 11.72	± 12.74

Weight			
Units: kg			
arithmetic mean	74.64	71.71	48.5
standard deviation	± 11.207	± 15.512	± 22.523
Body Mass Index (BMI)			
Units: kg/m^2			
arithmetic mean	25.06	27.22	24.29
standard deviation	± 3.345	± 6.611	± 8.327

Reporting group values	Cohort 3: Children (≥1 to <6 Years Old)	Total	
Number of subjects	3	29	
Age categorical			
Units: Subjects			
Children (2-11 years)	3	11	
Adolescents (12-17 years)	0	9	
Adults (18-64 years)	0	9	
Age continuous			
Units: years			
arithmetic mean	4.7		
standard deviation	± 0.58	-	
Gender categorical			
Units: Subjects			
Female	2	11	
Male	1	18	
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	0	5	
Not Hispanic or Latino	3	20	
Not Reported	0	4	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	0	1	
Black or African American	2	7	
White	1	21	
Height			
Units: cm			
arithmetic mean	107.7		
standard deviation	± 11.06	-	
Weight			
Units: kg			
arithmetic mean	18.3		
standard deviation	± 4.026	-	
Body Mass Index (BMI)			
Units: kg/m^2			
arithmetic mean	15.67		
standard deviation	± 0.551	-	

End points

End points reporting groups

Reporting group title	Cohort 1: Healthy Adults
Reporting group description:	
Azilsartan medoxomil 80 mg, tablets, orally, one day only	
Reporting group title	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg
Reporting group description:	
Azilsartan medoxomil 40-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.	
Reporting group title	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg
Reporting group description:	
Azilsartan medoxomil 20-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 20 to < 40 kg received a 20 mg dose, participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.	
Reporting group title	Cohort 3: Children (≥1 to <6 Years Old)
Reporting group description:	
Azilsartan medoxomil 0.66 mg/kg participant body weight, granules, reconstituted orally, one day only.	
Subject analysis set title	Cohort 1: Healthy Adults
Subject analysis set type	Per protocol
Subject analysis set description:	
Azilsartan medoxomil 80 mg, tablets, orally, one day only	
Subject analysis set title	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Azilsartan medoxomil 60 mg, tablets, orally, one day only	
Subject analysis set title	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Azilsartan medoxomil 40 mg, tablets, orally, one day only	
Subject analysis set title	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Azilsartan medoxomil 60 mg, tablets, orally, one day only	
Subject analysis set title	Cohort 2: Children (≥6 to <12 Years Old) 40 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Azilsartan medoxomil 40 mg, tablets, orally, one day only	
Subject analysis set title	Cohort 2: Children (≥6 to <12 Years Old) 20 mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Azilsartan medoxomil 20 mg, tablets, orally, one day only	
Subject analysis set title	Cohort 3: Children (≥1 to <6 Years Old)
Subject analysis set type	Per protocol
Subject analysis set description:	
Azilsartan medoxomil 0.66 mg/kg participant body weight, granules, reconstituted orally, one day only	

Primary: Area Under the Plasma Concentration-time Curve From Time 0 to Time of Last Quantifiable Concentration (AUC[0-tlqc]) for TAK-536

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to Time of Last Quantifiable Concentration (AUC[0-tlqc]) for TAK-536[1]

End point description:

AUC(0-tlqc) is a measure of total plasma exposure to the drug from Time 0 to Time of the Last Quantifiable Concentration (AUC[0-tlqc]).

End point type	Primary

End point timeframe:

Day 1

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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[2]
Units: ng.hr/mL				
arithmetic mean (standard deviation)	40613 (± 9609.6)	23889 (± 5383.8)	17423 (± 3559.7)	16056 (± 0)

Notes:

[2] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: ng.hr/mL				
arithmetic mean (standard deviation)	22556 (± 5792.6)	18691 (± 5489.9)	16963 (± 4948.4)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve From Time 0 to Time of Last Quantifiable Concentration (AUC[0-tlqc]) for TAK-536 Metabolite M-II

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to Time of Last Quantifiable Concentration (AUC[0-tlqc]) for TAK-536 Metabolite M-II[3]

End point description:

AUC(0-tlqc) is a measure of total plasma exposure to the drug from Time 0 to Time of the Last Quantifiable Concentration (AUC[0-tlqc]).

End point type	Primary

End point timeframe:

Day 1

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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[4]
Units: ng.hr/mL				
arithmetic mean (standard deviation)	11563 (± 3106.5)	7409 (± 78.6)	7428 (± 2120.7)	7392 (± 0)

Notes:

[4] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: ng.hr/mL				
arithmetic mean (standard deviation)	7929 (± 3502.6)	9130 (± 1338.3)	7285 (± 3626)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve From Time 0 to Infinity (AUC[0-inf]) for TAK-536

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to Infinity (AUC[0-inf]) for TAK-536[5]

End point description:

Area under the plasma concentration-time curve from time 0 to infinity, calculated as AUC(0-inf)=AUC(0-tlqc) + Clast/λz.

End point type	Primary

End point timeframe:

Day 1

Notes:

[5] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[6]
Units: ng.hr/mL				
arithmetic mean (standard deviation)	44820 (± 11680.7)	26411 (± 6703.1)	18686 (± 3720.4)	16563 (± 0)

Notes:

[6] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: ng.hr/mL				
arithmetic mean (standard deviation)	23792 (± 6157)	19543 (± 6181.1)	17771 (± 5263.1)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve From Time 0 to Infinity (AUC[0-inf]) for TAK-536 Metabolite M-II

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to Infinity (AUC[0-inf]) for TAK-536 Metabolite M-II[7]

End point description:

Area under the plasma concentration-time curve from time 0 to infinity, calculated as AUC(0-inf)=AUC(0-tlqc) + Clast/λz.

End point type	Primary

End point timeframe:

Day 1

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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[8]
Units: ng.hr/mL				
arithmetic mean (standard deviation)	19188 (± 6766)	10596 (± 1168.8)	12532 (± 3905.3)	8961 (± 0)

Notes:

[8] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: ng.hr/mL				
arithmetic mean (standard deviation)	11387 (± 5440.7)	14230 (± 3419.6)	9477 (± 4659.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) for TAK-536

End point title	Maximum Observed Plasma Concentration (Cmax) for TAK-

End point description:

Maximum observed plasma concentration (Cmax) is the peak plasma concentration of a drug after administration, obtained directly from the plasma concentration-time curve.

End point type	Primary

End point timeframe:

Day 1

Notes:

[9] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[10]
Units: ng/mL				
arithmetic mean (standard deviation)	5699 (± 1346.1)	3245 (± 106.1)	2512 (± 701.6)	2810 (± 0)

Notes:

[10] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: ng/mL				
arithmetic mean (standard deviation)	3858 (± 1363)	2960 (± 364.3)	3320 (± 656)	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) for TAK-536 Metabolite M-II

End point title	Maximum Observed Plasma Concentration (Cmax) for TAK-536 Metabolite M-II[11]

End point description:

Maximum observed plasma concentration (Cmax) is the peak plasma concentration of a drug after administration, obtained directly from the plasma concentration-time curve.

End point type	Primary

End point timeframe:

Day 1

Notes:

[11] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[12]
Units: ng/mL				
arithmetic mean (standard deviation)	736 (± 241.6)	480 (± 74.2)	535 (± 200.2)	514 (± 0)

Notes:

[12] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: ng/mL				
arithmetic mean (standard deviation)	561 (± 211.7)	561 (± 40.3)	488 (± 212.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Cmax (Tmax) for TAK-536

End point title	Time to Reach Cmax (Tmax) for TAK-536[13]

End point description:

Tmax: Time to reach the maximum plasma concentration (Cmax), equal to time (hours) to Cmax, as observed on Day 1.

End point type	Primary

End point timeframe:

Day 1

Notes:

[13] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[14]
Units: hr				
median (full range (min-max))	2 (2 to 4)	2.01 (2 to 2.02)	2 (1 to 2)	2 (2 to 2)

Notes:

[14] - Standard deviation or range cannot be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: hr				
median (full range (min-max))	2 (1.05 to 6)	2 (1.98 to 2)	1 (1 to 1)	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Cmax (Tmax) for TAK-536 Metabolite M-II

End point title	Time to Reach Cmax (Tmax) for TAK-536 Metabolite M-II[15]

End point description:

Tmax: Time to reach the maximum plasma concentration (Cmax), equal to time (hours) to Cmax, as observed on Day 1.

End point type	Primary

End point timeframe:

Day 1

Notes:

[15] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[16]
Units: hr				
median (full range (min-max))	6 (4 to 8)	5 (4 to 6)	6 (4 to 6.1)	6 (6 to 6)

Notes:

[16] - Standard deviation or range cannot be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: hr				
median (full range (min-max))	4.03 (4 to 8)	4 (4 to 8)	6 (6 to 6)	

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Elimination Half-life (T1/2) for TAK-536

End point title	Terminal Elimination Half-life (T1/2) for TAK-536[17]

End point description:

Terminal phase elimination half-life (T1/2) is the time required for half of the drug to be eliminated from the plasma.

End point type	Primary

End point timeframe:

Day 1

Notes:

[17] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[18]
Units: hr				
arithmetic mean (standard deviation)	7.35 (± 1.083)	7.74 (± 0.621)	5.76 (± 1.158)	5.07 (± 0)

Notes:

[18] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to	Cohort 2: Children (≥6 to	Cohort 3: Children (≥1 to	

	<12 Years Old) 40 mg	<12 Years Old) 20 mg	<6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: hr				
arithmetic mean (standard deviation)	5.75 (± 0.76)	5.37 (± 0.922)	4.59 (± 1.627)	

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Elimination Half-life (T1/2) for TAK-536 Metabolite M-II

End point title	Terminal Elimination Half-life (T1/2) for TAK-536 Metabolite M-II[19]

End point description:

Terminal phase elimination half-life (T1/2) is the time required for half of the drug to be eliminated from the plasma.

End point type	Primary

End point timeframe:

Day 1

Notes:

[19] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[20]
Units: hr				
arithmetic mean (standard deviation)	16.6 (± 6.87)	12.78 (± 2.915)	14 (± 2.414)	8.5 (± 0)

Notes:

[20] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: hr				
arithmetic mean (standard deviation)	11.56 (± 3.314)	13.97 (± 2.983)	10.35 (± 2.77)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL/F) for TAK-536

End point title	Apparent Oral Clearance (CL/F) for TAK-536[21]

End point description:

CL/F is apparent clearance of the drug from the plasma, expressed in L/hr.

End point type	Primary

End point timeframe:

Day 1

Notes:

[21] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[22]
Units: L/hr				
arithmetic mean (standard deviation)	1.52 (± 0.414)	1.88 (± 0.477)	1.78 (± 0.411)	2.9 (± 0)

Notes:

[22] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg	Cohort 3: Children (≥1 to <6 Years Old)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	3	
Units: L/hr				
arithmetic mean (standard deviation)	1.43 (± 0.427)	0.87 (± 0.232)	0.54 (± 0.134)	

Statistical analyses

No statistical analyses for this end point

Primary: Total Amount of Drug Excreted in Urine From Time 0 to 24 Hours Postdose (Ae[0-t]) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536)

End point title	Total Amount of Drug Excreted in Urine From Time 0 to 24 Hours Postdose (Ae[0-t]) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536)[23]

End point description:

End point type	Primary

End point timeframe:

Day 1

Notes:

[23] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	3	6	1[24]
Units: mg				
arithmetic mean (standard deviation)	10.65 (± 4.673)	4.56 (± 1.029)	2.89 (± 0.936)	4.59 (± 0)

Notes:

[24] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: mg				
arithmetic mean (standard deviation)	3.63 (± 2.125)	1.27 (± 0.58)		

Statistical analyses

No statistical analyses for this end point

Primary: Total Amount of Drug Excreted in Urine From Time 0 to 24 Hours Postdose (Ae[0-t]) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536 Metabolite M-II)

End point title	Total Amount of Drug Excreted in Urine From Time 0 to 24 Hours Postdose (Ae[0-t]) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536 Metabolite M-II)[25]

End point description:

End point type	Primary

End point timeframe:

Day 1

Notes:

[25] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	3	6	1[26]
Units: mg				
arithmetic mean (standard deviation)	6.6 (± 5.149)	2.93 (± 0.582)	2.73 (± 1.528)	4.43 (± 0)

Notes:

[26] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: mg				
arithmetic mean (standard deviation)	2.77 (± 1.197)	1.48 (± 0.284)		

Statistical analyses

No statistical analyses for this end point

Primary: Fraction of Unchanged Drug Excreted in Urine From 0 to 24 Hours Postdose (Fe%) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536)

End point title	Fraction of Unchanged Drug Excreted in Urine From 0 to 24 Hours Postdose (Fe%) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536)[27]

End point description:

Fe=[Ae(0-24)/dose]×100 (molecular weight adjusted for metabolites.

End point type	Primary

End point timeframe:

Day 1

Notes:

[27] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	3	6	1[28]
Units: percent				
arithmetic mean (standard deviation)	16.65 (± 7.302)	9.5 (± 2.144)	9.04 (± 2.925)	9.57 (± 0)

Notes:

[28] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: percent				
arithmetic mean (standard deviation)	11.36 (± 6.639)	7.94 (± 3.622)		

Statistical analyses

No statistical analyses for this end point

Primary: Fraction of Unchanged Drug Excreted in Urine From 0 to 24 Hours Postdose (Fe%) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536 Metabolite M-II)

End point title	Fraction of Unchanged Drug Excreted in Urine From 0 to 24 Hours Postdose (Fe%) (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536 Metabolite M-II)[29]

End point description:

Fe=[Ae(0-24)/dose]×100 (molecular weight adjusted for metabolites.

End point type	Primary

End point timeframe:

Day 1

Notes:

[29] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	3	6	1[30]
Units: percent				
arithmetic mean (standard deviation)	11.01 (± 8.581)	6.55 (± 1.293)	9.11 (± 5.094)	9.85 (± 0)

Notes:

[30] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: percent				
arithmetic mean (standard deviation)	9.22 (± 3.991)	9.89 (± 1.896)		

Statistical analyses

No statistical analyses for this end point

Primary: Renal Clearance (CLr) From 0 to 24 Hours Postdose (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536)

End point title	Renal Clearance (CLr) From 0 to 24 Hours Postdose (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536)[31]

End point description:

Renal clearance, calculated as CLr=Ae(0-24)/AUC(0-24).

End point type	Primary

End point timeframe:

Day 1

Notes:

[31] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[32]
Units: L/hr				
arithmetic mean (standard deviation)	0.28 (± 0.13)	0.22 (± 0.051)	0.17 (± 0.077)	0.29 (± 0)

Notes:

[32] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: L/hr				
arithmetic mean (standard deviation)	0.15 (± 0.069)	0.07 (± 0.011)		

Statistical analyses

No statistical analyses for this end point

Primary: Renal Clearance (CLr) From 0 to 24 Hours Postdose (for Cohorts 1 and 2

Urine Pharmacokinetic Endpoint for TAK-536 Metabolite M-II)

End point title	Renal Clearance (CLr) From 0 to 24 Hours Postdose (for Cohorts 1 and 2 Urine Pharmacokinetic Endpoint for TAK-536 Metabolite M-II)[33]

End point description:

Renal clearance, calculated as CLr=Ae(0-24)/AUC(0-24).

End point type	Primary

End point timeframe:

Day 1

Notes:

[33] - 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: No Statistical Analysis reported for this End Point.

End point values	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 60 mg	Cohort 1: Adolescents (≥12 to <17 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 60 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	2	6	1[34]
Units: L/hr				
arithmetic mean (standard deviation)	0.55 (± 0.309)	0.37 (± 0.084)	0.34 (± 0.146)	0.6 (± 0)

Notes:

[34] - Standard deviation can not be calculated for 1 participant.

End point values	Cohort 2: Children (≥6 to <12 Years Old) 40 mg	Cohort 2: Children (≥6 to <12 Years Old) 20 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: L/hr				
arithmetic mean (standard deviation)	0.36 (± 0.099)	0.16 (± 0.022)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

A treatment-emergent adverse event (TEAE) had an onset occurring after the first dose of study medication and within 14 days after the last dose of study medication or, if an SAE, within 30 days after last dose of study medication.

Adverse event reporting additional description:

At each visit the investigator assessed whether any subjective adverse events have occurred and had to document any occurrence of adverse events and clinically significant abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Cohort 1: Healthy Adults

Reporting group description:

Azilsartan medoxomil 80 mg, tablets, orally, one day only.

Reporting group title	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg

Reporting group description:

Azilsartan medoxomil 40-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.

Reporting group title	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg

Reporting group description:

Azilsartan medoxomil 20-60 mg, tablets, orally, one day only. Dose regimen was based on body weight. Participants 20 to < 40 kg received a 20 mg dose, participants 40 to < 80 kg received a 40 mg dose and participants 80 to 100 kg received a 60 mg dose.

Reporting group title	Cohort 3: Children (≥1 to <6 Years Old)

Reporting group description:

Azilsartan medoxomil 0.66 mg/kg participant body weight, granules, reconstituted orally, one day only.

Serious adverse events	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Cohort 3: Children (≥1 to <6 Years Old)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events			

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

Non-serious adverse events	Cohort 1: Healthy Adults	Cohort 1: Adolescents (≥12 to <17 Years Old) 40-60 mg	Cohort 2: Children (≥6 to <12 Years Old) 20-60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)	5 / 9 (55.56%)	3 / 8 (37.50%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 9 (0.00%)	2 / 9 (22.22%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Migraine			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Infusion site pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 9 (0.00%)	2 / 9 (22.22%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal			

disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infections and infestations			
Infected bites			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 3: Children (≥1 to <6 Years Old)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

General disorders and administration site conditions Infusion site pain subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0		
Infections and infestations Infected bites subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2010	• Safety endpoints were listed as additional endpoints. • Decided only safety data from pediatric subjects in Cohort 1 and 2 was required to be reviewed, and any adult subjects enrolled up to that time, prior to the commencement of Cohort 3. • Provided guidance on the continuation of subjects with emesis after dosing of study drug. • Height (or length) measurement for pediatric subjects was added.
14 February 2011	• Changed lower age limit of Cohort 3 from ≥6 months to ≥1 year. • Increased weight limit of Cohort 3 from 6.5 to 8.0 kg (17.6 lbs). • Determined that formal interim PK and safety analysis of Cohort 1 and 2 data was to be conducted.
07 December 2012	• Day 1 overnight stay was considered optional and based on investigator discretion. • Inclusion criterion 11 was updated to change the length of time that a subject must be on a stable dose of immunosuppressive therapy, after a renal transplant, from 60 days to 30 days.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported