



Clinical trial results:

A Single Blind, Randomized, Placebo Controlled, Repeat Dose, Dose Escalating Study Investigating Safety, Tolerability pharmacokinetics, Pharmacodynamics and the Beta-Cell Preserving Effect of Otelixizumab in New-Onset, Autoimmune Type 1 Diabetes Mellitus Patients

Summary

EudraCT number	2013-003296-34
Trial protocol	BE
Global end of trial date	27 September 2018

Results information

Result version number	v1 (current)
This version publication date	11 April 2019
First version publication date	11 April 2019

Trial information

Trial identification

Sponsor protocol code	116505
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	08 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of a single course of otelixizumab treatment on the acute and long term safety and tolerability of otelixizumab in NOT1DM patients.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	5
Adults (18-64 years)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was a multi-centered, single-blind, randomized (rand), placebo-controlled 6 Day repeat dose study to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics, efficacy and immunological profile of intravenously administered Otelixizumab (OTX) in New Onset Type 1 Diabetes Mellitus participants (par.).

Pre-assignment

Screening details:

A total of 30 par. were enrolled at different centers in Belgium, which was conducted from 12-Mar-2014 to 27-Sep-2018.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received 0.9% weight/volume Sodium Chloride solution for injection daily for 6 Days

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants were administered 0.9% weight/volume sodium chloride by intravenous infusion

Arm title	Otelixizumab 9 mg
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Arm description:

Participants received 1.5 mg of OTX (intravenous solution for infusion) daily for 6 Days

Arm type	Experimental
Investigational medicinal product name	Otelixizumab 9 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Otelixizumab will be provided as concentrated solution for infusion (5 mg/mL). The study medication will be diluted to 0.1 mg/mL in 0.9% sodium chloride and administered by intravenous infusion using a syringe pump

Arm title	Otelixizumab 18 mg
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Arm description:

Participants received 3 mg of OTX (intravenous solution for infusion) daily for 6 Days

Arm type	Experimental
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Investigational medicinal product name	Otelixizumab 18 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Otelixizumab will be provided as concentrated solution for infusion (5 mg/mL). The study medication will be diluted to 0.1 mg/mL in 0.9% sodium chloride and administered by intravenous infusion using a syringe pump

Arm title	Otelixizumab 27 mg
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Arm description:

Participants received 4.5 mg of OTX (intravenous solution for infusion) daily for 6 Days

Arm type	Experimental
Investigational medicinal product name	Otelixizumab 27 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Otelixizumab will be provided as concentrated solution for infusion (5 mg/mL). The study medication will be diluted to 0.1 mg/mL in 0.9% sodium chloride and administered by intravenous infusion using a syringe pump

Number of subjects in period 1^[1]	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg
Started	5	9	8
Completed	4	8	7
Not completed	1	1	1
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	1	-
Lost to follow-up	-	-	1

Number of subjects in period 1^[1]	Otelixizumab 27 mg
Started	7
Completed	7
Not completed	0
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Lost to follow-up	-

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: Overall number of participants were 30 of which only 29 were randomized

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received 0.9% weight/volume Sodium Chloride solution for injection daily for 6 Days	
Reporting group title	Otelixizumab 9 mg
Reporting group description:	
Participants received 1.5 mg of OTX (intravenous solution for infusion) daily for 6 Days	
Reporting group title	Otelixizumab 18 mg
Reporting group description:	
Participants received 3 mg of OTX (intravenous solution for infusion) daily for 6 Days	
Reporting group title	Otelixizumab 27 mg
Reporting group description:	
Participants received 4.5 mg of OTX (intravenous solution for infusion) daily for 6 Days	

Reporting group values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg
Number of subjects	5	9	8
Age categorical			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Subjects			
All Participants	5	9	8
Age Continuous			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Years			
arithmetic mean	24.8	22.4	20.5
standard deviation	± 4.44	± 2.13	± 4.31
Sex: Female, Male			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Subjects			
Female	2	3	3
Male	3	6	5
Race/Ethnicity, Customized			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Subjects			
White	5	9	8

Reporting group values	Otelixizumab 27 mg	Total	
Number of subjects	7	29	
Age categorical			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Subjects			
All Participants	7	29	

Age Continuous			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Years			
arithmetic mean	22.1		
standard deviation	± 3.98	-	
Sex: Female, Male			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Subjects			
Female	2	10	
Male	5	19	
Race/Ethnicity, Customized			
Safety Population comprised of participants who received at least one dose of study treatment. 1 participant withdrew after being randomized, prior to receiving any treatment.			
Units: Subjects			
White	7	29	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received 0.9% weight/volume Sodium Chloride solution for injection daily for 6 Days	
Reporting group title	Otelixizumab 9 mg
Reporting group description:	
Participants received 1.5 mg of OTX (intravenous solution for infusion) daily for 6 Days	
Reporting group title	Otelixizumab 18 mg
Reporting group description:	
Participants received 3 mg of OTX (intravenous solution for infusion) daily for 6 Days	
Reporting group title	Otelixizumab 27 mg
Reporting group description:	
Participants received 4.5 mg of OTX (intravenous solution for infusion) daily for 6 Days	

Primary: Number of participants with adverse events (AEs) related to cytokine release syndrome (CRS)

End point title	Number of participants with adverse events (AEs) related to cytokine release syndrome (CRS) ^[1]
End point description:	
An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. On treatment AEs have been reported. Safety Population comprised of all participants who received at least one dose of study treatment.	
End point type	Primary
End point timeframe:	
Up to Day 14	

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: There are no statistical analysis to report.

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[2]	9 ^[3]	8 ^[4]	7 ^[5]
Units: Participants	5	9	8	7

Notes:

[2] - Safety population

[3] - Safety population

[4] - Safety population

[5] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Epstein-Barr virus (EBV) viral load detection

End point title	Epstein-Barr virus (EBV) viral load detection ^[6]
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End point description:

Blood samples were collected for analysis of EBV viral load and detection was done by polymerase chain reaction (PCR). Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Week 3, Week 6, Week 8, Week 12, Week 24 and Week 96

Notes:

[6] - 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: There are no statistical analysis to report.

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[7]	9 ^[8]	8 ^[9]	7 ^[10]
Units: Copies per million cells				
geometric mean (geometric coefficient of variation)				
Week 3, n=5, 8, 8, 7	12.0 (± 32806.06)	438.5 (± 193067.66)	4266.1 (± 306867.44)	64870.6 (± 723.66)
Week 6, n=4, 9, 8, 7	28.1 (± 178623.77)	20.5 (± 77662.74)	398.2 (± 131086.12)	974.2 (± 19777.11)
Week 8, n=5, 9, 7, 5	3.5 (± 4755.63)	8.9 (± 22969.48)	17.0 (± 55312.01)	24.3 (± 3060948.75)
Week 12, n=4, 9, 8, 6	4.7 (± 12491.55)	15.8 (± 21359.16)	5.5 (± 15292.04)	33.2 (± 227953.09)
Week 24, n=4, 9, 7, 7	1.0 (± 0.00)	39.3 (± 52129.25)	15.9 (± 39905.91)	2.9 (± 4732.52)
Week 96, n=4, 9, 7, 7	1.0 (± 0.00)	2.3 (± 2166.53)	3.3 (± 13653.67)	5.9 (± 9925.87)

Notes:

[7] - Safety population

[8] - Safety population

[9] - Safety population

[10] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with abnormal laboratory results

End point title	Number of participants with abnormal laboratory results ^[11]
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End point description:

Blood samples were collected to analyze the laboratory parameters which included alanine aminotransferase (ALT), albumin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), bilirubin, calcium, chloride, creatinine, direct bilirubin, glucose, potassium, protein, sodium, urate, urea nitrogen, basophil, eosinophil, mean corpuscular haemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), erythrocytes, haematocrit, haemoglobin, leukocytes, lymphocytes, monocytes, neutrophils, platelets and reticulocytes. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Up to Month 24

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: There are no statistical analysis to report.

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[12]	9 ^[13]	8 ^[14]	7 ^[15]
Units: Participants				
ALT, Low, n= 5, 9, 8, 7	0	0	0	1
ALT, High, n= 5, 9, 8, 7	2	5	6	4
Albumin, Low, n= 5, 9, 8, 7	4	5	2	3
Albumin, High, n= 5, 9, 8, 7	1	4	1	0
ALP, Low, n= 5, 9, 8, 7	3	0	1	1
ALP, High, n= 5, 9, 8, 7	0	1	0	1
AST, Low, n= 5, 9, 8, 7	1	0	1	0
AST, High, n= 5, 9, 8, 7	1	4	5	5
Bilirubin, Low, n= 5, 9, 8, 7	2	2	2	1
Bilirubin, High, n= 5, 9, 8, 7	0	1	2	2
Calcium, Low, n= 5, 9, 8, 7	1	5	5	1
Calcium, High, n= 5, 9, 8, 7	0	1	1	0
Chloride, Low, n= 5, 9, 8, 7	0	2	0	1
Chloride, High, n= 5, 9, 8, 7	3	5	5	3
Creatinine, Low, n= 5, 9, 8, 7	1	0	2	1
Creatinine, High, n= 5, 9, 8, 7	0	3	0	0
Direct Bilirubin, Low, n= 1, 5, 4, 5	0	0	0	0
Direct Bilirubin, High, n= 1, 5, 4, 5	0	0	0	1
Glucose, Low, n= 5, 9, 8, 7	4	0	0	2
Glucose, High, n= 5, 9, 8, 7	2	2	1	3
Potassium, Low, n= 5, 9, 8, 7	0	3	3	2
Potassium, High, n= 5, 9, 8, 7	0	0	1	0
Protein, Low, n= 5, 9, 8, 7	2	3	7	3
Protein, High, n= 5, 9, 8, 7	0	0	0	0
Sodium, Low, n= 5, 9, 8, 7	1	0	1	2
Sodium, High, n= 5, 9, 8, 7	0	3	1	0
Urate, Low, n= 5, 9, 8, 7	1	6	1	6
Urate, High, n= 5, 9, 8, 7	0	0	0	1
Urea Nitrogen, Low, n= 5, 9, 8, 7	2	5	3	2
Urea Nitrogen, High, n= 5, 9, 8, 7	1	2	2	1
Basophils, Low, n= 5, 9, 8, 7	0	1	0	0
Basophils, High, n= 5, 9, 8, 7	0	0	1	0
Eosinophils, Low, n= 5, 9, 8, 7	0	1	0	0
Eosinophils, High, n= 5, 9, 8, 7	3	2	2	1
MCHC, Low, n= 5, 9, 8, 7	2	1	2	2
MCHC, High, n= 5, 9, 8, 7	1	5	4	4
MCH, Low, n= 5, 9, 8, 7	0	2	4	3
MCH, High, n= 5, 9, 8, 7	0	0	1	0
MCV, Low, n= 5, 9, 8, 7	0	3	3	2
MCV, High, n= 5, 9, 8, 7	0	0	0	0
Erythrocytes, Low, n= 5, 9, 8, 7	4	6	6	4
Erythrocytes, High, n= 5, 9, 8, 7	0	2	1	0

Hematocrit, Low, n= 5, 9, 8, 7	4	5	7	2
Hematocrit, High, n= 5, 9, 8, 7	1	0	0	0
Hemoglobin, Low, n= 5, 9, 8, 7	5	6	5	4
Hemoglobin, High, n= 5, 9, 8, 7	0	2	0	0
Leukocytes, Low, n= 5, 9, 8, 7	0	5	2	2
Leukocytes, High, n= 5, 9, 8, 7	3	1	1	1
Lymphocytes, Low, n= 5, 9, 8, 7	0	9	7	7
Lymphocytes, High, n= 5, 9, 8, 7	1	1	2	3
Monocytes, Low, n= 5, 9, 8, 7	0	1	0	2
Monocytes, High, n= 5, 9, 8, 7	0	0	0	1
Neutrophils, Low, n= 5, 9, 8, 7	0	2	2	2
Neutrophils, High, n= 5, 9, 8, 7	2	1	2	2
Platelets, Low, n= 5, 9, 8, 7	0	2	3	2
Platelets, High, n= 5, 9, 8, 7	0	0	2	0
Reticulocytes, Low, n= 1, 3, 4, 4	0	1	0	0
Reticulocytes, High, n= 1, 3, 4, 4	0	2	1	1

Notes:

[12] - Safety population

[13] - Safety population

[14] - Safety population

[15] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with increase in QT Interval Corrected for heart rate (QTc)

End point title	Number of participants with increase in QT Interval Corrected for heart rate (QTc) ^[16]
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End point description:

12-lead electrocardiograms (ECGs) were obtained in semi-supine position after 5 minutes rest for the participants at indicated time points to measure QTc.

End point type	Primary
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End point timeframe:

Up to Month 24

Notes:

[16] - 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: There are no statistical analysis to report.

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[17]	9 ^[18]	8 ^[19]	7 ^[20]
Units: Participants				
QTc Interval (Bazett's), Increase >60 millisec	0	0	0	0
QTc Interval (Fridericia), Increase >60 millisec	0	0	0	0

Notes:

[17] - Safety population

[18] - Safety population

[19] - Safety population

[20] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with abnormal vital sign results

End point title	Number of participants with abnormal vital sign results ^[21]
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End point description:

Vital signs were measured in semi-supine position after 5 minutes rest for the participants at indicated time points. Vital signs included systolic, diastolic blood pressure, pulse rate and respiratory rate

End point type	Primary
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End point timeframe:

Up to Month 24

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: There are no statistical analysis to report.

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[22]	9 ^[23]	8 ^[24]	7 ^[25]
Units: Participants				
number (not applicable)				
Systolic Blood Pressure, Low	1	1	2	1
Systolic Blood Pressure, High	1	0	1	1
Diastolic Blood Pressure, Low	2	5	4	1
Diastolic Blood Pressure, High	0	0	1	0
Pulse Rate, Low	0	0	0	1
Pulse Rate, High	1	2	3	2
Respiratory Rate, Low	0	1	0	0
Respiratory Rate, High	0	0	0	0

Notes:

[22] - Safety population

[23] - Safety population

[24] - Safety population

[25] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Free serum Otelixizumab concentrations by treatment

End point title	Free serum Otelixizumab concentrations by treatment ^[26]
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End point description:

Blood samples were collected at designated timepoints. Free serum Otelixizumab concentrations were calculated by linear and semi-logarithmic individual serum concentration-time profiles. Fully treated population comprised of all randomized participants who received the full 6 days of treatment based on

actual exposure data. 99999 indicates that data could not be calculated as >30% of samples were below the limit of quantification. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Pre-dose on Day 1,2,3,4,5,6 and 14; 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 9 hours, 16 hours post-dose on Day 1, and 1 hour post-dose on Day 6.

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical analysis to report.

End point values	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8 ^[27]	8 ^[28]	6 ^[29]	
Units: Nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1, Pre-dose, n=8, 8, 6	0.000 (± 99999)	0.000 (± 99999)	0.000 (± 99999)	
Day 1, 30 minutes, n=8, 8, 6	0.000 (± 99999)	0.444 (± 99999)	7.387 (± 4.8946)	
Day 1, 1 hour, n=8, 8, 6	0.513 (± 99999)	2.963 (± 99999)	12.542 (± 7.9086)	
Day 1, 2 hours, n=8, 8, 6	2.995 (± 99999)	7.606 (± 6.1836)	23.598 (± 14.4526)	
Day 1, 4 hours, n=7, 8, 6	6.600 (± 5.2773)	15.929 (± 9.8903)	41.457 (± 26.3827)	
Day 1, 6 hours, n=8, 8, 6	11.870 (± 5.0544)	24.899 (± 14.5630)	100.148 (± 79.4845)	
Day 1, 8 hours, n=8, 7, 6	70.088 (± 153.2593)	37.657 (± 19.8741)	146.298 (± 95.4089)	
Day 1, 9 hours, n=7, 8, 6	18.494 (± 6.0716)	102.865 (± 111.2186)	402.173 (± 246.4271)	
Day 1, 16 hours, n=7, 8, 6	0.000 (± 99999)	30.758 (± 23.3494)	212.487 (± 144.0899)	
Day 2, Pre-Dose, n=8, 8, 6	0.000 (± 99999)	7.329 (± 99999)	112.020 (± 124.1743)	
Day 3, Pre-Dose, n=8, 8, 6	0.000 (± 99999)	36.051 (± 35.6464)	420.228 (± 344.7569)	
Day 4, Pre-Dose, n=8, 8, 6	0.523 (± 99999)	114.993 (± 152.7864)	829.148 (± 473.9342)	
Day 5, Pre-Dose, n=8, 8, 6	9.550 (± 16.2697)	213.305 (± 257.3174)	1088.808 (± 542.8032)	
Day 6, Pre-Dose, n=8, 8, 6	4.416 (± 3.2896)	174.448 (± 258.4873)	1386.008 (± 623.1118)	
Day 6, 1 hour, n=8, 8, 6	413.488 (± 262.5248)	2048.336 (± 1889.7194)	2868.735 (± 771.5457)	
Day 14, n=7, 8, 5	0.523 (± 99999)	0.899 (± 99999)	12.474 (± 8.7977)	

Notes:

[27] - Fully Treated population

[28] - Fully Treated population

[29] - Fully Treated population

Statistical analyses

Secondary: Change from Baseline in C-Peptide weighted mean (area under curve from 0 to 120 minutes [AUC0-120 minutes]) from mixed meal tolerance test

End point title	Change from Baseline in C-Peptide weighted mean (area under curve from 0 to 120 minutes [AUC0-120 minutes]) from mixed meal tolerance test
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End point description:

Blood samples were collected at indicated time points to assess levels of C-peptide. Day -1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Mixed meal-stimulated C-peptide AUC was calculated from area under C-peptide/time curve from time 0 to 120 minutes, using trapezoidal rule. ITT treated population comprised of all randomized participants who received at least one dose of study treatment. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day-1), Month 3, Month 6, Month 12, Month 18 and Month 24

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[30]	9 ^[31]	8 ^[32]	7 ^[33]
Units: Nanomoles minute per liter				
arithmetic mean (standard deviation)				
Month 3, n=5, 8, 8, 7	0.175 (± 0.0797)	0.255 (± 0.2852)	0.118 (± 0.2462)	0.153 (± 0.1312)
Month 6, n=5, 8, 8, 7	0.118 (± 0.0895)	0.147 (± 0.3215)	-0.185 (± 0.2148)	0.076 (± 0.2788)
Month 12, n=5, 8, 8, 7	-0.103 (± 0.0552)	0.023 (± 0.3145)	-0.215 (± 0.2597)	-0.016 (± 0.3689)
Month 18, n=5, 8, 7, 7	-0.278 (± 0.1142)	0.015 (± 0.3903)	-0.295 (± 0.3105)	-0.201 (± 0.3132)
Month 24, n=4, 7, 7, 7	-0.296 (± 0.0962)	-0.042 (± 0.2905)	-0.349 (± 0.3917)	-0.165 (± 0.3729)

Notes:

[30] - Intent-To-Treat treated population

[31] - Intent-To-Treat treated population

[32] - Intent-To-Treat treated population

[33] - Intent-To-Treat treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in glucose weighted mean (area under curve from 0 to 120 minutes, AUC0-120 minutes) from mixed meal tolerance test

End point title	Change from Baseline in glucose weighted mean (area under curve from 0 to 120 minutes, AUC0-120 minutes) from mixed meal tolerance test
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End point description:

Blood samples were collected at indicated time points to assess levels of glucose. Day -1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Mixed meal-stimulated glucose was calculated from area under the glucose /time curve from time 0 to 120 minutes, using trapezoidal rule. Only those participants with data available at the

specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
End point timeframe:	
Baseline (Day-1), Month 3, Month 6, Month 12, Month 18 and Month 24	

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[34]	9 ^[35]	8 ^[36]	7 ^[37]
Units: Millmoles minute per liter				
arithmetic mean (standard deviation)				
Month 3, n=5, 8, 8, 7	1.382 (± 1.5801)	-0.550 (± 1.7140)	0.999 (± 3.3953)	0.641 (± 3.0009)
Month 6, n=5, 8, 8, 7	1.423 (± 2.9999)	-1.041 (± 1.5506)	0.643 (± 4.1751)	0.749 (± 2.7698)
Month 12, n=5, 8, 8, 7	2.314 (± 2.2718)	0.067 (± 2.0492)	1.875 (± 2.7440)	1.842 (± 3.2408)
Month 18, n=5, 8, 7, 7	3.142 (± 3.2172)	1.159 (± 2.4073)	2.676 (± 3.0803)	3.942 (± 1.9745)
Month 24, n=4, 7, 7, 7	4.029 (± 1.2365)	-1.807 (± 2.1615)	2.557 (± 3.9428)	3.435 (± 2.3714)

Notes:

[34] - ITT treated population

[35] - ITT treated population

[36] - ITT treated population

[37] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in C-Peptide weighted mean (area under curve from 60 to 140 minutes, [AUC 60-140 minutes]) from hyperglycemic clamp test

End point title	Change from Baseline in C-Peptide weighted mean (area under curve from 60 to 140 minutes, [AUC 60-140 minutes]) from hyperglycemic clamp test
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End point description:

Blood samples were collected at indicated time points to assess levels of C-peptide during hyperglycemic (H) phase. Day-1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from specified time point value. C-peptide AUC was calculated from area under C-peptide/time curve from time H60 to H140 minutes. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
End point timeframe:	
Baseline (Day-1), Month 6, Month 24	

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[38]	9 ^[39]	8 ^[40]	7 ^[41]
Units: Nanomoles minute per liter				
arithmetic mean (standard deviation)				
Month 6, n=5, 8, 8, 7	-0.037 (± 0.2107)	0.105 (± 0.2520)	-0.201 (± 0.2643)	0.006 (± 0.3011)
Month 24, n=4, 5, 7, 7	-0.423 (± 0.1630)	-0.273 (± 0.1552)	-0.373 (± 0.2308)	-0.344 (± 0.3397)

Notes:

[38] - ITT treated population

[39] - ITT treated population

[40] - ITT treated population

[41] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in glucose weighted mean (area under curve from 60 to 140 minutes, AUC60-140 minutes) from hyperglycemic clamp Test

End point title	Change from Baseline in glucose weighted mean (area under curve from 60 to 140 minutes, AUC60-140 minutes) from hyperglycemic clamp Test
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End point description:

Blood samples were collected at indicated time points to assess levels of glucose during hyperglycemic (H) phase. Day-1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Glucose AUC was calculated from area under the C-peptide/time curve from time H60 to H140 minutes. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day-1), Month 6 and Month 24

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[42]	9 ^[43]	8 ^[44]	7 ^[45]
Units: Millmoles minute per liter				
arithmetic mean (standard deviation)				
Month 6, n=5, 8, 8, 7	0.645 (± 1.0094)	0.415 (± 1.3255)	0.723 (± 1.5955)	1.074 (± 0.6264)
Month 24, n=4, 5, 7, 7	1.346 (± 1.1063)	-0.501 (± 3.2542)	0.094 (± 2.2642)	1.095 (± 1.3972)

Notes:

[42] - ITT treated population

[43] - ITT treated population

[44] - ITT treated population

[45] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in insulin sensitivity (IS) Index from hyperglycemic clamp test

End point title	Change from Baseline in insulin sensitivity (IS) Index from hyperglycemic clamp test
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End point description:

Insulin sensitivity index is defined as the ratio of glucose metabolized and average insulin concentration multiplied by 100 by hyperglycemic clamp test. Day-1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day-1), Month 6, Month 24

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[46]	9 ^[47]	8 ^[48]	7 ^[49]
Units: (100*mmol*I)/(pmol*kg*min)				
arithmetic mean (standard deviation)				
Month 6, n=5, 8, 7, 6	-0.0003 (± 0.00130)	-0.0000 (± 0.00030)	-0.0002 (± 0.00197)	-0.0002 (± 0.00066)
Month 24, n=4, 4, 6, 6	0.0037 (± 0.00591)	-0.0006 (± 0.00344)	-0.0013 (± 0.01299)	0.0023 (± 0.00351)

Notes:

[46] - ITT treated population

[47] - ITT treated population

[48] - ITT treated population

[49] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in mean daily insulin use

End point title	Change from Baseline in mean daily insulin use
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End point description:

Participants were asked to record their daily insulin usage thoroughly and accurately in a diary from 7 days prior to study visit. Day-1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day-1), Week 2, Week 3, Week 6, Week 8, Week 12, Week 24, Week 36, Week 48, Week 72 and Week 96

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[50]	9 ^[51]	8 ^[52]	7 ^[53]
Units: International unit				
arithmetic mean (standard deviation)				
Week 2, n=5, 8, 7, 6	-0.0901 (± 0.05997)	-0.0265 (± 0.07580)	0.0941 (± 0.12919)	-0.0741 (± 0.08855)
Week 3, n=5, 8, 8, 7	-0.1504 (± 0.06424)	-0.0424 (± 0.08708)	0.0706 (± 0.14989)	-0.0440 (± 0.08753)
Week 6, n=5, 4, 8, 7	-0.1727 (± 0.05431)	-0.1009 (± 0.12893)	-0.0332 (± 0.19098)	-0.1090 (± 0.11777)
Week 8, n=4, 7, 5, 6	-0.1566 (± 0.07033)	-0.1514 (± 0.15364)	-0.0666 (± 0.21066)	-0.1492 (± 0.14713)
Week 12, n=4, 8, 8, 7	-0.1850 (± 0.08007)	-0.1629 (± 0.14706)	-0.1115 (± 0.16950)	-0.1850 (± 0.20173)
Week 24, n=5, 8, 5, 7	-0.1449 (± 0.09069)	-0.1168 (± 0.20181)	0.0298 (± 0.13942)	-0.1678 (± 0.17308)
Week 36, n=4, 8, 7, 7	-0.0776 (± 0.13492)	-0.0673 (± 0.26527)	0.0701 (± 0.20840)	-0.1114 (± 0.21943)
Week 48, n=5, 8, 8, 7	-0.1221 (± 0.16778)	-0.0936 (± 0.24246)	0.0970 (± 0.15473)	-0.1155 (± 0.25461)
Week 72, n=5, 8, 7, 5	-0.1000 (± 0.23378)	0.0172 (± 0.43320)	0.1088 (± 0.07406)	0.0807 (± 0.27375)
Week 96, n=4, 6, 7, 7	-0.0390 (± 0.34885)	-0.0811 (± 0.34104)	0.1131 (± 0.16596)	0.1117 (± 0.19080)

Notes:

[50] - ITT treated population

[51] - ITT treated population

[52] - ITT treated population

[53] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin A1c

End point title	Change from Baseline in hemoglobin A1c
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End point description:

Hemoglobin A1C levels were measured at indicated time points. Day-1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day-1), Month 6, Month 12 and Month 24

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[54]	9 ^[55]	8 ^[56]	7 ^[57]
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)				

Month 6, n=5, 8, 8, 7	-3.26 (± 1.119)	-2.29 (± 1.883)	-0.68 (± 2.437)	-2.04 (± 2.141)
Month 12, n=5, 9, 8, 7	-3.26 (± 1.665)	-2.10 (± 2.125)	-1.15 (± 1.384)	-1.60 (± 2.985)
Month 24, n=4, 9, 7, 7	-2.53 (± 2.445)	-2.23 (± 1.736)	-0.33 (± 2.075)	-1.41 (± 2.174)

Notes:

[54] - ITT treated population

[55] - ITT treated population

[56] - ITT treated population

[57] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute body weight

End point title	Absolute body weight
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End point description:

Body weight was measured at indicated time points. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Day-1, Month 12, Month 18 and Month 24

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[58]	9 ^[59]	8 ^[60]	7 ^[61]
Units: Kilogram				
arithmetic mean (standard deviation)				
Day -1, n=5, 9, 8, 7	65.22 (± 10.608)	72.84 (± 16.118)	64.19 (± 9.545)	65.27 (± 8.714)
Month 12, n=5, 9, 8, 7	70.24 (± 12.691)	75.86 (± 15.503)	64.58 (± 9.851)	67.96 (± 8.373)
Month 18, n=5, 9, 7, 7	70.44 (± 13.209)	75.22 (± 16.504)	63.56 (± 8.658)	68.97 (± 10.167)
Month 24, n=4, 9, 7, 7	66.98 (± 11.226)	75.82 (± 17.507)	63.71 (± 8.037)	69.79 (± 8.689)

Notes:

[58] - ITT treated population

[59] - ITT treated population

[60] - ITT treated population

[61] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Time-normalized number of hypoglycemic and hyperglycemic events

End point title	Time-normalized number of hypoglycemic and hyperglycemic events
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End point description:

As per American Diabetes Association (ADA), hypoglycemia is defined as blood glucose level ≤ 70 milligram/deciliter (mg/dl) and hyperglycemia is defined as blood glucose level > 250 mg/dL. Hypoglycaemic and hyperglycaemic events will be recorded in a diary whenever they occur, along with the start and stop dates. Mean number of events is defined as the average number of events reported per subject. Normalization is expressed by dividing number of events by length of reporting period in month (1 month = 30 days). Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Up to Month 24

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4 ^[62]	9 ^[63]	7 ^[64]	7 ^[65]
Units: Number of events				
arithmetic mean (standard deviation)				
Hypoglycemia	14.13 (\pm 3.533)	21.45 (\pm 2.383)	7.74 (\pm 1.105)	24.55 (\pm 3.508)
Hyperglycemia	2.79 (\pm 0.698)	11.03 (\pm 1.225)	14.13 (\pm 2.019)	8.48 (\pm 1.211)

Notes:

[62] - ITT treated population

[63] - ITT treated population

[64] - ITT treated population

[65] - ITT treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from Baseline in percentage (%) in CD4+ cells

End point title	Relative change from Baseline in percentage (%) in CD4+ cells
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End point description:

Whole blood samples were collected and analyzed by flow cytometry. Day 1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Relative change from Baseline (percentage) was calculated as change from Baseline relative to Baseline in percentage. 99999 indicates that standard deviation could not be calculated for a single participant. 99999 indicates that data was not collected. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Day 1 (30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 9 hours, 12 hours, 16 hours), Day 2, Day 3, Day 4, Day 5, Day 6 (1 hour), Day 14

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[66]	9 ^[67]	8 ^[68]	7 ^[69]
Units: Percentage				
arithmetic mean (standard deviation)				
Day 1, 30 minutes, n=5, 7, 8, 6	-2.2331 (± 8.06090)	15.7568 (± 9.45733)	22.3101 (± 11.38275)	37.9286 (± 7.06740)
Day 1, 1 hour, n=5, 7, 8, 6	-0.9229 (± 3.79426)	24.8673 (± 8.97161)	33.2356 (± 10.06318)	40.8432 (± 17.12371)
Day 1, 2 hours, n=5, 7, 8, 6	4.6329 (± 10.59418)	32.0976 (± 13.50078)	42.2579 (± 11.17916)	54.2045 (± 9.65956)
Day 1, 4 hours, n=5, 7, 8, 6	-1.8509 (± 9.27472)	31.4853 (± 18.78336)	49.3861 (± 14.33838)	49.1721 (± 30.22147)
Day 1, 6 hours, n=5, 7, 8, 6	3.3922 (± 6.75373)	58.4446 (± 9.17750)	70.8026 (± 8.26487)	67.9378 (± 25.45192)
Day 1, 8 hours, n=5, 7, 7, 6	6.9714 (± 8.64363)	58.4772 (± 9.97693)	76.5366 (± 12.00112)	69.8593 (± 23.77517)
Day 1, 9 hours, n=1, 6, 0, 0	18.8383 (± 99999)	58.2218 (± 11.84589)	999999 (± 999999)	999999 (± 999999)
Day 1, 12 hours, n=4, 0, 7, 6	1.1168 (± 9.94441)	999999 (± 999999)	72.0336 (± 10.97106)	72.4138 (± 28.39518)
Day 1, 16 hours, n=4, 6, 8, 6	-1.9654 (± 4.50998)	47.1603 (± 7.15517)	79.1078 (± 8.03676)	75.8997 (± 24.65609)
Day 2, n=5, 7, 8, 6	5.8586 (± 11.64080)	38.9846 (± 10.09414)	67.5197 (± 8.13498)	71.3820 (± 20.92599)
Day 3, n=5, 7, 8, 6	8.4017 (± 21.57257)	47.8814 (± 8.46678)	77.5903 (± 8.78800)	88.1872 (± 3.79283)
Day 4, n=5, 7, 8, 6	-2.2685 (± 9.15020)	48.5169 (± 11.02802)	82.0325 (± 10.26798)	91.6139 (± 1.52341)
Day 5, n=5, 7, 8, 6	9.4816 (± 10.25461)	64.5703 (± 8.16040)	88.1950 (± 6.33948)	94.2542 (± 1.59484)
Day 6, n=5, 7, 8, 6	4.6145 (± 5.61446)	70.6624 (± 7.58163)	89.9853 (± 4.21710)	95.1333 (± 1.79263)
Day 6, 1 hour, n=5, 7, 8, 6	8.0058 (± 7.53027)	93.5215 (± 2.42406)	91.9917 (± 2.78804)	95.3978 (± 1.70448)
Day 14, n=5, 6, 8, 4	16.0448 (± 15.71866)	18.3627 (± 15.59835)	17.6415 (± 27.54591)	38.7962 (± 17.92367)

Notes:

[66] - Fully treated population

[67] - Fully treated population

[68] - Fully treated population

[69] - Fully treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from Baseline in percentage (%) in CD8+ cells

End point title	Relative change from Baseline in percentage (%) in CD8+ cells
End point description:	
Whole blood samples were collected and analyzed by flow cytometry. Day1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Relative change from baseline (%) was calculated as change from Baseline relative to Baseline in %. 99999 indicates that standard deviation could not be calculated for a single participant. 999999 indicates that data was not collected. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).	
End point type	Secondary

End point timeframe:

Day 1 (30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 9 hours, 12 hours, 16 hours), Day 2, Day 3, Day 4, Day 5, Day 6 (1 hour), Day 14

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[70]	9 ^[71]	8 ^[72]	7 ^[73]
Units: Percentage				
arithmetic mean (standard deviation)				
Day 1, 30 minutes, n=5, 7, 8, 6	1.4489 (± 5.86548)	13.6045 (± 6.84553)	18.4972 (± 10.57226)	35.6721 (± 7.81791)
Day 1, 1 hour, n=5, 7, 8, 6	3.9227 (± 3.52082)	23.2571 (± 8.77440)	29.9262 (± 9.11960)	37.1052 (± 15.47566)
Day 1, 2 hours, n=5, 7, 8, 6	5.7591 (± 7.62243)	29.7916 (± 10.08248)	36.7030 (± 11.18167)	48.2854 (± 10.33624)
Day 1, 4 hours, n=5, 7, 8, 6	2.4574 (± 5.34591)	27.9312 (± 15.06025)	40.2754 (± 12.70208)	41.5574 (± 26.91586)
Day 1, 6 hours, n=5, 7, 8, 6	5.2570 (± 5.13603)	50.6248 (± 8.12251)	63.2777 (± 9.16749)	61.0355 (± 22.44049)
Day 1, 8 hours, n=5, 7, 7, 6	3.0516 (± 5.05296)	50.0586 (± 13.15793)	64.0559 (± 8.96743)	64.6389 (± 23.37406)
Day 1, 9 hours, n=1, 6, 0, 0	12.0124 (± 99999)	47.3877 (± 10.18779)	999999 (± 999999)	999999 (± 999999)
Day 1, 12 hours, n=4, 0, 7, 6	4.6297 (± 1.55778)	999999 (± 999999)	63.0325 (± 11.60295)	68.2523 (± 25.41788)
Day 1, 16 hours, n=4, 6, 8, 6	2.4031 (± 9.29601)	36.5804 (± 11.00323)	73.7619 (± 9.27676)	73.7870 (± 23.65616)
Day 2, n=5, 7, 8, 6	11.5153 (± 12.44266)	32.3389 (± 17.53306)	63.2076 (± 11.90764)	68.8582 (± 23.13445)
Day 3, n=5, 7, 8, 6	9.6580 (± 17.96579)	38.6763 (± 10.50068)	73.4518 (± 13.11370)	86.3391 (± 4.07679)
Day 4, n=5, 7, 8, 6	1.4965 (± 9.56563)	39.4735 (± 13.72429)	78.2797 (± 13.97813)	89.7661 (± 2.38427)
Day 5, n=5, 7, 8, 6	13.1690 (± 10.31403)	55.7138 (± 7.92647)	84.6850 (± 10.08105)	92.6561 (± 1.66146)
Day 6, n=5, 7, 8, 6	9.5352 (± 4.64977)	62.6915 (± 6.12617)	87.5358 (± 6.72558)	93.6820 (± 1.51640)
Day 6, 1 hour, n=5, 7, 8, 6	9.6315 (± 7.30255)	90.8426 (± 2.43623)	91.3298 (± 3.00883)	93.9939 (± 1.50147)
Day 14, n=5, 6, 8, 4	21.2448 (± 18.40147)	19.6382 (± 18.17904)	20.1594 (± 27.60057)	33.4359 (± 23.03254)

Notes:

[70] - Fully treated population

[71] - Fully treated population

[72] - Fully treated population

[73] - Fully treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in free CD3 on CD8+ cells

End point title	Change from Baseline in free CD3 on CD8+ cells
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End point description:

Whole blood samples were drawn and analyzed by flow cytometry. Day 1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. 99999 indicates that standard deviation could not be calculated for a single participant. 999999 indicates that data was not collected. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Day 1 (30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 9 hours, 12 hours, 16 hours), Day 2, Day 3, Day 4, Day 5, Day 6 (1 hour), Day 14

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[74]	9 ^[75]	8 ^[76]	7 ^[77]
Units: Copies per cell				
arithmetic mean (standard deviation)				
Day 1, 30 minutes, n=5, 7, 8, 6	-1570.2 (± 7996.97)	-17344.6 (± 8219.24)	-33177.1 (± 26046.74)	-46590.5 (± 14242.51)
Day 1, 1 hour, n=5, 7, 8, 6	-5367.8 (± 4454.93)	-30170.0 (± 11702.96)	-52164.3 (± 25780.68)	-45971.2 (± 17371.50)
Day 1, 2 hours, n=5, 7, 8, 6	-7599.6 (± 9683.28)	-38063.3 (± 12268.28)	-64195.5 (± 30475.25)	-63303.5 (± 19743.02)
Day 1, 4 hours, n=5, 7, 8, 6	-2668.2 (± 7081.48)	-37523.3 (± 21827.29)	-70708.9 (± 35060.26)	-50216.3 (± 33433.24)
Day 1, 6 hours, n=5, 7, 8, 6	-7434.0 (± 6566.98)	-65821.7 (± 14778.18)	-109702.0 (± 36004.22)	-75299.7 (± 24515.25)
Day 1, 8 hours, n=5, 7, 7, 6	-5118.8 (± 9260.84)	-64346.1 (± 16499.07)	-113884.9 (± 36548.70)	-79778.2 (± 25001.56)
Day 1, 9 hours, n=1, 6, 0, 0	-14630.0 (± 99999)	-62113.7 (± 17114.28)	999999 (± 999999)	999999 (± 999999)
Day 1, 12 hours, n=4, 0, 7, 6	-7671.0 (± 3453.02)	999999 (± 999999)	-111484.0 (± 37822.49)	-84085.8 (± 27533.48)
Day 1, 16 hours, n=4, 6, 8, 6	-2398.0 (± 12735.14)	-48607.8 (± 17774.03)	-126378.6 (± 34284.38)	-91537.5 (± 23378.53)
Day 2, n=5, 7, 8, 6	-16282.6 (± 18931.53)	-42379.1 (± 25223.07)	-108857.0 (± 36292.51)	-85611.5 (± 24571.30)
Day 3, n=5, 7, 8, 6	-12613.4 (± 23082.56)	-50757.1 (± 16662.32)	-126037.9 (± 39171.31)	-112220.0 (± 20740.64)
Day 4, n=5, 7, 8, 6	-2479.6 (± 14120.73)	-52064.6 (± 22177.41)	-133794.1 (± 38684.37)	-116816.5 (± 22469.30)
Day 5, n=5, 7, 8, 6	-19504.4 (± 14161.40)	-72058.3 (± 13158.75)	-144613.4 (± 35791.57)	-120512.7 (± 22578.38)
Day 6, n=5, 7, 8, 6	-13905.4 (± 6365.89)	-81326.7 (± 14410.25)	-149202.1 (± 32099.88)	-121836.0 (± 22706.98)
Day 6, 1 hour, n=5, 7, 8, 6	-14414.4 (± 10131.25)	-118000.6 (± 18946.75)	-155565.6 (± 29776.06)	-122237.2 (± 22786.52)
Day 14, n=5, 6, 8, 4	-30658.2 (± 25814.70)	-25656.7 (± 23202.59)	-34478.6 (± 46509.48)	-49846.8 (± 42800.88)

Notes:

[74] - Fully treated population

[75] - Fully treated population

[76] - Fully treated population

[77] - Fully treated population

Statistical analyses

Secondary: Change from Baseline in free CD3 on CD4+ cells

End point title	Change from Baseline in free CD3 on CD4+ cells
End point description:	
Whole blood samples were drawn and analyzed by flow cytometry. Day 1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. 99999 indicates that standard deviation could not be calculated for a single participant. 999999 indicates that data was not collected. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).	
End point type	Secondary
End point timeframe:	
Day 1 (30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 9 hours, 12 hours, 16 hours), Day 2, Day 3, Day 4, Day 5, Day 6 (1 hour), Day 14	

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[78]	9 ^[79]	8 ^[80]	7 ^[81]
Units: Copies per cell				
arithmetic mean (standard deviation)				
Day 1, 30 minutes, n=5, 7, 8, 6	5529.0 (± 13037.93)	-26310.0 (± 15691.77)	-46612.6 (± 31524.47)	-61053.8 (± 16266.15)
Day 1, 1 hour, n=5, 7, 8, 6	2819.2 (± 8108.55)	-41955.9 (± 16287.89)	-68726.5 (± 33738.60)	-63524.8 (± 26817.94)
Day 1, 2 hours, n=5, 7, 8, 6	-5833.0 (± 17972.31)	-54111.1 (± 23197.46)	-86880.5 (± 37961.85)	-87013.2 (± 20852.00)
Day 1, 4 hours, n=5, 7, 8, 6	2651.6 (± 14138.56)	-54076.3 (± 34638.82)	-101829.5 (± 45896.19)	-73042.7 (± 45129.43)
Day 1, 6 hours, n=5, 7, 8, 6	-5072.0 (± 11737.82)	-97871.0 (± 18824.51)	-143635.8 (± 41952.00)	-104097.7 (± 36063.45)
Day 1, 8 hours, n=5, 7, 7, 6	-10668.4 (± 11325.47)	-97642.4 (± 17931.01)	-156878.1 (± 38450.32)	-107788.0 (± 34304.89)
Day 1, 9 hours, n=1, 6, 0, 0	-31435.0 (± 99999)	-98963.5 (± 25253.18)	999999 (± 999999)	999999 (± 999999)
Day 1, 12 hours, n=4, 0, 7, 6	-4958.5 (± 15637.79)	999999 (± 999999)	-150231.0 (± 46611.02)	-111627.8 (± 43965.70)
Day 1, 16 hours, n=4, 6, 8, 6	4546.3 (± 7628.46)	-79792.2 (± 16063.80)	-159376.9 (± 40492.21)	-117485.2 (± 35848.96)
Day 2, n=5, 7, 8, 6	-9071.4 (± 22730.36)	-64674.3 (± 14881.25)	-136989.0 (± 40208.17)	-111246.8 (± 30955.42)
Day 3, n=5, 7, 8, 6	-9750.2 (± 28173.66)	-80703.6 (± 19670.68)	-156782.3 (± 42746.51)	-141892.0 (± 28600.19)
Day 4, n=5, 7, 8, 6	4442.8 (± 16258.54)	-81174.3 (± 21094.09)	-165042.3 (± 42878.04)	-147344.5 (± 28442.20)
Day 5, n=5, 7, 8, 6	-14696.4 (± 15969.14)	-107817.7 (± 16112.46)	-177310.9 (± 40876.20)	-151768.5 (± 30266.62)
Day 6, n=5, 7, 8, 6	-7848.0 (± 10416.76)	-118246.4 (± 17896.58)	-180424.5 (± 37325.84)	-153238.7 (± 30828.00)
Day 6, 1 hour, n=5, 7, 8, 6	-12708.6 (± 8424.98)	-156241.0 (± 14748.58)	-184362.0 (± 36070.44)	-153638.3 (± 30779.71)
Day 14, n=5, 6, 8, 4	-25564.4 (± 24902.78)	-31243.3 (± 25714.52)	-37536.4 (± 55570.83)	-70890.5 (± 40581.96)

Notes:

- [78] - Fully treated population
- [79] - Fully treated population
- [80] - Fully treated population
- [81] - Fully treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bound CD3 copies on CD4+ cells

End point title	Change from Baseline in bound CD3 copies on CD4+ cells
End point description:	
Whole blood samples were drawn and analyzed by flow cytometry. Day 1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. 99999 indicates that standard deviation could not be calculated for a single participant. 999999 indicates that data was not collected. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).	
End point type	Secondary
End point timeframe:	
Day 1 (30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 9 hours, 12 hours, 16 hours), Day 2, Day 3, Day 4, Day 5, Day 6 (1 hour), Day 14	

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[82]	9 ^[83]	8 ^[84]	7 ^[85]
Units: Copies per cell				
arithmetic mean (standard deviation)				
Day 1, 30 minutes, n=5, 7, 8, 6	-54.0 (± 103.13)	29059.1 (± 15150.15)	27538.5 (± 12441.29)	28035.7 (± 14672.79)
Day 1, 1 hour, n=5, 7, 8, 6	-10.2 (± 82.62)	39472.3 (± 16401.81)	43911.8 (± 14701.05)	38406.5 (± 19297.11)
Day 1, 2 hours, n=5, 7, 8, 6	27.6 (± 133.59)	54116.3 (± 14159.80)	56840.6 (± 15756.66)	47028.2 (± 24507.94)
Day 1, 4 hours, n=5, 7, 8, 6	-50.4 (± 113.62)	62635.7 (± 24380.73)	54693.1 (± 16678.89)	42730.2 (± 24609.04)
Day 1, 6 hours, n=5, 7, 8, 6	-77.4 (± 168.73)	86518.1 (± 23953.89)	74664.6 (± 5837.58)	49078.8 (± 27502.89)
Day 1, 8 hours, n=5, 7, 7, 6	13.6 (± 203.64)	86801.1 (± 24642.24)	60435.0 (± 24147.90)	51092.2 (± 25386.18)
Day 1, 9 hours, n=1, 6, 0, 0	-36.0 (± 999999)	55085.3 (± 14474.39)	999999 (± 999999)	999999 (± 999999)
Day 1, 12 hours, n=4, 0, 7, 6	-2.8 (± 188.70)	999999 (± 999999)	57280.0 (± 7920.20)	34176.7 (± 22339.84)
Day 1, 16 hours, n=4, 6, 8, 6	62.3 (± 278.48)	33286.2 (± 10303.10)	46080.4 (± 7254.50)	28515.0 (± 13537.67)
Day 2, n=5, 7, 8, 6	-120.8 (± 157.70)	14676.3 (± 4819.20)	27994.6 (± 7683.11)	23777.3 (± 10220.98)
Day 3, n=5, 7, 8, 6	-56.4 (± 209.56)	15982.6 (± 5415.43)	23383.9 (± 7380.09)	19095.8 (± 4142.74)
Day 4, n=5, 7, 8, 6	-199.0 (± 221.61)	12522.1 (± 4472.75)	17241.8 (± 3135.36)	14843.3 (± 3645.33)

Day 5, n=5, 7, 8, 6	-31.4 (± 334.36)	9679.6 (± 3432.37)	5748.1 (± 2499.44)	6979.3 (± 4026.59)
Day 6, n=5, 7, 8, 6	-103.4 (± 138.02)	4856.7 (± 4683.55)	3671.9 (± 1663.91)	4700.3 (± 2723.61)
Day 6, 1 hour, n=5, 7, 8, 6	-22.2 (± 385.45)	15972.9 (± 4968.41)	4262.9 (± 2221.09)	4658.3 (± 2789.87)
Day 14, n=5, 6, 8, 4	-111.2 (± 227.74)	-874.7 (± 2068.49)	688.0 (± 513.77)	1506.3 (± 2330.70)

Notes:

[82] - Fully treated population

[83] - Fully treated population

[84] - Fully treated population

[85] - Fully treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bound CD3 copies on CD8+ cells

End point title	Change from Baseline in bound CD3 copies on CD8+ cells
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End point description:

Whole blood samples were drawn and analyzed by flow cytometry. Day 1 was considered as Baseline. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. 99999 indicates that standard deviation could not be calculated for a single participant. 999999 indicates that data was not collected. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Day 1 (30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 9 hours, 12 hours, 16 hours), Day 2, Day 3, Day 4, Day 5, Day 6 (1 hour), Day 14

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[86]	9 ^[87]	8 ^[88]	7 ^[89]
Units: Copies per cell				
arithmetic mean (standard deviation)				
Day 1, 30 minutes, n=5, 7, 8, 6	10.8 (± 168.01)	20952.1 (± 9089.08)	22141.3 (± 9619.64)	23518.7 (± 12011.07)
Day 1, 1 hour, n=5, 7, 8, 6	85.8 (± 253.77)	28365.3 (± 9711.56)	34147.9 (± 11206.05)	32445.0 (± 16424.62)
Day 1, 2 hours, n=5, 7, 8, 6	101.2 (± 265.29)	35963.7 (± 6942.11)	42469.1 (± 13977.93)	38510.7 (± 19273.02)
Day 1, 4 hours, n=5, 7, 8, 6	76.0 (± 209.69)	41046.0 (± 14859.06)	43492.8 (± 15811.41)	43477.2 (± 28963.40)
Day 1, 6 hours, n=5, 7, 8, 6	-130.8 (± 273.14)	68337.3 (± 22986.71)	77279.4 (± 14115.24)	55195.8 (± 27523.26)
Day 1, 8 hours, n=5, 7, 7, 6	-60.4 (± 242.85)	68342.4 (± 27742.23)	70935.4 (± 10888.79)	50511.3 (± 25067.72)
Day 1, 9 hours, n=1, 6, 0, 0	50.0 (± 99999)	46941.7 (± 15418.31)	999999 (± 999999)	999999 (± 999999)
Day 1, 12 hours, n=4, 0, 7, 6	-9.8 (± 267.43)	999999 (± 999999)	56618.7 (± 8092.43)	40765.8 (± 21505.21)
Day 1, 16 hours, n=4, 6, 8, 6	30.8 (± 353.27)	35124.7 (± 31051.56)	47713.4 (± 7841.92)	29753.0 (± 15501.29)

Day 2, n=5, 7, 8, 6	-41.2 (± 263.98)	14020.9 (± 2453.61)	26096.8 (± 5228.98)	22559.8 (± 13107.67)
Day 3, n=5, 7, 8, 6	-29.0 (± 351.20)	13502.1 (± 6856.86)	19841.5 (± 4986.13)	20615.5 (± 11473.73)
Day 4, n=5, 7, 8, 6	-90.0 (± 332.42)	11065.7 (± 5053.88)	17923.5 (± 2476.65)	17694.8 (± 8442.57)
Day 5, n=5, 7, 8, 6	49.0 (± 412.48)	7781.6 (± 2908.32)	7139.3 (± 2922.96)	9209.5 (± 5670.67)
Day 6, n=5, 7, 8, 6	-59.4 (± 291.67)	4706.7 (± 4049.36)	4795.4 (± 2544.14)	6093.3 (± 3673.79)
Day 6, 1 hour, n=5, 7, 8, 6	10.0 (± 566.43)	20140.3 (± 6799.16)	6011.8 (± 3638.55)	6167.5 (± 3965.76)
Day 14, n=5, 6, 8, 4	-84.4 (± 321.06)	-783.3 (± 1407.22)	564.3 (± 374.97)	1082.3 (± 1638.04)

Notes:

[86] - Fully treated population

[87] - Fully treated population

[88] - Fully treated population

[89] - Fully treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-drug antibody binding

End point title	Number of participants with anti-drug antibody binding
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End point description:

Samples were analyzed for the presence of anti-Otelixizumab antibodies using a validated immunoelectrochemiluminescent (ECL) assay.

End point type	Secondary
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End point timeframe:

Day-1, Month 3 and Month 6

End point values	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg	Otelixizumab 27 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[90]	9 ^[91]	8 ^[92]	7 ^[93]
Units: Participants				
Day -1, Negative	3	9	8	6
Day-1, Positive	2	0	0	1
Month 3, Negative	3	0	0	0
Month 3, Positive	2	9	8	7
Month 3, Newly Positive	0	9	8	6
Month 3, Negative who were Positive previously	0	0	0	0
Month 6, Negative	3	0	0	0
Month 6, Positive	2	8	8	7
Month 6, Newly Positive	0	0	0	0
Month 6, Negative who were Positive previously	0	0	0	0

Notes:

[90] - Safety population

[91] - Safety population

[92] - Safety population

[93] - Safety population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On treatment serious adverse events (SAEs) and non-serious AEs were collected from the start of study treatment up to 36 months.

Adverse event reporting additional description:

Safety population was used. Safety population comprised of all participants who received at least one dose of a study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants received 0.9% weight/volume Sodium Chloride solution for injection daily for 6 Days

Reporting group title	Otelixizumab 9 mg
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Reporting group description:

Participants received 1.5 mg of OTX (intravenous solution for infusion) daily for 6 Days

Reporting group title	Otelixizumab 18 mg
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Reporting group description:

Participants received 3 mg of OTX (intravenous solution for infusion) daily for 6 Days

Reporting group title	Otelixizumab 27 mg
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Reporting group description:

Participants received 4.5 mg of OTX (intravenous solution for infusion) daily for 6 Days

Serious adverse events	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	2 / 9 (22.22%)	1 / 8 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (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
Fibula fracture			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (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
Infections and infestations			

Cytomegalovirus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (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

Serious adverse events	Otelixizumab 27 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibula fracture			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cytomegalovirus infection			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic disorder			
subjects affected / exposed	0 / 7 (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: 0 %

Non-serious adverse events	Placebo	Otelixizumab 9 mg	Otelixizumab 18 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	9 / 9 (100.00%)	8 / 8 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Thrombophlebitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Nail operation			

subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Wisdom teeth removal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 9 (33.33%)	6 / 8 (75.00%)
occurrences (all)	0	3	11
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	3 / 8 (37.50%)
occurrences (all)	0	1	3
Chills			
subjects affected / exposed	0 / 5 (0.00%)	3 / 9 (33.33%)	0 / 8 (0.00%)
occurrences (all)	0	4	0
Peripheral swelling			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Inflammation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	1	2
Application site scab			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Facial pain			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1
Infusion site reaction subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Nodule subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Reproductive system and breast disorders Balanoposthitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 2	0 / 8 (0.00%) 0
Nipple pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	3 / 9 (33.33%) 6	2 / 8 (25.00%) 2
Cough subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1
Asthma subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Depressive symptom			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Intentional self-injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT Prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Haematocrit decreased			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Heart rate irregular subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Injury, poisoning and procedural complications			
Ligament sprain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Limb injury subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1
Clavicle fracture subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Concussion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Fibula fracture subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Hand fracture subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Joint injury			

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Post procedural complication			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Repetitive strain injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 5 (80.00%)	9 / 9 (100.00%)	8 / 8 (100.00%)
occurrences (all)	25	45	25
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	2	1	1
Dizziness postural			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Memory impairment			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Migraine subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1
Syncope subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Blood and lymphatic system disorders			
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 9 (11.11%) 2	1 / 8 (12.50%) 1
Anaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Eosinophilia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Lymphopenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	2 / 8 (25.00%) 2
Leukocytosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1
Monocytosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	0 / 8 (0.00%) 0

Ear and labyrinth disorders			
Ear disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Motion sickness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Tinnitus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 5 (40.00%)	5 / 9 (55.56%)	8 / 8 (100.00%)
occurrences (all)	2	7	16
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	4 / 9 (44.44%)	6 / 8 (75.00%)
occurrences (all)	0	9	10
Abdominal pain upper			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	6 / 8 (75.00%)
occurrences (all)	1	1	7
Abdominal pain			
subjects affected / exposed	2 / 5 (40.00%)	3 / 9 (33.33%)	3 / 8 (37.50%)
occurrences (all)	5	4	3
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	3 / 9 (33.33%)	1 / 8 (12.50%)
occurrences (all)	1	4	2
Constipation			
subjects affected / exposed	2 / 5 (40.00%)	0 / 9 (0.00%)	2 / 8 (25.00%)
occurrences (all)	4	0	2
Aphthous ulcer			

subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	0	1	6
Abdominal distension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gingival recession			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Tongue disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 5 (20.00%)	4 / 9 (44.44%)	7 / 8 (87.50%)
occurrences (all)	1	12	14
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	2 / 9 (22.22%)	1 / 8 (12.50%)
occurrences (all)	0	3	1
Alopecia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 9 (33.33%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	2 / 9 (22.22%)	2 / 8 (25.00%)
occurrences (all)	0	2	2
Rash erythematous			
subjects affected / exposed	0 / 5 (0.00%)	2 / 9 (22.22%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Skin exfoliation			
subjects affected / exposed	0 / 5 (0.00%)	3 / 9 (33.33%)	0 / 8 (0.00%)
occurrences (all)	0	3	0

Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Dermatitis acneiform			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Dermatitis contact			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Generalised erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rash generalised			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Microalbuminuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 5 (40.00%)	3 / 9 (33.33%)	5 / 8 (62.50%)
occurrences (all)	6	3	5
Arthralgia			

subjects affected / exposed	0 / 5 (0.00%)	3 / 9 (33.33%)	4 / 8 (50.00%)
occurrences (all)	0	4	8
Myalgia			
subjects affected / exposed	1 / 5 (20.00%)	3 / 9 (33.33%)	2 / 8 (25.00%)
occurrences (all)	1	4	2
Pain in extremity			
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Arthritis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 5 (40.00%)	6 / 9 (66.67%)	4 / 8 (50.00%)
occurrences (all)	5	10	7
Gastroenteritis			
subjects affected / exposed	1 / 5 (20.00%)	3 / 9 (33.33%)	3 / 8 (37.50%)
occurrences (all)	1	4	4
Influenza			
subjects affected / exposed	1 / 5 (20.00%)	5 / 9 (55.56%)	1 / 8 (12.50%)
occurrences (all)	1	5	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	2 / 8 (25.00%)
occurrences (all)	0	1	3
Onychomycosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Body tinea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2

Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cytomegalovirus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gingival abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Herpes virus infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Subcutaneous abscess			
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Tooth abscess subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0
Vaginal infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1
Metabolism and nutrition disorders			
Hypoglycaemia subjects affected / exposed occurrences (all)	5 / 5 (100.00%) 434	9 / 9 (100.00%) 646	8 / 8 (100.00%) 210
Hyperglycaemia subjects affected / exposed occurrences (all)	5 / 5 (100.00%) 118	9 / 9 (100.00%) 380	7 / 8 (87.50%) 360
Decreased appetite subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	2 / 8 (25.00%) 2
Iron deficiency subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 9 (11.11%) 2	0 / 8 (0.00%) 0
Metabolic disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	2 / 9 (22.22%) 2	0 / 8 (0.00%) 0
Diabetic ketoacidosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	1 / 8 (12.50%) 2
Increased appetite subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 9 (0.00%) 0	1 / 8 (12.50%) 1
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 9 (11.11%) 1	0 / 8 (0.00%) 0

Non-serious adverse events	Otelixizumab 27 mg		
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Phlebitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Thrombophlebitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Nail operation			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Wisdom teeth removal			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Peripheral swelling			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Influenza like illness			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Application site scab			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Facial pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Infusion site reaction			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nodule			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Nipple pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	4		
Cough			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Depressive symptom			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Intentional self-injury			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Stress			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	3		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Electrocardiogram QT Prolonged			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Haematocrit decreased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Heart rate irregular			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Clavicle fracture			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Concussion			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Contusion			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Fibula fracture			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hand fracture			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Joint injury			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Laceration			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Post procedural complication			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Repetitive strain injury			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nervous system disorders			
Headache			

subjects affected / exposed	7 / 7 (100.00%)		
occurrences (all)	32		
Dizziness			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Dizziness postural			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Memory impairment			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	6		
Anaemia			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Eosinophilia			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

Leukocytosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2		
Leukopenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Monocytosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Neutropenia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Ear and labyrinth disorders Ear disorder subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Motion sickness subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Tinnitus subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Vertigo subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	7 / 7 (100.00%) 15		
Vomiting subjects affected / exposed occurrences (all)	7 / 7 (100.00%) 12		
Abdominal pain upper			

subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Aphthous ulcer			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gingival recession			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Tongue disorder			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 7 (100.00%)		
occurrences (all)	9		
Pruritus			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		

Alopecia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Rash erythematous			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Skin exfoliation			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Generalised erythema			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Rash generalised			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Microalbuminuria			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	6		
Myalgia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Arthritis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 7 (71.43%)		
occurrences (all)	11		
Gastroenteritis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

Influenza			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Onychomycosis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Body tinea			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Cytomegalovirus infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastrointestinal infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gingival abscess			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Herpes virus infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Subcutaneous abscess			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vaginal infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	7 / 7 (100.00%)		
occurrences (all)	622		
Hyperglycaemia			
subjects affected / exposed	7 / 7 (100.00%)		
occurrences (all)	215		
Decreased appetite			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Iron deficiency			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Metabolic disorder			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Diabetic ketoacidosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Increased appetite			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2014	Amend_01: Addition of unblinded Pharmacy Monitor to table summarising blinding status of personnel; endpoint in table updated to include insulin measurement for 7 days before all outpatient visits; endpoint of glucose added when performing Mixed Meal Tolerance test and clamp procedures; clarification of time period for collecting information in the screening period; removal of T Cell Receptor complexes and clarification of CD3 requirements throughout protocol; change of volume required to purge the Intravenous infusion line and total volume filled into syringe, and removal of "micopore" from description; the following changes to the Time and Events Tables: clarification that insulin should be recorded for 7 days before all outpatient visits; addition of Day 6 to footnote; clarification that glucose will be collected in addition to C-peptide during the hyperglycaemic clamp procedure; addition of Electrocardiograms at 6 hours post start of infusion clarification of which Electrocardiograms will be triplicate or single measures; addition of T Cell Receptor deep sequencing at 24 months to Biomarker Assay Table; clarification that Mixed Meal Tolerance test will be at least 7 days prior to the first dose of study drug; clarification that c-peptide and glucose samples will be shipped within 3 weeks of collection; clarification that the hyperglycaemic range of 180-240 milligram per deciliter during 140 minutes for consistency with blood sampling time points.
02 April 2014	Amend_02: Hyperglycaemic events is included in the follow up endpoints and the Time and Events table to be consistent with the applicable secondary objective; rephrased "Immuno-Assay for syphilis test" in order to allow for different types of tests; increased the overage volume required to remain in the syringe for infusion; clarified the start of Adverse Events recording.
18 June 2014	Amend_03: The third medical monitor has changed, therefore contact information for the replacement is included. The eligibility inclusion criterion was changed from two to one positive autoantibody associated with Type 1 Diabetes Mellitus
28 July 2014	Amend_3.1: Clarified that within each cohort administration of study treatment for the first three patients will be staggered by at least three days across each centre.
11 February 2015	Amend_04: To increase flexibility for patients, dosing on Day 4, 5 & 6 may be performed on an out-patient basis if the Investigator is satisfied with the clinical status of the patient; clarification that if the infusion needs to be reduced or temporarily stopped the Investigator should first consult with the Medical Monitor who will consult the Sponsor, unless there is an immediate safety hazard, in this case the Investigator can inform the Medical Monitor afterwards; clarified that insulin use is to be recorded prior to each visit and phone call; clarification that the decision to replace a patient is to be based on the reason for withdrawal; inclusion criteria amended; screen failure data are to be collected; assessments following patient withdrawal clarified; clarified that infusion kits are supplied to sites; assessment of Epstein Barr Virus reactivation now conducted at 6 weeks after the first active dose; blinding status amended to clarify that only the patient is blinded and not site staff; requirement for pharmacy staff to document that investigational product shipping conditions were 2-8°C included; anti-emetic added as a permitted concomitant medication, window of ± 1 day added to Day 14, 21 visits & Week 4 telephone call; Dosing and Follow-up amended to include a phone call at Week 4 to discuss Adverse Events (AEs) with patient and addition of assessments at Week 6; endpoints amended to reflect the change to visits at Week 4 and Week 6; Detail for Vitals, Electrocardiogram and Pharmacokinetic and Pharmacodynamic Monitoring over the Infusion Period amended to include Electrocardiogram at 3 hours and to clarify that assessments may stop at 3 hours post dose; clarification of cytokine release syndrome adverse events grading system and stopping criteria in Section; Cytokine Release Syndrome (CRS) AEs; clarification on requirements for bilirubin samples included

18 August 2015	Amend_05: The assay for screening Epstein Barr Virus ImmunoglobulinG and ImmunoglobulinM assessment was clarified in exclusion criterion and in the Risk Management section; exclusion criterion was split into two exclusion criterias to clarify Epstein Barr Virus ImmunoglobulinM, ImmunoglobulinG and Viral load requirements for the interpretation of the results: a footnote was added to Table; Stopping Criteria for Cytokine Release Syndrome-Adverse Events to provide further clarification regarding when individual stopping criteria are met; the dose preparation section was updated to clarify that an additional maximum of 30 minutes is allowed for dose preparation tasks and that if 6 hours is exceeded, the syringe and infusion materials must be replaced; Epstein Barr Virus serology samples to assess ImmunoglobulinG and ImmunoglobulinM included for Day -1 in the Time and Events Table; Dosing and Follow-Up.
12 September 2016	Amend_06: Clarifications were made to the exploratory biomarker objectives and endpoints. Significant changes were: the addition of Th17 cells to the objective to assess the effect of orelizumab on circulating lymphocytes; the addition of viral antigens to the endpoints to assess the effect of orelizumab on the frequency of cytokine-producing antigen specific T cells; the addition of transcriptomic gene expression changes to the objective to assess the effect of orelizumab on the clonal repertoire of circulating T cell populations; and clarification that the suppression activity of circulating T lymphocytes may be further evaluated by adapting assay conditions, possibly through adding and/or blocking of stimuli. The Time and Events table was updated to show requirement for telephone calls at Month 36, 48 and 60. Month 24 exploratory biomarkers are now being routinely collected and are not subject to the results of Month 12 biomarker analysis. In addition, it was clarified that Month 24 exploratory biomarker samples will be collected and only analysed after review of safety endpoints from Month 12 and not efficacy endpoints as previously stated. Minor clarifications related to the Month 12 Interim Analyses were included.
11 September 2017	Amend_07: All details of how the currently used Ensure powder (Abbott) is prepared has been removed from the Mixed Meal Tolerance Test. This has been amended because the manufacturer (Abbott) has discontinued the currently used powder and the new product has a slightly different formulation.
26 October 2017	Amend_08: Data which emerged from an interim analysis carried out in this study showed a prompt regain of immune competence observed in treated subjects and consequent rapid resolution of Epstein Barr Virus reactivation, both clinically and virologically. The long term EBV related Post-Transplant Lymphoproliferative Disorder risk, as observed in solid organ transplant on a chronic immune suppression therapy, is negligible. Therefore, all references to month 48 and 60 have been removed as no patient currently enrolled in the study has reached month 48 of follow up. For the patients who have yet to complete their 24 month visit, this visit will be treated as a final visit and for those who have gone past month 24, they will be followed up with a final communication or visit (final follow up) upon approval of this protocol amendment. Data from the literature identified a causal relationship between the degree of immunosuppression and an increased incidence of Epstein Barr Virus related Post Transplant Lymphoproliferative Disorders and for this reason a long-term follow-up was implemented at the start of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported