Clinical trial results:
Phase 2a Study to Evaluate the Efficacy and Safety of MEDI2070 in Subjects with Moderate to Severe Crohn's Disease Who Have Failed or Are Intolerant to Anti-tumor Necrosis Factor-alpha Therapy

Summary

EudraCT number	2012-004098-26
Trial protocol	DE CZ HU IT ES FR
Global end of trial date	14 December 2016

Results information

Result version number	v1 (current)
This version publication date	07 April 2018
First version publication date	07 April 2018

Trial information

Trial identification

Sponsor protocol code	D5170C00001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	MedImmune
Sponsor organisation address	Milstein Building, Granta Park, Cambridge, United Kingdom, CB21 6GH
Public contact	Robert A Gasser, MedImmune, 1 3013982450, gasserr@medimmune.com
Scientific contact	Robert A Gasser, MedImmune, 1 3013982450, gasserr@medimmune.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	14 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of MEDI2070 versus placebo to induce a clinical effect (defined as at least a 100-point reduction in Crohn's Disease Activity Index [CDAI] from baseline) or remission at Week 8 in subjects with moderate to severe Crohn’s Disease.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and was consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements, and any conditions required by a regulatory authority and/or Institutional Review Board/ Independent Ethics Committee that approved this study. Subjects signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2013
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 States: 31
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Poland: 6
Worldwide total number of subjects	121
EEA total number of subjects	66

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)	121
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 174 subjects were screened between 01Feb2013 and 26Feb2014 across 9 countries (USA, Canada, Czech Republic, France, Germany, Hungary, Italy, Poland, and Spain).

Pre-assignment

Screening details:

Out of 174 screened subjects, 53 were considered screen failures. A total of 121 subjects were randomized, of which 2 did not receive study drugs and 119 were treated in the study.

Period 1

Period 1 title	Double-Blind Induction Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received IV Placebo at Week 0 and Week 4.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo (matching to MEDI2070 700 mg) was administered by intravenous (IV) infusion at Week 0 (Day 1) and Week 4 in double-blind period. Placebo was delivered in 5.0% weight/volume (w/v) dextrose in a volume of 100 mL over a minimum of 60 minutes using an infusion pump.

Arm title	MEDI2070 700mg

Arm description:

Subject received IV MEDI2070 700mg at Week 0 and Week 4.

Arm type	Experimental
Investigational medicinal product name	MEDI2070
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

MEDI2070 700mg was administered by IV infusion at Week 0 (Day 1) and Week 4 in double-blind period. MEDI2070 was delivered in 5.0% w/v dextrose in a volume of 100 mL over a minimum of 60 minutes using an infusion pump.

Number of subjects in period 1[1]	Placebo	MEDI2070 700mg
Started	60	59
Completed	52	52
Not completed	8	7
Consent withdrawn by subject	5	3
Adverse event, non-fatal	-	1
Subject not entered in open label period	3	1
Lost to follow-up	-	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Total subjects enrolled worldwide were 121; of which 2 subjects were randomized but not treated. Those 2 subject were not included in mITT population and data for those 2 subjects were not captured for baseline characteristics.

Period 2

Period 2 title	Open-Label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/MEDI2070 210mg

Arm description:

Subjects randomized to placebo arm in double-blind period received 210 mg SC MEDI2070 every 4 weeks (Q4W) during the 100-week, open-label treatment period.

Arm type	Experimental
Investigational medicinal product name	MEDI2070
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI2070 210 mg was administered by subcutaneous (SC) injection every 4 weeks (Q4W) between Week 12 and Week 112 in open-label period.

Arm title	MEDI2070 700mg/MEDI2070 210mg

Arm description:

Subjects randomized to MEDI2070 700mg arm in double-blind period received 210 mg SC MEDI2070 Q4W during the 100-week, open-label treatment period.

Arm type	Experimental
Investigational medicinal product name	MEDI2070
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

MEDI2070 210 mg was administered by SC injection every 4 weeks (Q4W) between Week 12 and Week 112 in open-label period.

Number of subjects in period 2	Placebo/MEDI2070 210mg	MEDI2070 700mg/MEDI2070 210mg
Started	52	52
Completed	33	24
Not completed	19	28
Consent withdrawn by subject	9	19
Adverse event, non-fatal	1	-
Not specified	1	3
Lost to follow-up	3	4
Development of study-specific withdrawal criteria	5	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received IV Placebo at Week 0 and Week 4.	
Reporting group title	MEDI2070 700mg
Reporting group description:	
Subject received IV MEDI2070 700mg at Week 0 and Week 4.	

Reporting group values	Placebo	MEDI2070 700mg	Total
Number of subjects	60	59	119
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	60	59	119
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	38.1	34.8	
standard deviation	± 10.7	± 11.1	-
Gender, Male/Female Units: Subjects			
Female	37	37	74
Male	23	22	45
CDAI score Units: Scores on a scale			
arithmetic mean	312.4	325.0	
standard deviation	± 56.3	± 59.2	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received IV Placebo at Week 0 and Week 4.	
Reporting group title	MEDI2070 700mg
Reporting group description:	
Subject received IV MEDI2070 700mg at Week 0 and Week 4.	
Reporting group title	Placebo/MEDI2070 210mg
Reporting group description:	
Subjects randomized to placebo arm in double-blind period received 210 mg SC MEDI2070 every 4 weeks (Q4W) during the 100-week, open-label treatment period.	
Reporting group title	MEDI2070 700mg/MEDI2070 210mg
Reporting group description:	
Subjects randomized to MEDI2070 700mg arm in double-blind period received 210 mg SC MEDI2070 Q4W during the 100-week, open-label treatment period.	

Primary: Percentage of Subjects With Crohn's Disease Activity Index (CDAI) Response at Week 8

End point title	Percentage of Subjects With Crohn's Disease Activity Index (CDAI) Response at Week 8
End point description:	
A CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over 7 days includes subject reported symptoms, physician-assessed signs, and laboratory markers. CDAI score = Sum of weighted scores for subjective items (number of liquid/soft stools, degree of abdominal pain, general well-being); and objective items (associated signs, use of anti-diarrhoeal medication, abdominal mass, haematocrit, daily morning temperature, body weight). CDAI scores range approximately from 0 to 600, higher scores indicating greater disease activity. The CDAI response at Week 8 is defined as either CDAI score of less than (<) 150 or CDAI reduction from baseline of at least 100 points, where baseline was last non-missing observation prior to first administration of the study drug. Modified Intent-to-treat (mITT) population was analysed for this end point, which included all subjects who were randomized and received at least 1 dose of study drug in double-blind period.	
End point type	Primary
End point timeframe:	
Week 8	

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Percentage of subjects				
number (not applicable)	26.7	49.2		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v MEDI2070 700mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Regression, Logistic
Parameter estimate	Risk Difference
Point estimate	22.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	8.3
upper limit	36.8

Secondary: Percentage of Subjects With CDAI Remission at Week 8

End point title	Percentage of Subjects With CDAI Remission at Week 8

End point description:

The CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over 7 days and includes subject reported symptoms, physician-assessed signs, and laboratory markers. The CDAI score is calculated by summing weighted scores for subjective items (number of liquid or very soft stools, the degree of abdominal pain over a week and general well-being; and objective items (associated signs, use of anti-diarrhoeal medication, abdominal mass, haematocrit, daily morning temperature, and body weight). The CDAI scores range approximately from 0 to 600, with higher scores indicating greater disease activity. The CDAI score of < 150 represent CDAI remission. Subjects in the mITT population were analysed for this end point.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Percentage of subjects				
number (not applicable)	15	27.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With CDAI-100 Point Improvement at Week 8

End point title	Percentage of Subjects With CDAI-100 Point Improvement at Week 8

End point description:

The CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over

7 days and includes subject reported symptoms, physician-assessed signs, and laboratory markers. The CDAI score is calculated by summing weighted scores for subjective items (number of liquid or very soft stools, the degree of abdominal pain over a week and general well-being; and objective items (associated signs, use of anti-diarrhoeal medication, abdominal mass, haematocrit, daily morning temperature, and body weight). The CDAI scores range approximately from 0 to 600, with higher scores indicating greater disease activity. CDAI 100-point improvement is defined as a reduction from baseline in CDAI score of at least 100 points/scores, where baseline was the latest nonmissing observation prior to first administration of the study drug. Subjects in the mITT population were analysed for this end point.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Percentage of subjects				
number (not applicable)	25	45.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With CDAI-70 Point Improvement at Week 8

End point title	Percentage of Subjects With CDAI-70 Point Improvement at Week 8

End point description:

The CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over 7 days and includes subject reported symptoms, physician-assessed signs, and laboratory markers. The CDAI score is calculated by summing weighted scores for subjective items (number of liquid or very soft stools, the degree of abdominal pain over a week and general well-being; and objective items (associated signs, use of anti-diarrhoeal medication, abdominal mass, haematocrit, daily morning temperature, and body weight). The CDAI scores range approximately from 0 to 600, with higher scores indicating greater disease activity. CDAI 70-point improvement is defined as a reduction from baseline in CDAI score of at least 70 points/scores, where baseline was the latest nonmissing observation prior to first administration of the study drug. Subjects in the mITT population were analysed for this end point.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Percentage of subjects				
number (not applicable)	46.7	52.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With CDAI Response at Week 12

End point title	Percentage of Subjects With CDAI Response at Week 12

End point description:

The CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over 7 days and includes subject reported symptoms, physician-assessed signs, and laboratory markers. The CDAI score is calculated by summing weighted scores for subjective items (number of liquid or very soft stools, the degree of abdominal pain over a week and general well-being; and objective items (associated signs, use of anti-diarrhoeal medication, abdominal mass, haematocrit, daily morning temperature, and body weight). The CDAI scores range approximately from 0 to 600, with higher scores indicating greater disease activity. CDAI response is defined by either a CDAI score of < 150 or a CDAI reduction from baseline of at least 100 points, where baseline was the latest non-missing observation prior to first administration of the study drug. Subjects in the mITT population were analysed for this end point.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Percentage of subjects				
number (not applicable)	28.3	37.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI Total Score at Week 8

End point title	Change from Baseline in CDAI Total Score at Week 8

End point description:

The CDAI is a multi-item instrument which measures severity of active Crohn's Disease monitored over 7 days and includes subject reported symptoms, physician-assessed signs, and laboratory markers. The CDAI score is calculated by summing weighted scores for subjective items (number of liquid or very soft stools, the degree of abdominal pain over a week and general well-being; and objective items (associated signs, use of anti-diarrhoeal medication, abdominal mass, haematocrit, daily morning temperature, and body weight). The CDAI scores range approximately from 0 to 600, with higher scores indicating greater disease activity. Subjects in the mITT population were analysed for this end point.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	52		
Units: Scores on a scale				
least squares mean (standard error)	-62.7 (± 13.5)	-99.0 (± 15.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) in Double-blind Period

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) in Double-blind Period

End point description:

An Adverse Event (AE) is any unfavourable and unintended sign, symptoms, or diseases temporally associated with use of study drug, whether or not considered related to study drug. A serious adverse event (SAE) is any AE that resulted in death, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, lifethreatening, a congenital anomaly/birth defect, or an important medical event. The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug (Day 1) to 36 weeks post treatment (approximately 48 weeks). The safety population was analysed for this end point, which included all subjects who received any amount of study drug.

End point type	Secondary

End point timeframe:

From study drug administration (Day 1) to 36 weeks post last blinded dose (up to 48 weeks)

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Subjects				
Any TEAEs	41	40		
Any TESAEs	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With TEAEs and TESAEs in Open-label Period

End point title	Number of Subjects With TEAEs and TESAEs in Open-label Period

End point description:

An AE is any unfavourable and unintended sign, symptoms, or diseases temporally associated with use of study drug, whether or not considered related to study drug. A SAE is any AE that resulted in death, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, lifethreatening, a congenital anomaly/birth defect, or an important medical event. The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug (Day 1) to 36 weeks post treatment (approximately 148 weeks). Open-label population was analysed for this endpoint, which included all subjects who were enrolled in the 100-week, open-label treatment period and have at least one dose of open-label MEDI2070 210 mg SC treatment.

End point type	Secondary

End point timeframe:

From first open-label dose administration (Week 12) to 36 weeks post last dose (up to 148 weeks)

End point values	Placebo/MEDI2070 210mg	MEDI2070 700mg/MEDI2070 210mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Subjects				
Any TEAEs	44	43		
Any TESAEs	8	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinical Laboratory Abnormalities Reported as TEAEs in Double-blind Period

End point title	Number of Subjects with Clinical Laboratory Abnormalities Reported as TEAEs in Double-blind Period

End point description:

The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug (Day 1) to 36 weeks post treatment (up to approximately 48 weeks). Subjects in the safety population were analysed for this end point.

End point type	Secondary

End point timeframe:

From study drug administration (Day 1) to 36 weeks post last blinded dose (up to 48 weeks)

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Subjects				
Anaemia	2	1		
Leukopenia	0	1		
Neutropenia	0	1		
Urine analysis abnormal	1	0		
Urine abnormality	0	1		
Urine bilirubin increased	0	1		
Proteinuria	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinical Laboratory Abnormalities Reported as TEAEs in Open-label Period

End point title	Number of Subjects with Clinical Laboratory Abnormalities Reported as TEAEs in Open-label Period

End point description:

The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug (Day 1) to 36 weeks post treatment (up to approximately 148 weeks). Open-label population was analysed for this endpoint, which included all subjects who were enrolled in the 100-week, open-label treatment period and have at least one dose of open-label MEDI2070 210 mg SC treatment.

End point type	Secondary

End point timeframe:

From first open-label dose administration (Week 12) to 36 weeks post last dose (up to 148 weeks)

End point values	Placebo/MEDI2070 210mg	MEDI2070 700mg/MEDI2070 210mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Subjects				
Anaemia	5	5		
Lymphocyte count decreased	0	1		
Lymphopenia	0	1		
Neutrophil count increased	0	1		
Platelet count increased	0	1		
Red cell distribution width increased	0	1		
White blood cell count decreased	0	1		
Chromaturia	0	1		
Blood uric acid increased	1	0		
Hypokalaemia	1	1		
Hepatic enzyme increased	0	1		
Hyperlipidemia	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Signs Abnormalities Reported as TEAEs in Double-blind Period

End point title	Number of Subjects With Vital Signs Abnormalities Reported as TEAEs in Double-blind Period

End point description:

The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug (Day 1) to 36 weeks post treatment (approximately 48 weeks). Subjects in the safety population were analysed for this end point.

End point type	Secondary

End point timeframe:

From study drug administration (Day 1) to 36 weeks post last blinded dose (up to 48 weeks)

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Signs Abnormalities Reported as TEAEs in Open-label Period

End point title	Number of Subjects With Vital Signs Abnormalities Reported as TEAEs in Open-label Period

End point description:

The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug (Day 1) to 36 weeks post treatment (approximately 148 weeks). Open-label population was analysed for this endpoint, which included all subjects who were enrolled in the 100-week, open-label treatment period and have at least one dose of open-label MEDI2070 210 mg SC treatment.

End point type	Secondary

End point timeframe:

From first open-label dose administration (Week 12) to 36 weeks post last dose (up to 148 weeks)

End point values	Placebo/MEDI2070 210mg	MEDI2070 700mg/MEDI2070 210mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Mean Serum Concentration of MEDI2070 in Double-blind Period

End point title	Maximum Mean Serum Concentration of MEDI2070 in Double-blind Period

End point description:

Pharmacokinetic (PK) population included all subjects who received at least one dose of MEDI2070 (either in double-blind period or in open-label period) and had at least one PK sample that was above the lower limit of quantification was considered for this end point. Serum concentration of MEDI2070 for subject in 'Placebo' arm is not applicable for this time frames and is reported by an arbitrary value (99999). Here, 'n' denotes number of subjects analysed for specified time points.

End point type	Secondary

End point timeframe:

Post-dose on Week 0 (Day 1); pre and post-dose on Week 4; pre-dose on Week 8

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Week 0 Post-dose (n= 60, 58)	99999 (± 99999)	186 (± 83.8)		
Week 4 Pre-dose (n= 54, 53)	99999 (± 99999)	37.4 (± 52.3)		
Week 4 Post-dose (n= 52, 51)	99999 (± 99999)	209 (± 68.9)		
Week 8 Post-dose (n= 55, 51)	99999 (± 99999)	39.2 (± 18.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Mean Serum Concentration of MEDI2070 in Open-label Period

End point title	Maximum Mean Serum Concentration of MEDI2070 in Open-label Period

End point description:

The PK population included all subjects who received at least one dose of MEDI2070 (either in double-blind period or in open-label period) and had at least one PK sample that was above the lower limit of quantification was considered for this end point. Serum concentration of MEDI2070 for subject in 'Placebo' arm is not applicable for pre-dose Week 12 time frame and is reported by an arbitrary value (99999). Here, 'n' denotes number of subjects analysed for specified time points.

End point type	Secondary

End point timeframe:

Pre-dose on Weeks 12, 24, and 112

End point values	Placebo/MEDI2070 210mg	MEDI2070 700mg/MEDI2070 210mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Week 12 Pre-dose (51, 52)	99999 (± 99999)	16.7 (± 11.8)		
Week 24 Pre-dose (n= 48, 43)	14.5 (± 7.0)	15.1 (± 6.38)		
Week 112 Pre-dose (n= 24, 20)	18.3 (± 7.73)	22.4 (± 7.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Anti-drug Antibody (ADA) to MEDI2070 in Double-blind Period

End point title	Number of Subjects With Positive Anti-drug Antibody (ADA) to MEDI2070 in Double-blind Period

End point description:

The PK population included all subjects who received at least one dose of MEDI2070 (either in double-blind period or in open-label period) and had at least one PK sample that was above the lower limit of quantification was considered for this end point.

End point type	Secondary

End point timeframe:

Baseline (Week0/Day 1) up to 28 week post last dose (approximately 36 weeks)

End point values	Placebo	MEDI2070 700mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	59		
Units: Subjects	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With ADA Positive to MEDI2070 in Open-label Period

End point title	Number of Subjects With ADA Positive to MEDI2070 in Open-label Period

End point description:

The PK population included all subjects who received at least one dose of MEDI2070 (either in double-blind period or in open-label period) and had at least one PK sample that was above the lower limit of quantification was considered for this end point.

End point type	Secondary

End point timeframe:

Up to 28 week post last dose (approximately 140 weeks)

End point values	Placebo/MEDI2070 210mg	MEDI2070 700mg/MEDI2070 210mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Subjects	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From study drug administration (Day 1) to 36 weeks post last dose (approximately 148 weeks)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received IV Placebo at Week 0 and Week 4.	
Reporting group title	MEDI2070 700mg
Reporting group description:	
Subjects received IV MEDI2070 700mg at Week 0 and Week 4.	
Reporting group title	Placebo/MEDI2070 210mg
Reporting group description:	
Subjects who completed the placebo treatment in double-blind period were entered in open-label period to receive SC MEDI2070 210mg Q4W starting from Week 12 to Week 112.	
Reporting group title	MEDI2070 700mg/MEDI2070 210mg
Reporting group description:	
Subjects who completed IV MEDI2070 700 mg treatment in double-blind period were entered in open-label period to receive SC MEDI2070 210mg Q4W starting from Week 12 to Week 112.	

Serious adverse events	Placebo	MEDI2070 700mg	Placebo/MEDI2070 210mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 60 (8.33%)	5 / 59 (8.47%)	8 / 52 (15.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Intestinal anastomosis complication			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental exposure to product			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Shock			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adverse drug reaction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	2 / 60 (3.33%)	2 / 59 (3.39%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cellulitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MEDI2070 700mg/MEDI2070 210mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 52 (23.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Intestinal anastomosis complication			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Accidental exposure to product			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Shock			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Pyrexia				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adverse drug reaction				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Crohn's disease				
subjects affected / exposed	6 / 52 (11.54%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Nephrolithiasis				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Myalgia				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 52 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Peritonitis			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Placebo	MEDI2070 700mg	Placebo/MEDI2070 210mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 60 (63.33%)	38 / 59 (64.41%)	43 / 52 (82.69%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 60 (0.00%)	3 / 59 (5.08%)	1 / 52 (1.92%)
occurrences (all)	0	4	1
Headache			
subjects affected / exposed	4 / 60 (6.67%)	10 / 59 (16.95%)	12 / 52 (23.08%)
occurrences (all)	5	11	62
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 60 (6.67%)	1 / 59 (1.69%)	5 / 52 (9.62%)
occurrences (all)	4	2	7
Asthenia			
subjects affected / exposed	1 / 60 (1.67%)	2 / 59 (3.39%)	1 / 52 (1.92%)
occurrences (all)	1	2	1
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 59 (1.69%)	5 / 52 (9.62%)
occurrences (all)	1	1	6
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 60 (10.00%)	6 / 59 (10.17%)	9 / 52 (17.31%)
occurrences (all)	10	7	15
Crohn's disease			
subjects affected / exposed	3 / 60 (5.00%)	3 / 59 (5.08%)	6 / 52 (11.54%)
occurrences (all)	3	3	6
Diarrhoea			
subjects affected / exposed	4 / 60 (6.67%)	0 / 59 (0.00%)	7 / 52 (13.46%)
occurrences (all)	4	0	7
Nausea			
subjects affected / exposed	3 / 60 (5.00%)	3 / 59 (5.08%)	5 / 52 (9.62%)
occurrences (all)	3	5	5
Vomiting			
subjects affected / exposed	2 / 60 (3.33%)	3 / 59 (5.08%)	8 / 52 (15.38%)
occurrences (all)	2	3	55
Constipation			
subjects affected / exposed	1 / 60 (1.67%)	2 / 59 (3.39%)	0 / 52 (0.00%)
occurrences (all)	2	2	0
Toothache			
subjects affected / exposed	1 / 60 (1.67%)	2 / 59 (3.39%)	4 / 52 (7.69%)
occurrences (all)	1	2	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 60 (3.33%)	3 / 59 (5.08%)	5 / 52 (9.62%)
occurrences (all)	2	3	7
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 60 (10.00%)	9 / 59 (15.25%)	8 / 52 (15.38%)
occurrences (all)	6	9	12
Sinusitis			
subjects affected / exposed	4 / 60 (6.67%)	0 / 59 (0.00%)	3 / 52 (5.77%)
occurrences (all)	5	0	6

Gastroenteritis			
subjects affected / exposed	0 / 60 (0.00%)	2 / 59 (3.39%)	5 / 52 (9.62%)
occurrences (all)	0	2	5
Gastroenteritis viral			
subjects affected / exposed	2 / 60 (3.33%)	1 / 59 (1.69%)	2 / 52 (3.85%)
occurrences (all)	2	1	2
Influenza			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	8 / 52 (15.38%)
occurrences (all)	1	0	10
Upper respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 59 (1.69%)	8 / 52 (15.38%)
occurrences (all)	1	1	8
Bronchitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 59 (1.69%)	5 / 52 (9.62%)
occurrences (all)	1	1	5
Urinary tract infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	4 / 52 (7.69%)
occurrences (all)	1	0	5

Non-serious adverse events	MEDI2070 700mg/MEDI2070 210mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 52 (80.77%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	11 / 52 (21.15%)		
occurrences (all)	28		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Asthenia			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	7		

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	5		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	10 / 52 (19.23%)		
occurrences (all)	14		
Crohn's disease			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	9		
Diarrhoea			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	9		
Nausea			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	9		
Vomiting			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	7		
Toothache			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	8		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 52 (28.85%)		
occurrences (all)	31		
Sinusitis			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Gastroenteritis viral			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2012	• Exclusion Criterion revised to include eye disorders (not including refraction errors), neurological disorders, myocardial infarction or acute coronary syndrome within 12 months prior to screening • Three items added to the list of reasons for discontinuation of study drug: recurrence of significant Crohn's disease symptoms, according to investigator judgment, subject develops a malignant neoplasm, and mycobacterial infections, systemic fungal infections, or viral infections requiring hospitalization or parenteral antiviral therapy . • For subjects permanently discontinued from study drug, instruction was added that investigators were to refer subjects for appropriate medical care in coordination with subject's personal physician • Requirement added that subjects be followed for at least 6 hours after IV administration of first dose of study drug and, if no adverse reaction, 2 hours after administration of second dose

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported