



Clinical trial results:

Phase II, dose ranging, efficacy study of anti-thymocyte globulin (ATG) within 6 weeks of diagnosis of type 1 diabetes (T1D)

Summary

EudraCT number	2019-003265-17
Trial protocol	BE DE FI SI AT IT DK
Global end of trial date	16 December 2024

Results information

Result version number	v1 (current)
This version publication date	27 July 2025
First version publication date	27 July 2025

Trial information

Trial identification

Sponsor protocol code	S63466
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04509791
WHO universal trial number (UTN)	-
Other trial identifiers	University of Cambridge Department of Paediatrics : MELD-ATG 2020-1

Notes:

Sponsors

Sponsor organisation name	University of Cambridge
Sponsor organisation address	Francis Crick Ave, Cambridge, United Kingdom,
Public contact	MELD-ATG Trial Coordinator, Univeristy of Cambridge, +44 01223762944, MELD-ATG@medschl.cam.ac.uk
Scientific contact	MELD-ATG Trial Coordinator, Univeristy of Cambridge, +44 01223762944, MELD-ATG@medschl.cam.ac.uk
Sponsor organisation name	University Hospitals Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	MELD-ATG@uzleuven.be, University Hospitals Leuven Department of Clinical and Experimental Medicine, 0032 16342129, MELD-ATG@uzleuven.be
Scientific contact	MELD-ATG@uzleuven.be, University Hospitals Leuven Department of Clinical and Experimental Medicine, 0032 16342129, MELD-ATG@uzleuven.be

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	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 December 2024
Global end of trial reached?	Yes
Global end of trial date	16 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine the changes in stimulated C-peptide response over the first two hours of a mixed meal tolerance test (MMTT) at 12 months for 2.5mg/kg ATG arm versus the placebo.
- Conditional on finding a statistical difference between the 2.5mg/kg ATG arm and placebo, to identify the minimally effective dose (lowest dose significantly different to placebo) amongst the doses studied in the trial using change in stimulated C-peptide response over the first two hours of a MMTT at 12 months versus placebo.

Protection of trial subjects:

NA

Background therapy:

insulin therapy

Evidence for comparator:

NA

Actual start date of recruitment	01 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	Slovenia: 15
Country: Number of subjects enrolled	United Kingdom: 38
Country: Number of subjects enrolled	Austria: 13
Country: Number of subjects enrolled	Belgium: 43
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	152
EEA total number of subjects	114

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)	56
Adolescents (12-17 years)	71
Adults (18-64 years)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment officially started in November 2020 (Belgium). Recruitment in Germany, the UK, Slovenia and Austria started in 2021. Recruitment in Denmark & Italy started in 2022. In 2023, recruitment started in Finland.

Recruitment was officially completed in January 2024.

Pre-assignment

Screening details:

Major inclusion criteria: T1DM diagnosis <9 weeks of planned treatment day 1, random C-peptide levels ≥ 200 pmol/L, presence of ≥ 1 diabetes-related autoantibody (GADA, IA-2A or ZnT8A)

Major exclusion criteria: T2DM, evidence of tuberculosis infection, requiring use of immunosuppressive or immunomodulative agents (e.g. use of systemic steroids)

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

The web-based randomisation system Sealed Envelope was used for randomising. Both patients and the study teams were blinded to the treatment allocation. The pharmacy team was unblinded to the treatment allocation, in order to be able to prepare the infusion. The medical monitor was unblinded for safety review and the monitors for reviewing the study team and pharmacy teams.

Emergency unblinding for safety reasons was possible during the entire trial (responsibility of the investigator).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

IV sodium chloride solution (0.9%)

Arm title	Middle dose 1 - 0.1mg/kg ATG
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Arm description:

Low dose Anti-thymocyte globulin (ATG) - 0.1mg/kg

Arm type	Experimental
Investigational medicinal product name	Anti-thymocyte globulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

IV - Low dose Anti-thymocyte globulin - 0.1mg/kg in sodium chloride solution (0.9%)

Arm title	Middle dose 2 - 0.5mg/kg ATG
Arm description:	
Low dose Anti-thymocyte globulin (ATG) - 0.5mg/kg	
Arm type	Experimental
Investigational medicinal product name	Anti-thymocyte globulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion
Dosage and administration details:	
IV - Low dose Anti-thymocyte globulin - 0.5mg/kg in sodium chloride solution (0.9%)	
Arm title	Middle dose 3 - 1.5mg/kg ATG
Arm description:	
Low dose Anti-thymocyte globulin (ATG) - 1.5mg/kg	
Arm type	Experimental
Investigational medicinal product name	Anti-thymocyte globulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion
Dosage and administration details:	
IV - Low dose Anti-thymocyte globulin - 1.0mg/kg in sodium chloride solution (0.9%)	
Arm title	High dose - 2.5mg/kg ATG
Arm description:	
High dose Anti-thymocyte globulin (ATG) - 2.5mg/kg	
Arm type	Experimental
Investigational medicinal product name	Anti-thymocyte globulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion
Dosage and administration details:	
IV - High dose Anti-thymocyte globulin - 2.5mg/kg in sodium chloride solution (0.9%)	

Number of subjects in period 1^[1]	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG
Started	31	6	35
Completed	30	5	32
Not completed	1	1	3
Consent withdrawn by subject	1	-	1
Lost to follow-up	-	1	2

Number of subjects in period 1^[1]	Middle dose 3 - 1.5mg/kg ATG	High dose - 2.5mg/kg ATG
Started	12	33

Completed	9	32
Not completed	3	1
Consent withdrawn by subject	1	-
Lost to follow-up	2	1

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: The number of subject enrolled worldwide resembles the number of subjects that have been screened for this trial. The number of subjects in the baseline period resembles the number of subjects that have been screened and found to be eligible for participation in the trial and have therefore had a baseline visit during which baseline data were collected for primary and secondary outcomes. Statistical analyses were carried out according to a intention-to-treat principle.

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo -	
Reporting group title	Middle dose 1 - 0.1mg/kg ATG
Reporting group description:	
Low dose Anti-thymocyte globulin (ATG) - 0.1mg/kg	
Reporting group title	Middle dose 2 - 0.5mg/kg ATG
Reporting group description:	
Low dose Anti-thymocyte globulin (ATG) - 0.5mg/kg	
Reporting group title	Middle dose 3 - 1.5mg/kg ATG
Reporting group description:	
Low dose Anti-thymocyte globulin (ATG) - 1.5mg/kg	
Reporting group title	High dose - 2.5mg/kg ATG
Reporting group description:	
High dose Anti-thymocyte globulin (ATG) - 2.5mg/kg	

Reporting group values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG
Number of subjects	31	6	35
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Children (5-11)	6	0	7
Adolescents (12-17)	21	4	22
Adults (18-25)	4	2	6
Gender categorical			
Units: Subjects			
Female	10	3	22
Male	21	3	13
Ethnicity			
Units: Subjects			
Europe (excl Nordic countries)	26	6	27
Africa	1	0	1
Asia - including Turkey	0	0	2
Mixed	2	0	1
Nordic (Norway Sweden Denmark Finland Iceland Faro)	2	0	4
Diabetes-related autoantibodies			

Number of diabetes-related autoantibodies present at baseline			
Units: Subjects			
1 autoantibody	0	1	3
2 autoantibodies	5	1	8
3 autoantibodies	16	1	9
4 autoantibodies	10	3	15
BMI			
Units: kg/m ²			
arithmetic mean	20.18	23.3	19.39
standard deviation	± 3.68	± 3.76	± 3.25
Glycated hemoglobin			
Glycated hemoglobin (%) at baseline			
Units: Percentage			
arithmetic mean	7.64	7.2	7.89
standard deviation	± 1.1	± 0.66	± 1.32
Insulin dose-adjusted A1c			
Insulin dose-adjusted A1c (IDAA1C) at baseline			
Units: Index			
arithmetic mean	9.34	8.32	9.56
standard deviation	± 1.78	± 1.05	± 2.02
C-peptide AUC			
C-peptide AUC from 2-hour MMTT (nmol/L/min) at baseline			
Units: nmol/L/min			
median	0.79	1.06	0.83
inter-quartile range (Q1-Q3)	0.62 to 0.97	0.8 to 1.63	0.67 to 1.15
Time from T1D diagnosis to randomization			
Time from T1D diagnosis to randomization in days			
Units: days			
median	54	51	50
inter-quartile range (Q1-Q3)	47 to 57	43 to 58	40 to 56

Reporting group values	Middle dose 3 - 1.5mg/kg ATG	High dose - 2.5mg/kg ATG	Total
Number of subjects	12	33	117
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Children (5-11)	1	7	21
Adolescents (12-17)	8	21	76
Adults (18-25)	3	5	20
Gender categorical			
Units: Subjects			
Female	8	20	63

Male	4	13	54
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Ethnicity			
Units: Subjects			
Europe (excl Nordic countries)	9	27	95
Africa	1	1	4
Asia - including Turkey	1	1	4
Mixed	0	1	4
Nordic (Norway Sweden Denmark Finland Iceland Faro	1	3	10
Diabetes-related autoantibodies			
Number of diabetes-related autoantibodies present at baseline			
Units: Subjects			
1 autoantibody	1	1	6
2 autoantibodies	1	10	25
3 autoantibodies	3	12	41
4 autoantibodies	7	10	45
BMI			
Units: kg/m ²			
arithmetic mean	19.83	19.62	
standard deviation	± 3.77	± 3.46	-
Glycated hemoglobin			
Glycated hemoglobin (%) at baseline			
Units: Percentage			
arithmetic mean	7.97	7.88	
standard deviation	± 1.35	± 1.17	-
Insulin dose-adjusted A1c			
Insulin dose-adjusted A1c (IDAA1C) at baseline			
Units: Index			
arithmetic mean	9.45	9.51	
standard deviation	± 2.19	± 1.67	-
C-peptide AUC			
C-peptide AUC from 2-hour MMTT (nmol/L/min) at baseline			
Units: nmol/L/min			
median	0.86	0.81	
inter-quartile range (Q1-Q3)	0.70 to 1.30	0.68 to 0.95	-
Time from T1D diagnosis to randomization			
Time from T1D diagnosis to randomization in days			
Units: days			
median	48	51	
inter-quartile range (Q1-Q3)	34 to 57	40 to 56	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo -	
Reporting group title	Middle dose 1 - 0.1mg/kg ATG
Reporting group description:	
Low dose Anti-thymocyte globulin (ATG) - 0.1mg/kg	
Reporting group title	Middle dose 2 - 0.5mg/kg ATG
Reporting group description:	
Low dose Anti-thymocyte globulin (ATG) - 0.5mg/kg	
Reporting group title	Middle dose 3 - 1.5mg/kg ATG
Reporting group description:	
Low dose Anti-thymocyte globulin (ATG) - 1.5mg/kg	
Reporting group title	High dose - 2.5mg/kg ATG
Reporting group description:	
High dose Anti-thymocyte globulin (ATG) - 2.5mg/kg	

Primary: Changes of C-peptide response during a MMTT - 12 months post treatment

End point title	Changes of C-peptide response during a MMTT - 12 months post treatment
End point description:	
The differences in changes in area under the stimulated C-peptide response curve over the first 2 hours of a MMTT at 12 months post treatment.	
End point type	Primary
End point timeframe:	
12 months post treatment	

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: nmol/L/min				
log mean (confidence interval 95%)	0.411403434 (0.348140202 to 0.474666666)	0.562477373 (0.417939595 to 0.70701505)	0.513130606 (0.451309393 to 0.574952020)	0.466454545 (0.360205959 to 0.572703232)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: nmol/L/min				
log mean (confidence interval 95%)	0.535193737			

(0.473115656
to
0.597271717)

Statistical analyses

Statistical analysis title	Primary outcome (placebo v. 2.5mg/kg dose)
Statistical analysis description: A mixed effects longitudinal model was used on the transformed $\ln(\text{AUC C-peptide}+1)$ data (baseline, 3-, 6- and 12-months) adjusting for baseline C-peptide data in the model as an outcome. The model assumes that the repeated measures follow a multivariate normal distribution and allows randomized participants with missing timepoint data to be incorporated under a Missing At Random (MAR) assumption.	
Comparison groups	High dose - 2.5mg/kg ATG v Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.05 ^[2]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.124
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.043
upper limit	0.205
Variability estimate	Standard error of the mean
Dispersion value	0.0415

Notes:

[1] - The primary hypothesis of comparing 2.5mg/kg ATG to placebo. Assuming this SD and comparing 2.5mg/kg ATG to placebo on the transformed $\ln(\text{AUC C-peptide}+1)$ scale, 32 participants in each arm provided over 90% power at a 5% significance level to detect a change of 0.22 nmol/L/min using a two-sided two-sample t-test.

[2] - If the 2.5mg/kg dose was found not to be statistically significant, no further tests would have been carried out, forming a gatekeeping procedure for the primary endpoint and the family wise error rate controlled at 5%.

Statistical analysis title	Primary outcome (placebo v. 0.5mg/kg dose)
Statistical analysis description: Given a significant effect for the 2.5mg/kg ATG versus placebo mean difference, the middle dose level (0.5mg/kg ATG) was compared to the placebo dose at the 5% level using the Wald test.	
Comparison groups	Placebo v Middle dose 2 - 0.5mg/kg ATG
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.05 ^[4]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.102

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.021
upper limit	0.183
Variability estimate	Standard error of the mean
Dispersion value	0.041

Notes:

[3] - Given a significant effect for the 2.5mg/kg ATG versus placebo mean difference, the middle dose level (0.5mg/kg ATG) was compared to the placebo dose at the 5% level using the Wald test.

[4] - If the 2.5mg/kg dose was found not to be statistically significant, no further tests would have been carried out, forming a gatekeeping procedure for the primary endpoint and the family wise error rate controlled at 5%.

Primary: Changes in CD4/CD8 ratio - 12 months post treatment

End point title	Changes in CD4/CD8 ratio - 12 months post treatment
End point description: Changes in CD4/CD8 ratio - 12 months post treatment	
End point type	Primary
End point timeframe: 12 months post treatment	

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: units				
geometric mean (confidence interval 95%)	1.98045 (1.832757 to 2.128143)	2.257679 (1.969606 to 2.545753)	1.947787 (1.803551 to 2.092023)	1.489817 (1.273482 to 1.706152)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units				
geometric mean (confidence interval 95%)	1.395302 (1.250049 to 1.540555)			

Statistical analyses

Statistical analysis title	Secondary - CD4/CD8 (placebo v. 2.5mg/kg dose)
Statistical analysis description: Comparable linear mixed effects models were fitted to secondary outcome, ratio of CD4/CD8. This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.	
Comparison groups	Placebo v High dose - 2.5mg/kg ATG

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 ^[5]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.585
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	-0.43
Variability estimate	Standard error of the mean
Dispersion value	0.079

Notes:

[5] - This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Statistical analysis title	Secondary - CD4/CD8 (placebo v. 0.5mg/kg dose)
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Statistical analysis description:

Comparable linear mixed effects models were fitted to secondary outcomes, CD4/CD8 ratio of absolute counts. This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Comparison groups	Placebo v Middle dose 2 - 0.5mg/kg ATG
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 ^[6]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.033
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.186
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.078

Notes:

[6] - This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Secondary: Changes of C-peptide response during a MMTT - 3 months post treatment

End point title	Changes of C-peptide response during a MMTT - 3 months post treatment
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End point description:

The differences in changes in area under the stimulated C-peptide response curve over the first 2 hours of a MMTT at 3 months post treatment.

End point type	Secondary
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End point timeframe:

3 months post treatment

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: nmol/L/min				
log mean (confidence interval 95%)	0.576156262 (0.527184949 to 0.6251275)	0.708432626 (0.618357979 to 0.798507272)	0.6284462 (0.5808083 to 0.6760841)	0.6039400 (0.538042525 to 0.669837676)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: nmol/L/min				
log mean (confidence interval 95%)	0.6238126 (0.5760606 to 0.6715645)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes of C-peptide response during a MMTT - 6 months post treatment

End point title	Changes of C-peptide response during a MMTT - 6 months post treatment
End point description: The differences in changes in area under the stimulated C-peptide response curve over the first 2 hours of a MMTT at 6 months post treatment.	
End point type	Secondary
End point timeframe: 6 months post treatment	

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	34	9
Units: nmol/L/min				
log mean (confidence interval 95%)	0.5052018 (0.4495933 to 0.5608104)	0.661471212 (0.545831919 to 0.777110606)	0.5953023 (0.5412028 to 0.649401818)	0.5914197 (0.5082453 to 0.6745941)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: nmol/L/min				
log mean (confidence interval 95%)	0.587397777 (0.533288080 to 0.641507474)			

Statistical analyses

No statistical analyses for this end point

Secondary: HbA1c (mmol/mol) - 3 months post treatment

End point title	HbA1c (mmol/mol) - 3 months post treatment
End point description:	
Changes in HbA1c 3 months post treatment	
End point type	Secondary
End point timeframe:	
3 months post treatment	

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: mmol/mol				
geometric mean (confidence interval 95%)	46.9532354 (43.5213982 to 50.3850835)	43.9032028 (35.9700494 to 51.8363672)	46.5149825 (43.2876378 to 49.7423271)	45.7195261 (40.3307750 to 51.1082663)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mmol/mol				
geometric mean (confidence interval 95%)	47.9692171 (44.7286156 to 51.2098186)			

Statistical analyses

No statistical analyses for this end point

Secondary: HbA1c (mmol/mol) - 6 months post treatment

End point title	HbA1c (mmol/mol) - 6 months post treatment
End point description: Changes in HbA1c 6 months post treatment	
End point type	Secondary
End point timeframe: 6 months post treatment	

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: mmol/mol				
log mean (confidence interval 95%)	50.6954671 (47.1621432 to 54.2287800)	42.9364016 (34.6840121 to 51.1887912)	45.7402257 (42.4184217 to 49.0620187)	46.6922509 (40.8662086 to 52.5182931)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mmol/mol				
log mean (confidence interval 95%)	48.2148026 (44.8391187 to 51.5904975)			

Statistical analyses

No statistical analyses for this end point

Secondary: HbA1c (mmol/mol) - 12 months post treatment

End point title	HbA1c (mmol/mol) - 12 months post treatment
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End point description:	
Changes in HbA1c 12 months post treatment	
End point type	Secondary
End point timeframe:	
12 months post treatment	

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: mmol/mol				
log mean (confidence interval 95%)	53.8019479 (50.2996515 to 57.3042443)	43.7714647 (35.4721023 to 52.0708161)	48.3601802 (45.0188570 to 51.7014924)	49.2193307 (43.0644458 to 55.3742157)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mmol/mol				
log mean (confidence interval 95%)	49.8691909 (46.4764031 to 53.2619788)			

Statistical analyses

Statistical analysis title	Secondary outcome HbA1c (placebo v. 2.5mg/kg dose)
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Statistical analysis description:

Comparable linear mixed effects models were fitted to secondary outcomes, glycated hemoglobin (%) (HbA1c). This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Comparison groups	Placebo v High dose - 2.5mg/kg ATG
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 ^[7]
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.08

Variability estimate	Standard error of the mean
Dispersion value	0.223

Notes:

[7] - This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Statistical analysis title	Secondary outcome HbA1c (placebo v. 0.5mg/kg dose)
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Statistical analysis description:

Comparable linear mixed effects models were fitted to secondary outcomes, glycated hemoglobin (%) (HbA1c). This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Comparison groups	Placebo v Middle dose 2 - 0.5mg/kg ATG
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [8]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.221

Notes:

[8] - This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Secondary: Insulin use - 3 months post treatment

End point title	Insulin use - 3 months post treatment
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End point description:

Changes in insuline use 3 months post treatment

End point type	Secondary
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End point timeframe:

3 months post treatment

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: units/24hr/kg				
geometric mean (confidence interval 95%)	0.38407939 (0.31251384 to 0.45564485)	0.26222 (0.100212121 to 0.424227979)	0.401080505 (0.333150101 to 0.469010909)	0.415460808 (0.303360404 to 0.527561111)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units/24hr/kg				
geometric mean (confidence interval 95%)	0.4144191 (0.344957 to 0.4838813)			

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin use - 6 months post treatment

End point title	Insulin use - 6 months post treatment
End point description:	Changes in insuline use 6 months post treatment
End point type	Secondary
End point timeframe:	6 months post treatment

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: units/24hr/kg				
geometric mean (confidence interval 95%)	0.4735686 (0.40003848 to 0.5467524)	0.2778695 (0.1156906 to 0.4400483)	0.4447685 (0.3754506 to 0.5140863)	0.3759515 (0.2597446 to 0.4921584)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units/24hr/kg				
geometric mean (confidence interval 95%)	0.4194426 (0.3499787 to 0.4889064)			

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin use - 12 months post treatment

End point title	Insulin use - 12 months post treatment
End point description:	
Changes in insuline use 12 months post treatment	
End point type	Secondary
End point timeframe:	
12 months post treatment	

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: units/24hr/kg				
geometric mean (confidence interval 95%)	0.5380983 (0.4664981 to 0.6096986)	0.3946814 (0.2325022 to 0.5568606)	0.5253224 (0.455307 to 0.5953379)	0.4686962 (0.3479719 to 0.5894206)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units/24hr/kg				
geometric mean (confidence interval 95%)	0.5024111 (0.4322181 to 0.5726042)			

Statistical analyses

Statistical analysis title	Secondary - insulin use (placebo v. 2.5mg/kg dose)
Statistical analysis description:	
Comparable linear mixed effects models were fitted to secondary outcome, insulin use (mg/kg/24hrs). This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.	
Comparison groups	Placebo v High dose - 2.5mg/kg ATG
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 ^[9]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.128
upper limit	0.056

Variability estimate	Standard error of the mean
Dispersion value	0.047

Notes:

[9] - This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Statistical analysis title	Secondary - insulin use (placebo v. 0.5mg/kg dose)
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Statistical analysis description:

Comparable linear mixed effects models were fitted to secondary outcome, insulin use (mg/kg/24hrs). This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Comparison groups	Placebo v Middle dose 2 - 0.5mg/kg ATG
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 ^[10]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.104
upper limit	0.079
Variability estimate	Standard error of the mean
Dispersion value	0.047

Notes:

[10] - This secondary outcome was not included in the multiplicity control so individual findings should be interpreted as exploratory.

Secondary: Changes in CD4/CD8 ratio - 3 months post treatment

End point title	Changes in CD4/CD8 ratio - 3 months post treatment
End point description:	Changes in CD4/CD8 ratio - 3 months post treatment
End point type	Secondary
End point timeframe:	3 months post treatment

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: units				
geometric mean (confidence interval 95%)	2.061071 (1.912452 to 2.20969)	2.018107 (1.730033 to 2.30618)	1.799619 (1.656212 to 1.943027)	1.537151 (1.331781 to 1.742521)

End point values	High dose - 2.5			
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	mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units				
geometric mean (confidence interval 95%)	1.225702 (1.0806 to 1.370804)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in CD4/CD8 ratio - 6 months post treatment

End point title	Changes in CD4/CD8 ratio - 6 months post treatment
End point description:	Changes in CD4/CD8 ratio - 6 months post treatment
End point type	Secondary
End point timeframe:	6 months post treatment

End point values	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG	Middle dose 3 - 1.5mg/kg ATG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	5	32	9
Units: units				
geometric mean (confidence interval 95%)	2.076863 (1.927256 to 2.22647)	2.056617 (1.768544 to 2.34469)	1.931648 (1.786584 to 2.076712)	1.633123 (1.4225777 to 1.84367)

End point values	High dose - 2.5mg/kg ATG			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: units				
geometric mean (confidence interval 95%)	1.271815 (1.126561 to 1.417068)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From time of written informed consent until 12 months post treatment

Adverse event reporting additional description:

Any untoward medical occurrence in a participant or clinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with this treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo -

Reporting group title	Middle dose 1 - 0.1mg/kg ATG
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Reporting group description:

Low dose Anti-thymocyte globulin (ATG) - 0.1mg/kg

Reporting group title	Middle dose 2 - 0.5mg/kg ATG
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Reporting group description:

Low dose Anti-thymocyte globulin (ATG) - 0.5mg/kg

Reporting group title	Middle dose 3 - 1.5mg/kg ATG
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Reporting group description:

Low dose Anti-thymocyte globulin (ATG) - 1.5mg/kg

Reporting group title	High dose - 2.5mg/kg ATG
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Reporting group description:

High dose Anti-thymocyte globulin (ATG) - 2.5mg/kg

Serious adverse events	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Overdose as per trial allocation			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (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
Overdose as per trial allocation and as per protocol			

alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (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
Dose error			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (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
Immune system disorders			
Suspected serum sickness			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation and urinary retention			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (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
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Subcutaneous infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (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

Serious adverse events	Middle dose 3 - 1.5mg/kg ATG	High dose - 2.5mg/kg ATG	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	5 / 33 (15.15%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Overdose as per trial allocation			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose as per trial allocation and as per protocol			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dose error			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Suspected serum sickness			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation and urinary retention			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Myalgia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Subcutaneous infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo	Middle dose 1 - 0.1mg/kg ATG	Middle dose 2 - 0.5mg/kg ATG
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)	6 / 6 (100.00%)	35 / 35 (100.00%)
Vascular disorders			
Flushing			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Hypertension			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hypotension			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	2 / 31 (6.45%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences (all)	3	0	2
Phlebitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

<p>Surgical and medical procedures</p> <p>Insulin therapy (admission to start insulin pump therapy)</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 31 (3.23%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>1 / 35 (2.86%)</p> <p>1</p>
<p>Tooth extraction</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 31 (6.45%)</p> <p>2</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>0 / 35 (0.00%)</p> <p>0</p>
<p>General disorders and administration site conditions</p> <p>Chills</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 31 (6.45%)</p> <p>2</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>7 / 35 (20.00%)</p> <p>9</p>
<p>Face edema</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 31 (0.00%)</p> <p>0</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>1 / 35 (2.86%)</p> <p>1</p>
<p>Fatigue</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 31 (12.90%)</p> <p>11</p>	<p>3 / 6 (50.00%)</p> <p>4</p>	<p>7 / 35 (20.00%)</p> <p>9</p>
<p>Influenza-like illness</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 31 (3.23%)</p> <p>1</p>	<p>1 / 6 (16.67%)</p> <p>1</p>	<p>2 / 35 (5.71%)</p> <p>3</p>
<p>Infusion site pruritus</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 31 (0.00%)</p> <p>0</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>1 / 35 (2.86%)</p> <p>1</p>
<p>Injection site reaction</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 31 (0.00%)</p> <p>0</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>1 / 35 (2.86%)</p> <p>1</p>

Malaise alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	0 / 6 (0.00%) 0	3 / 35 (8.57%) 3
Non-cardiac chest pain alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 6 (16.67%) 1	1 / 35 (2.86%) 1
Peripheral edema alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Pain alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Pyrexia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	10 / 31 (32.26%) 13	2 / 6 (33.33%) 2	18 / 35 (51.43%) 23
Immune system disorders Cytokine release syndrome alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 6 (33.33%) 2	8 / 35 (22.86%) 9
Hypersensitivity alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Seasonal allergy alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Serum sickness alternative dictionary used: MedDRA 27			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	11 / 35 (31.43%) 11
Reproductive system and breast disorders			
Amenorrhea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	3 / 35 (8.57%)
occurrences (all)	1	0	7
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	5 / 31 (16.13%)	0 / 6 (0.00%)	5 / 35 (14.29%)
occurrences (all)	8	0	6
Dyspnea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Laryngeal inflammation			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	5 / 31 (16.13%)	1 / 6 (16.67%)	4 / 35 (11.43%)
occurrences (all)	9	1	8
Rhinitis allergic			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Rhinorrhea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	2 / 31 (6.45%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Tachypnea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Wheezing			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Eating disorder			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Stress			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Accidental overdose			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ankle fracture			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Dose calculation error			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Fracture			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Head injury			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Infusion related reaction			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	4 / 35 (11.43%)
occurrences (all)	2	0	4
Injury			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Limb injury			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Procedural pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Soft tissue injury			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Upper limb fracture			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Wrist fracture			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Gilbert's syndrome			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	2 / 6 (33.33%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Tachycardia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	1 / 6 (16.67%) 1	1 / 35 (2.86%) 4
Headache alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	18 / 31 (58.06%) 53	4 / 6 (66.67%) 9	24 / 35 (68.57%) 64
Lethargy alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Migraine alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Paresthesia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Syncope alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Tremor alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 6 (16.67%) 1	0 / 35 (0.00%) 0
Blood and lymphatic system disorders Anemia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Leukocytosis alternative dictionary used: MedDRA 27			

subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Lymphadenopathy			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	6 / 31 (19.35%)	2 / 6 (33.33%)	12 / 35 (34.29%)
occurrences (all)	6	2	14
Monocytopenia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	4 / 35 (11.43%)
occurrences (all)	1	0	7
Neutrophilia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	2
Middle ear infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Vertigo			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Chalazion			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Conjunctival hemorrhage			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dry eye			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Eye edema			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Eye pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Periorbital edema			
alternative dictionary used: MedDRA 27			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Gastrointestinal disorders			
Abdominal distension alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Abdominal pain alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	7 / 31 (22.58%) 14	3 / 6 (50.00%) 5	11 / 35 (31.43%) 12
Celiac disease alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Constipation alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 6 (16.67%) 1	0 / 35 (0.00%) 0
Diarrhea alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	5 / 31 (16.13%) 6	0 / 6 (0.00%) 0	5 / 35 (14.29%) 6
Dyspepsia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 6 (16.67%) 1	0 / 35 (0.00%) 0
Dysphagia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Epigastric discomfort alternative dictionary used: MedDRA 27			

subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Nausea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	6 / 31 (19.35%)	1 / 6 (16.67%)	6 / 35 (17.14%)
occurrences (all)	10	1	8
Oral mucosal blistering			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Tongue blistering			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Toothache			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	2 / 31 (6.45%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	1
Vomiting			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	4 / 31 (12.90%)	0 / 6 (0.00%)	7 / 35 (20.00%)
occurrences (all)	4	0	8
Hepatobiliary disorders			
Hyperbilirubinemia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Acne			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	1
Alopecia			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Angioedema			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Eczema			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	4 / 35 (11.43%)
occurrences (all)	1	0	5
Erythema			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Lipohypertrophy			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Night sweats			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Skin pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Perioral dermatitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Pruritus			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	4 / 35 (11.43%)
occurrences (all)	1	0	4
Purpura			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Rash			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	8 / 31 (25.81%)	2 / 6 (33.33%)	6 / 35 (17.14%)
occurrences (all)	9	4	8
Skin hypopigmentation			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Skin ulcer			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Spider naevus			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Urticaria			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Vitiligo			
alternative dictionary used: MedDRA 27			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Renal and urinary disorders			
Cystitis non-infective alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Dysuria alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Urinary retention alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	3 / 35 (8.57%) 3
Back pain alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Bone pain alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Joint effusion alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Muscle spasms alternative dictionary used: MedDRA 27			

subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Myalgia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	8 / 31 (25.81%)	3 / 6 (50.00%)	4 / 35 (11.43%)
occurrences (all)	13	3	5
Neck pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Acrodermatitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
COVID-19 infection			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	3 / 31 (9.68%)	1 / 6 (16.67%)	3 / 35 (8.57%)
occurrences (all)	3	1	3
Conjunctivitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	3 / 35 (8.57%)
occurrences (all)	1	0	3
Enterobiasis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Epstein-Barr virus infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Eye infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Fungal foot infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Impetigo			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	9 / 31 (29.03%)	2 / 6 (33.33%)	9 / 35 (25.71%)
occurrences (all)	12	3	14

<p>Infective exacerbation of asthma</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 31 (0.00%)</p> <p>0</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>0 / 35 (0.00%)</p> <p>0</p>
<p>Influenza</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 31 (3.23%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>1 / 35 (2.86%)</p> <p>2</p>
<p>Laryngitis</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 31 (6.45%)</p> <p>2</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>0 / 35 (0.00%)</p> <p>0</p>
<p>Lymph gland infection</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 31 (3.23%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>0 / 35 (0.00%)</p> <p>0</p>
<p>Nail infection</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 31 (0.00%)</p> <p>0</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>1 / 35 (2.86%)</p> <p>2</p>
<p>Nasopharyngitis</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>11 / 31 (35.48%)</p> <p>17</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>10 / 35 (28.57%)</p> <p>17</p>
<p>Oral herpes</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 31 (3.23%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>0 / 35 (0.00%)</p> <p>0</p>
<p>Otitis media</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 31 (6.45%)</p> <p>2</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	<p>1 / 35 (2.86%)</p> <p>1</p>
<p>Parasitic gastroenteritis</p> <p>alternative dictionary used: MedDRA 27</p>			

subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Paronychia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Pharyngitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	4 / 31 (12.90%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	5	0	1
Rhinitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	2 / 31 (6.45%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	3
Scarlet fever			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Sepsis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 31 (3.23%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	3 / 35 (8.57%)
occurrences (all)	0	0	4
Tooth infection			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 31 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	1	0

Tracheobronchitis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Upper respiratory tract infection alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Urinary tract infection alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Varicella alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Vulvovaginal candidiasis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Metabolism and nutrition disorders			
Decreased appetite alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Hyperglycemia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 6 (0.00%) 0	0 / 35 (0.00%) 0
Hypoglycemia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 6 (0.00%) 0	1 / 35 (2.86%) 1
Iron deficiency alternative dictionary used: MedDRA 27			

subjects affected / exposed	0 / 31 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1

Non-serious adverse events	Middle dose 3 - 1.5mg/kg ATG	High dose - 2.5mg/kg ATG	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	33 / 33 (100.00%)	
Vascular disorders			
Flushing			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Hypertension			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hypotension			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	3 / 33 (9.09%)	
occurrences (all)	1	3	
Phlebitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Insulin therapy (admission to start insulin pump therapy)			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Tooth extraction			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chills			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	3 / 12 (25.00%)	10 / 33 (30.30%)
occurrences (all)	3	18
Face edema		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Fatigue		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	4 / 12 (33.33%)	8 / 33 (24.24%)
occurrences (all)	5	14
Influenza-like illness		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	4 / 33 (12.12%)
occurrences (all)	1	6
Infusion site pruritus		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Injection site reaction		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Malaise		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	2
Non-cardiac chest pain		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Peripheral edema		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	2

Pain alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Pyrexia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 5	18 / 33 (54.55%) 30	
Immune system disorders Cytokine release syndrome alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	11 / 33 (33.33%) 16	
Hypersensitivity alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Seasonal allergy alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Serum sickness alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	6 / 12 (50.00%) 6	27 / 33 (81.82%) 27	
Reproductive system and breast disorders Amenorrhea alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Dysmenorrhea alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Respiratory, thoracic and mediastinal			

disorders			
Cough			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	4 / 33 (12.12%)	
occurrences (all)	1	4	
Dyspnea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Epistaxis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Laryngeal inflammation			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Nasal congestion			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	2 / 12 (16.67%)	1 / 33 (3.03%)	
occurrences (all)	2	1	
Oropharyngeal pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	2 / 12 (16.67%)	5 / 33 (15.15%)	
occurrences (all)	2	7	
Rhinitis allergic			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Rhinorrhea			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	4 / 33 (12.12%)	
occurrences (all)	1	5	
Tachypnea			
alternative dictionary used: MedDRA 27			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Throat irritation</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Wheezing</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>	<p>1 / 33 (3.03%)</p> <p>1</p> <p>0 / 33 (0.00%)</p> <p>0</p> <p>0 / 33 (0.00%)</p> <p>0</p>	
<p>Psychiatric disorders</p> <p>Anxiety</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Eating disorder</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Stress</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>	<p>0 / 33 (0.00%)</p> <p>0</p> <p>1 / 33 (3.03%)</p> <p>1</p> <p>0 / 33 (0.00%)</p> <p>0</p>	
<p>Injury, poisoning and procedural complications</p> <p>Accidental overdose</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ankle fracture</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dose calculation error</p> <p>alternative dictionary used: MedDRA 27</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>	<p>1 / 33 (3.03%)</p> <p>1</p> <p>0 / 33 (0.00%)</p> <p>0</p>	

subjects affected / exposed	0 / 12 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	3
Fracture		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Head injury		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Infusion related reaction		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	2 / 12 (16.67%)	5 / 33 (15.15%)
occurrences (all)	3	6
Injury		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Limb injury		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Procedural pain		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Soft tissue injury		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Upper limb fracture		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0

Wrist fracture alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Congenital, familial and genetic disorders Gilbert's syndrome alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Cardiac disorders Palpitations alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all) Tachycardia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	1 / 33 (3.03%) 1 2 / 33 (6.06%) 3	
Nervous system disorders Dizziness alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all) Headache alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all) Lethargy alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all) Migraine alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2 8 / 12 (66.67%) 18 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	2 / 33 (6.06%) 2 23 / 33 (69.70%) 48 1 / 33 (3.03%) 1 0 / 33 (0.00%) 0	

Paresthesia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Syncope alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Tremor alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Blood and lymphatic system disorders Anemia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	4 / 33 (12.12%) 4	
Leukocytosis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Leukopenia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Lymphadenopathy alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 33 (6.06%) 3	
Lymphopenia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 6	14 / 33 (42.42%) 17	
Monocytopenia alternative dictionary used: MedDRA 27			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Neutropenia</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Neutrophilia</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Thrombocytopenia</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>1 / 12 (8.33%)</p> <p>1</p>	<p>1 / 33 (3.03%)</p> <p>1</p> <p>1 / 33 (3.03%)</p> <p>1</p> <p>2 / 33 (6.06%)</p> <p>2</p> <p>3 / 33 (9.09%)</p> <p>3</p>	
<p>Ear and labyrinth disorders</p> <p>Ear pain</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Middle ear infection</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vertigo</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>	<p>0 / 33 (0.00%)</p> <p>0</p> <p>0 / 33 (0.00%)</p> <p>0</p> <p>1 / 33 (3.03%)</p> <p>1</p>	
<p>Eye disorders</p> <p>Chalazion</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Conjunctival hemorrhage</p> <p>alternative dictionary used: MedDRA 27</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	<p>0 / 33 (0.00%)</p> <p>0</p>	

subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Dry eye			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Eye edema			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Eye pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Periorbital edema			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal distension			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	4 / 12 (33.33%)	9 / 33 (27.27%)	
occurrences (all)	4	16	
Celiac disease			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Constipation			
alternative dictionary used: MedDRA 27			

subjects affected / exposed	2 / 12 (16.67%)	1 / 33 (3.03%)
occurrences (all)	2	2
Diarrhea		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	5 / 33 (15.15%)
occurrences (all)	1	7
Dyspepsia		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Dysphagia		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Epigastric discomfort		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Nausea		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	13 / 33 (39.39%)
occurrences (all)	2	25
Oral mucosal blistering		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Tongue blistering		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Toothache		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0

Vomiting alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	10 / 33 (30.30%) 18	
Hepatobiliary disorders Hyperbilirubinemia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Skin and subcutaneous tissue disorders Acne alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Alopecia alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Angioedema alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 33 (0.00%) 0	
Ecchymosis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Eczema alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Erythema alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 33 (0.00%) 0	
Hyperhidrosis			

alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Lipohypertrophy			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Night sweats			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Skin pain			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	2	
Perioral dermatitis			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Pruritus			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	3 / 12 (25.00%)	10 / 33 (30.30%)	
occurrences (all)	3	10	
Purpura			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rash			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	3 / 33 (9.09%)	
occurrences (all)	1	3	
Skin hypopigmentation			
alternative dictionary used: MedDRA 27			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	<p>0 / 33 (0.00%)</p> <p>0</p>	
<p>Skin ulcer</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	<p>0 / 33 (0.00%)</p> <p>0</p>	
<p>Spider naevus</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	<p>1 / 33 (3.03%)</p> <p>1</p>	
<p>Urticaria</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	<p>2 / 33 (6.06%)</p> <p>2</p>	
<p>Vitiligo</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 12 (8.33%)</p> <p>1</p>	<p>0 / 33 (0.00%)</p> <p>0</p>	
<p>Renal and urinary disorders</p> <p>Cystitis non-infective</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	<p>0 / 33 (0.00%)</p> <p>0</p>	
<p>Dysuria</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p>	<p>1 / 33 (3.03%)</p> <p>1</p>	
<p>Urinary retention</p> <p>alternative dictionary used: MedDRA 27</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 12 (8.33%)</p> <p>1</p>	<p>0 / 33 (0.00%)</p> <p>0</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>alternative dictionary used: MedDRA 27</p>			

subjects affected / exposed	3 / 12 (25.00%)	1 / 33 (3.03%)
occurrences (all)	3	1
Back pain		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Bone pain		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)
occurrences (all)	1	0
Joint effusion		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Muscle spasms		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Muscular weakness		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)
occurrences (all)	1	0
Musculoskeletal stiffness		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)
occurrences (all)	1	0
Myalgia		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	2 / 12 (16.67%)	10 / 33 (30.30%)
occurrences (all)	2	10
Neck pain		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)
occurrences (all)	1	0

Pain in extremity alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 33 (6.06%) 3	
Infections and infestations Acrodermatitis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Bronchitis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 33 (0.00%) 0	
COVID-19 infection alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	2 / 33 (6.06%) 3	
Conjunctivitis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 33 (3.03%) 1	
Enterobiasis alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Epstein-Barr virus infection alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 33 (0.00%) 0	
Eye infection alternative dictionary used: MedDRA 27 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 33 (3.03%) 1	
Fungal foot infection alternative dictionary used: MedDRA 27			

subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Gastroenteritis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Impetigo		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Infection		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	3 / 12 (25.00%)	12 / 33 (36.36%)
occurrences (all)	4	15
Infective exacerbation of asthma		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Influenza		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Laryngitis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Lymph gland infection		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Nail infection		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	2

Nasopharyngitis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	9 / 33 (27.27%)
occurrences (all)	0	19
Oral herpes		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Otitis media		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Parasitic gastroenteritis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Paronychia		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Pharyngitis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	1 / 12 (8.33%)	1 / 33 (3.03%)
occurrences (all)	1	2
Rhinitis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	3
Scarlet fever		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Sepsis		
alternative dictionary used: MedDRA 27		

subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Skin infection		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Tonsillitis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Tooth infection		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Tracheobronchitis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Upper respiratory tract infection		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Urinary tract infection		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Varicella		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Vulvovaginal candidiasis		
alternative dictionary used: MedDRA 27		
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1

Metabolism and nutrition disorders			
Decreased appetite			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Hyperglycemia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hypoglycemia			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	0 / 12 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Iron deficiency			
alternative dictionary used: MedDRA 27			
subjects affected / exposed	1 / 12 (8.33%)	0 / 33 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 September 2020	<p>V2.0</p> <ul style="list-style-type: none">• 11.3.1 updated to comply with recommendations from Clinical Trial Facilitation Group (CTFG) regarding contraception for women of childbearing potential.• 12.4.3 CTCAE V5.0 to be used for clinical assessment of AE severity.• 16.4 updated with additional information on trial termination criteria.• 17.2 source data requirements updated according to sponsor requirements• 11.4 and Appendix 5 updated to include the maximum volume per visit for blood sampling• Clarification throughout regarding physical exam and vital sign requirements per visit.
13 January 2021	<p>V3.0 (UK only)</p> <ul style="list-style-type: none">• 2.1 updated to include pharmacy contributors• 2.2 updated to include Trial Statistician• 3.0 abbreviations updated (PT and APTT)• 8.2 and trial design figure updated to clarify the trial design• 9.1.2 Exclusion criterion #3 updated:<ul style="list-style-type: none">- Evidence of renal dysfunction with creatinine greater than 1.5 times the ULN at screening, adjusted for the age of the patient- New addition: Clinically significant clotting disorder, according to local reference ranges• 9.2.2 updated to remove repetition regarding trial design now covered in 8.2• 9.2.4 updated to remove requirement to discuss with CI before emergency unblinding by investigators• 11.4, 11.7, 11.8 and 11.9 updated to add clotting tests (PT and APTT) and updated of schedule of assessments• Correction of heading numbers in section 11 and minor typos throughout

11 February 2021	<p>V4.0 Protocol V4.0 includes the above changes made for Protocol V3.0, and in addition:</p> <ul style="list-style-type: none"> • 2.2 Updated trial coordination contacts • 5.0 treatment preparation conditions corrected in trial flow chart • 8.6.2 addition of total daily insulin dose (units/kg) to secondary objectives • 8.7.3 Addition of RNA profiling to the exploratory outcome measures • 9.1.2 Exclusion criterion #3 updated to include: <ul style="list-style-type: none"> o Any history of malignancies, other than skin: "other than skin" removed o Known allergy to ATG or to similar products: New addition: "or hypersensitivity to rabbit proteins or to any of the excipients" o Pregnant and breastfeeding women • 10.1.1.7: Update on ATG administration: "This includes the requirement for administering IMP and observing the participant in a hospital setting under medical supervision" • 10.1.1.9: Update on the use of drugs: "Drugs not listed in 10.1.1.9 will be also permitted per investigators discretion and should be listed in the eCRF" • 11.4.1 Clarification regarding hepatitis B (surface antigen) and hepatitis C (antibody) serology testing requirements • 13.1.1.2: Update of management of allergic reactions • 13.1.2.3: Addition of anaphylaxis and management • 13.1.4 Haematological effects management diagram corrected • 17.1 Removal of the statement that the eCRF allows "live (immediate) entry during participant's trial visit"
17 February 2021	<p>V4.1</p> <ul style="list-style-type: none"> • 13.1.4: Old haematological effects management figure had not been deleted in error in V4.0. Corrected.

18 February 2021	<p>V5.0 (Germany only) Response to German PEI Deficiencies abbreviations updated (PT and APTT)</p> <p>5.0 18 FEB 2021 • 3.0</p> <ul style="list-style-type: none"> • 4.0 Synopsis updated (trial design, exclusion criteria, clotting studies, withdrawal criteria) • 8.2 Trial design clarified, including updated trial diagram • 9.1.2 Exclusion criteria updated: <ul style="list-style-type: none"> o #3 – now includes “Clinically significant clotting disorder, according to local reference ranges” o #9 – removal of “except skin” o #13 – addition of “hypersensitivity to rabbit proteins or to any of the excipients” o #15 – new exclusion criteria added for pregnant and breastfeeding women • 9.2.4 updated to remove requirement to discuss with CI before emergency unblinding by investigators • 9.3 “Discontinuation from trial follow up visits should be the last possible solution” added • 10.1.1.7 Requirement for administering IMP and observing the participant in a hospital setting under medical supervision and that medical personnel and equipment must be readily at hand to provide emergency treatment if necessary • 10.1.1.9 “Drugs not listed in 10.1.1.9 will be also permitted per investigators discretion and should be listed in the eCRF” added • 11.4, 11.7 and 11.8 updated to add clotting tests (PT and APTT) • 11.9 Schedule of Assessments updated to include PT and APTT • 13.1.2.2 Allergic reactions grade 3 now require permanent treatment discontinuation • 13.1.2.3 New section on management of anaphylaxis • Correction of heading numbers in section 11
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01 April 2022	<p>V6.0</p> <ul style="list-style-type: none"> • Alignment of Protocol V5.0 (Germany only) and Protocol V4.1 <p>Changes made for V4.1 to align with V5.0:</p> <ul style="list-style-type: none"> o Section 10.1.1.7 ATG preparation, dose and administration: Medical personnel and equipment must be readily at hand to provide emergency treatment if necessary, including in case of anaphylaxis (protocol section 13.1.2.3). <p>Changes made for V5.0 to align with V4.1:</p> <ul style="list-style-type: none"> o Update on the trial coordination, Protocol contributions and contact details o Section 4. Trial synopsis: <ul style="list-style-type: none"> - Total daily insulin dose is part of the secondary objectives - Creatinine levels should be evaluated according/adjusted to the age of the patients - Screening for Hepatitis B and C adapted (Hepatitis B: screening for surface antigen, Hepatitis C: screening for antibodies) o Section 5. - Trial flow chart corrected o Section 8.6.2 Secondary objective - total daily insulin dose added to the secondary objectives o Section 8.7.3 Exploratory outcome measures: RNA profiling is added o Section 9.1.2 Creatinine levels should be evaluated according/adjusted to the age of the patient o Section 9.2 Information on cohorts is removed (already subject to Section 8.2) o Section 11.4.1 Screening assessments: correction in screening for Hepatitis B and C o Section 13.1.4 - Haematological effects management diagram corrected o Section 17.1 - Removal of the statement that the eCRF allows "live (immediate) entry during participant's trial visit" <ul style="list-style-type: none"> • Contact details section adapted • Section 4. Trial Synopsis: <ul style="list-style-type: none"> Unblinding procedure: The independent medical safety monitor, monitors, trial statisticians and pharmacy will be unblinded Update on physical examination during the follow-up visits • Section 4. Trial Synopsis: <ul style="list-style-type: none"> Update on the procedure of approach • Section 9.2.3: <ul style="list-style-type: none"> Unblinding procedure: The independent medical safety monitor, monitors, trial statisticians and pharmacy will be unblinded • Section 10.3.1 Pharmacy responsibilities
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34876434>