Clinical trial results:
Safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple subcutaneous doses of NNC0365-3769 (Mim8) in healthy subjects and in subjects with haemophilia A with or without factor VIII inhibitors

Summary

EudraCT number	2019-000465-20
Trial protocol	DE GB ES AT BG PL IT
Global end of trial date	06 October 2023

Results information

Result version number	v1 (current)
This version publication date	21 April 2024
First version publication date	21 April 2024

Trial information

Trial identification

Sponsor protocol code	NN7769-4513

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04204408
WHO universal trial number (UTN)	U1111-1227-4220

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety and tolerability of subcutaneous Mim8 in healthy subjects and in subjects with severe haemophilia A with or without FVIII inhibitors

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and International Council for Harmonisation (ICH) Good Clinical Practice, including archiving of essential documents (2016), and 21 Code of Federal Regulations (CFR) 312.120.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 48
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Türkiye: 5
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	100
EEA total number of subjects	74

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	6
Adults (18-64 years)	94
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

SAD part was conducted at one site in Germany. MAD part was conducted at 18 sites in 11 countries: (Austria, Bulgaria, Italy, Japan, South Africa, Switzerland, United Kingdom)-1, Poland-2, Spain-2, Turkey-3 and United States-4. EXP was conducted at 9 sites in 6 countries: (Italy, Spain, Switzerland, United Kingdom)-1, Poland-2 and United States-3.

Pre-assignment

Screening details:

The trial had phase 1 SAD part and phase 2 MAD part, conducted in an overlapping fashion. MAD phase had a main and extension period. After completing 12-week treatment in the main period, subjects continued treatment for up to 148 weeks in the extension period. The trial also included an exploratory biomarker cohort of emicizumab-treated subjects.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Single ascending dose (SAD) cohort 1

Arm description:

Subjects received a single dose of 0.6 milligrams (mg) Mim8 (NNC0365-3769) subcutaneously.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 0.6 milligrams (mg) Mim8 (NNC0365-3769) subcutaneously.

Arm title	SAD cohort 2

Arm description:

Subjects received a single dose of 3 milligrams (mg) Mim8 subcutaneously.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 3 milligrams (mg) Mim8 subcutaneously.

Arm title	SAD cohort 3

Arm description:

Subjects received a single dose of 12 milligrams (mg) Mim8 subcutaneously.

Arm type	Experimental

Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 12 milligrams (mg) Mim8 subcutaneously.

Arm title	SAD cohort 4

Arm description:

Subjects received a single dose of 24 milligrams (mg) Mim8 subcutaneously.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 24 milligrams (mg) Mim8 subcutaneously.

Arm title	SAD cohort 5

Arm description:

Subjects received a single dose of 29 milligrams (mg) Mim8 subcutaneously.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 29 milligrams (mg) Mim8 subcutaneously.

Arm title	SAD cohort 6

Arm description:

Subjects received a single dose of 48 milligrams (mg) Mim8 subcutaneously.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received a single dose of 48 milligrams (mg) Mim8 subcutaneously.

Arm title	SAD placebo

Arm description:

Subjects received a single dose of placebo matched with Mim8 subcutaneously.

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

Dosage and administration details:
Subjects received a single dose of placebo matched with Mim8 subcutaneously.

Arm title	Multiple ascending dose (MAD) cohort 1
Arm description:	
Subjects received 1.0/1.2 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received 1.0/1.2 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm title	MAD cohort 2
Arm description:	
Subjects received 2.4/3.8 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received 2.4/3.8 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm title	MAD cohort 3
Arm description:	
Subjects received 11.0/15.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received 11.0/15.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm title	MAD cohort 4
Arm description:	
Subjects received 41.0/60.0 milligrams (mg) dose of Mim8 subcutaneously once monthly for 12-weeks.	
Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received 41.0/60.0 milligrams (mg) dose of Mim8 subcutaneously once monthly for 12-weeks.	
Arm title	MAD cohort 5

Arm description:	
Subjects received 24.0/35.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received 24.0/35.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Arm title	Exploratory biomarker cohort: Naive
Arm description:	
Subjects received emicizumab in accordance with standard of care of the prescribed product.	
Arm type	Experimental
Investigational medicinal product name	Emicizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received emicizumab in accordance with standard of care of the prescribed product.	
Arm title	Exploratory biomarker cohort: Non-Naive
Arm description:	
Subjects received emicizumab in accordance with standard of care of the prescribed product.	
Arm type	Experimental
Investigational medicinal product name	Emicizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received emicizumab in accordance with standard of care of the prescribed product.	

Number of subjects in period 1	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3
Started	6	6	6
Full analysis set (FAS)	6	6	6
Safety analysis set (SAS)	6	6	6
Completed	5	5	6
Not completed	1	1	0
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	SAD cohort 4	SAD cohort 5	SAD cohort 6
Started	6	6	6

Full analysis set (FAS)	6	6	6
Safety analysis set (SAS)	6	6	6
Completed	6	6	5
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	1

Number of subjects in period 1	SAD placebo	Multiple ascending dose (MAD) cohort 1	MAD cohort 2
Started	12	7	9
Full analysis set (FAS)	12	7	9
Safety analysis set (SAS)	12	7	9
Completed	12	7	8
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	MAD cohort 3	MAD cohort 4	MAD cohort 5
Started	8	8	10
Full analysis set (FAS)	8	8	10
Safety analysis set (SAS)	8	8	10
Completed	8	8	10
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Exploratory biomarker cohort: Naive	Exploratory biomarker cohort: Non-Naive
Started	7	3
Full analysis set (FAS)	7	3
Safety analysis set (SAS)	7	3
Completed	6	3
Not completed	1	0
Consent withdrawn by subject	-	-
Adverse event, non-fatal	-	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Single ascending dose (SAD) cohort 1
Reporting group description: Subjects received a single dose of 0.6 milligrams (mg) Mim8 (NNC0365-3769) subcutaneously.	
Reporting group title	SAD cohort 2
Reporting group description: Subjects received a single dose of 3 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 3
Reporting group description: Subjects received a single dose of 12 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 4
Reporting group description: Subjects received a single dose of 24 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 5
Reporting group description: Subjects received a single dose of 29 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 6
Reporting group description: Subjects received a single dose of 48 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD placebo
Reporting group description: Subjects received a single dose of placebo matched with Mim8 subcutaneously.	
Reporting group title	Multiple ascending dose (MAD) cohort 1
Reporting group description: Subjects received 1.0/1.2 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	MAD cohort 2
Reporting group description: Subjects received 2.4/3.8 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	MAD cohort 3
Reporting group description: Subjects received 11.0/15.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	MAD cohort 4
Reporting group description: Subjects received 41.0/60.0 milligrams (mg) dose of Mim8 subcutaneously once monthly for 12-weeks.	
Reporting group title	MAD cohort 5
Reporting group description: Subjects received 24.0/35.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	Exploratory biomarker cohort: Naive
Reporting group description: Subjects received emicizumab in accordance with standard of care of the prescribed product.	
Reporting group title	Exploratory biomarker cohort: Non-Naive
Reporting group description: Subjects received emicizumab in accordance with standard of care of the prescribed product.	

Reporting group values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3
Number of subjects	6	6	6

Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	6
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	32.7	30.7	35.3
standard deviation	± 7.8	± 4.4	± 5.8
Gender Categorical Units: Subjects			
Male	6	6	6

Reporting group values	SAD cohort 4	SAD cohort 5	SAD cohort 6
Number of subjects	6	6	6
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	6
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	28.8	32.5	28.0
standard deviation	± 7.6	± 8.2	± 5.7
Gender Categorical Units: Subjects			
Male	6	6	6

Reporting group values	SAD placebo	Multiple ascending dose (MAD) cohort 1	MAD cohort 2
Number of subjects	12	7	9
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	1	2
Adults (18-64 years)	12	6	7
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	27.5	30.3	35.8
standard deviation	± 6.2	± 10.1	± 17.0
Gender Categorical			
Units: Subjects			
Male	12	7	9

Reporting group values	MAD cohort 3	MAD cohort 4	MAD cohort 5
Number of subjects	8	8	10
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	1	2	0
Adults (18-64 years)	7	6	10
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	32.8	32.3	36.7
standard deviation	± 11.4	± 15.3	± 13.2
Gender Categorical			
Units: Subjects			
Male	8	8	10

Reporting group values	Exploratory biomarker cohort: Naive	Exploratory biomarker cohort: Non-Naive	Total
Number of subjects	7	3	100
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	6
Adults (18-64 years)	7	3	94
From 65-84 years	0	0	0

85 years and over	0	0	0

Age Continuous Units: years			
arithmetic mean	29.7	34.7	
standard deviation	± 8.3	± 4.5	-
Gender Categorical Units: Subjects			
Male	7	3	100

End points

End points reporting groups

Reporting group title	Single ascending dose (SAD) cohort 1
Reporting group description: Subjects received a single dose of 0.6 milligrams (mg) Mim8 (NNC0365-3769) subcutaneously.	
Reporting group title	SAD cohort 2
Reporting group description: Subjects received a single dose of 3 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 3
Reporting group description: Subjects received a single dose of 12 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 4
Reporting group description: Subjects received a single dose of 24 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 5
Reporting group description: Subjects received a single dose of 29 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD cohort 6
Reporting group description: Subjects received a single dose of 48 milligrams (mg) Mim8 subcutaneously.	
Reporting group title	SAD placebo
Reporting group description: Subjects received a single dose of placebo matched with Mim8 subcutaneously.	
Reporting group title	Multiple ascending dose (MAD) cohort 1
Reporting group description: Subjects received 1.0/1.2 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	MAD cohort 2
Reporting group description: Subjects received 2.4/3.8 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	MAD cohort 3
Reporting group description: Subjects received 11.0/15.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	MAD cohort 4
Reporting group description: Subjects received 41.0/60.0 milligrams (mg) dose of Mim8 subcutaneously once monthly for 12-weeks.	
Reporting group title	MAD cohort 5
Reporting group description: Subjects received 24.0/35.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.	
Reporting group title	Exploratory biomarker cohort: Naive
Reporting group description: Subjects received emicizumab in accordance with standard of care of the prescribed product.	
Reporting group title	Exploratory biomarker cohort: Non-Naive
Reporting group description: Subjects received emicizumab in accordance with standard of care of the prescribed product.	
Subject analysis set title	MAD Extension Cohort 1
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects received a 1.0/1.2 milligrams (mg) of Mim8 subcutaneously once weekly for 148 weeks after 12-weeks treatment period (up to 160 weeks in total).	
Subject analysis set title	MAD Extension Cohort 2

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a 2.4/3.8 milligrams (mg) of Mim8 subcutaneously once weekly for 148 weeks after 12-weeks treatment period (up to 160 weeks in total).

Subject analysis set title	MAD Extension Cohort 3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a 11.0/15.0 milligrams (mg) of Mim8 subcutaneously once weekly for 148 weeks after 12-weeks treatment period (up to 160 weeks in total).

Subject analysis set title	MAD Extension Cohort 4
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a 41.0/60.0 milligrams (mg) of Mim8 subcutaneously once monthly for 148 weeks after 12-weeks treatment period (up to 160 weeks in total).

Subject analysis set title	MAD Extension Cohort 5
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a 24.0/35.0 milligrams (mg) of Mim8 subcutaneously once weekly for 148 weeks after 12-weeks treatment period (up to 160 weeks in total).

Subject analysis set title	MAD Extension Maintenance (QW)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a 6.0/11.0 milligrams (mg) of Mim8 subcutaneously once weekly for 148 weeks after 12-weeks treatment period (up to 160 weeks in total).

Subject analysis set title	MAD Extension Maintenance (QM)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received a 30.0/46.0 milligrams (mg) of Mim8 subcutaneously once monthly for 148 weeks after 12-weeks treatment period (up to 160 weeks in total).

Primary: Single ascending dose (SAD) part: Number of treatment emergent adverse events

End point title	Single ascending dose (SAD) part: Number of treatment emergent adverse events[1][2]

End point description:

Number of treatment emergent adverse events from time of dosing (Day 1) to Week 16 is presented. An adverse event (AE) is any untoward medical occurrence in a clinical trial subject that is temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Treatment emergent adverse events (TEAEs) were defined as AEs occurring after the first trial product administration and until week 16. The SAS included all subjects exposed to the trial product.

End point type	Primary

End point timeframe:

From time of dosing (Day 1) to Week 16

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Events				
number (not applicable)	8	9	7	11

End point values	SAD cohort 5	SAD cohort 6	SAD placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	12	
Units: Events				
number (not applicable)	6	14	24	

Statistical analyses

No statistical analyses for this end point

Primary: Extensíon to the MAD part: Number of treatment emergent adverse events

End point title	Extensíon to the MAD part: Number of treatment emergent adverse events[3]

End point description:

Number of treatment emergent adverse events from Week 12 up to Week 176 (16 weeks after last dose) is presented. An adverse event (AE) is any untoward medical occurrence in a clinical trial subject that is temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Treatment emergent adverse events (TEAEs) were defined as AEs occurring after the first trial product administration and until 16 weeks after the last dose. The SAS included all subjects exposed to the trial product.

End point type	Primary

End point timeframe:

From Week 12 up to Week 176 (16 weeks after last dose)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As per the end point the data were provided for safety analysis and so no statistical analysis was specified.

End point values	MAD Extension Cohort 1	MAD Extension Cohort 2	MAD Extension Cohort 3	MAD Extension Cohort 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	13	11	8
Units: Events				
number (not applicable)	6	36	31	19

End point values	MAD Extension Cohort 5	MAD Extension Maintenance (QW)	MAD Extension Maintenance (QM)	

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	31	9	
Units: Events				
number (not applicable)	16	56	10	

Statistical analyses

No statistical analyses for this end point

Primary: Multiple ascending dose (MAD) part: Number of treatment emergent adverse events

End point title	Multiple ascending dose (MAD) part: Number of treatment emergent adverse events[4][5]

End point description:

Number of treatment emergent adverse events from time of dosing (Day 1) to Week 12 is presented. An adverse event (AE) is any untoward medical occurrence in a clinical trial subject that is temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Treatment emergent adverse events (TEAEs) were defined as AEs occurring after the first trial product administration and until 16 weeks after the last dose. The SAS included all subjects exposed to the trial product.

End point type	Primary

End point timeframe:

From time of first dosing (day 1) to week 12

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.
[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	8	8
Units: Events	1	12	10	8

End point values	MAD cohort 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Events	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: Number of injection site reactions

End point title	Single ascending dose (SAD) part: Number of injection site reactions[6]

End point description:

Number of injection site reactions from time of dosing (day 1) to week 16 is presented. The SAS included all subjects exposed to the trial product.

End point type	Secondary

End point timeframe:

From time of dosing (day 1) to week 16

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Events				
number (not applicable)	0	1	0	0

End point values	SAD cohort 5	SAD cohort 6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Events				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: Relative change in D-dimer

End point title	Single ascending dose (SAD) part: Relative change in D-

End point description:

Relative change in D-dimer (measured in nanograms per milliliter (ng/mL)) from baseline (day 1) to week 16 is presented. The SAS included all subjects exposed to the trial product. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Percentage change in D-dimer				
number (not applicable)	16.09	84.51	68.49	1.30

End point values	SAD cohort 5	SAD cohort 6	SAD placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	12	
Units: Percentage change in D-dimer				
number (not applicable)	40.09	31.43	30.62	

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: Relative change in prothrombin fragment 1 and 2

End point title	Single ascending dose (SAD) part: Relative change in prothrombin fragment 1 and 2[8]

End point description:

Relative change in prothrombin fragment 1 and 2 (measured in picomoles per liter (pmol/L)) from baseline (day 1) to week 16 is presented. The SAS included all subjects exposed to the trial product. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Percentage change in prothrombin				
number (not applicable)	50.67	89.14	18.48	4.13

End point values	SAD cohort 5	SAD cohort 6	SAD placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	12	

Units: Percentage change in prothrombin				
number (not applicable)	30.39	61.55	35.20	

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: Relative change in fibrinogen

End point title	Single ascending dose (SAD) part: Relative change in fibrinogen[9]

End point description:

Relative change in fibrinogen (measured in gram per liter (g/L)) from baseline (day 1) to week 16 is presented. The SAS included all subjects exposed to the trial product. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Percentage change in fibrinogen				
number (not applicable)	-11.77	28.56	14.16	-12.78

End point values	SAD cohort 5	SAD cohort 6	SAD placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	12	
Units: Percentage change in fibrinogen				
number (not applicable)	-9.32	-8.08	0.92	

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: Relative change in platelets

End point title	Single ascending dose (SAD) part: Relative change in

End point description:

Relative change in platelets (measured in 10^9 per liter (10^9/L)) from baseline (day 1) to week 16 is presented. The SAS included all subjects exposed to the trial product. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Percentage change in platelets				
number (not applicable)	-3.46	7.52	12.14	-4.48

End point values	SAD cohort 5	SAD cohort 6	SAD placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	12	
Units: Percentage change in platelets				
number (not applicable)	1.39	2.84	-2.14	

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: Cmax, SD: the maximum concentration of Mim8 after a single dose

End point title	Single ascending dose (SAD) part: Cmax, SD: the maximum concentration of Mim8 after a single dose[11]

End point description:

Maximum concentration of Mim8 after a single dose from baseline (day 1) to week 16 is presented. The FAS included all subjects with at least one valid pharmacokinetics (PK) or pharmacodynamics (PD) assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)	0.060 (± 0.013)	0.316 (± 0.071)	0.769 (± 0.143)	1.432 (± 0.360)

End point values	SAD cohort 5	SAD cohort 6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)	2.803 (± 0.497)	3.544 (± 0.840)		

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: t1/2, SD: the terminal half-life of Mim8 after a single dose

End point title	Single ascending dose (SAD) part: t1/2, SD: the terminal half-life of Mim8 after a single dose[12]

End point description:

Terminal half-life of Mim8 after a single dose from baseline (day 1) to week 16 is presented. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Days				
arithmetic mean (standard deviation)	26.901 (± 3.143)	32.944 (± 3.343)	30.857 (± 4.508)	32.062 (± 4.504)

End point values	SAD cohort 5	SAD cohort 6		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Days				
arithmetic mean (standard deviation)	30.332 (± 2.624)	31.323 (± 6.406)		

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: AUC0-inf, SD: the area under the Mim8 concentration-time curve from time 0 to infinity after a single dose

End point title	Single ascending dose (SAD) part: AUC0-inf, SD: the area under the Mim8 concentration-time curve from time 0 to infinity after a single dose[13]

End point description:

Area under the Mim8 concentration-time curve from time 0 to infinity after a single dose from baseline (day 1) to week 16 is presented. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Microgram*day per milliliter (µg*day/mL)				
arithmetic mean (standard deviation)	3.011 (± 0.436)	17.649 (± 4.574)	42.051 (± 11.702)	81.518 (± 27.892)

End point values	SAD cohort 5	SAD cohort 6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Microgram*day per milliliter (µg*day/mL)				
arithmetic mean (standard deviation)	135.189 (± 18.163)	194.439 (± 67.607)		

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: Change in activated partial thromboplastin time

End point title	Single ascending dose (SAD) part: Change in activated partial thromboplastin time[14]

End point description:

Change in activated partial thromboplastin time from baseline (day 1) to week 16 is presented. The Activated Partial Thromboplastin Time (aPTT) assay records the time for clot formation. It includes both the time for activation of FVIII and the time for FVIIIa to support FIXa activity and thereby facilitate clotting. It measures the number of seconds it takes for a clot to form in a sample of blood after substances (reagents) are added. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Seconds				
arithmetic mean (standard deviation)	75.2 (± 9.4)	53.8 (± 6.5)	48.2 (± 3.9)	38.8 (± 5.2)

End point values	SAD cohort 5	SAD cohort 6	SAD placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	12	
Units: Seconds				
arithmetic mean (standard deviation)	37.7 (± 3.8)	37.0 (± 2.8)	95.8 (± 11.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Single ascending dose (SAD) part: tmax, SD: the time to maximum concentration of Mim8 after a single dose

End point title	Single ascending dose (SAD) part: tmax, SD: the time to maximum concentration of Mim8 after a single dose[15]

End point description:

Time to maximum concentration of Mim8 after a single dose from baseline (day 1) to week 16 is presented. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 16

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Single ascending dose (SAD) cohort 1	SAD cohort 2	SAD cohort 3	SAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	6	6
Units: Days				
arithmetic mean (standard deviation)	9.993 (± 2.535)	8.594 (± 4.137)	11.662 (± 1.493)	8.653 (± 3.982)

End point values	SAD cohort 5	SAD cohort 6		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Days				
arithmetic mean (standard deviation)	8.992 (± 1.073)	11.979 (± 1.439)		

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (weekly and monthly dosing): Number of injection site reactions

End point title	MAD part (weekly and monthly dosing): Number of injection site reactions[16]

End point description:

Number of injection site reactions from time of first dosing (day 1) to week 12 is presented. The SAS included all subjects exposed to the trial product.

End point type	Secondary

End point timeframe:

From time of first dosing (day 1) to week 12

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	8	8
Units: Events				
number (not applicable)	0	2	1	0

End point values	MAD cohort 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Events				
number (not applicable)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (weekly and monthly dosing): Relative change in D-dimer

End point title	MAD part (weekly and monthly dosing): Relative change in D-dimer[17]

End point description:

Relative change in D-dimer (measured in milligrams per liter (mg/L)) from baseline (day 1) to week 12 is presented. The SAS included all subjects exposed to the trial product. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 12

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	8
Units: Percentage change in D-dimer				
number (not applicable)	12.23	27.16	2.48	18.17

End point values	MAD cohort 5			
Subject group type	Reporting group			
Number of subjects analysed	10			

Units: Percentage change in D-dimer				
number (not applicable)	9.81			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (weekly and monthly dosing): Occurrence of anti-Mim8 antibodies

End point title	MAD part (weekly and monthly dosing): Occurrence of anti-Mim8 antibodies[18]

End point description:

Number of subjects with occurrence of anti-Mim8 antibodies from baseline (day 1) to week 12 is presented. The SAS included all subjects exposed to the trial product.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 12

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	8	8
Units: Subjects	0	0	0	0

End point values	MAD cohort 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (weekly and monthly dosing): Relative change in fibrinogen

End point title	MAD part (weekly and monthly dosing): Relative change in fibrinogen[19]

End point description:

Relative change in fibrinogen (measured in gram per liter (g/L)) from baseline (day 1) to week 12 is presented. The SAS included all subjects exposed to the trial product. Number of subjects

analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 12

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	8
Units: Percentage change in fibrinogen				
number (not applicable)	3.80	-4.95	-16.63	-12.41

End point values	MAD cohort 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage change in fibrinogen				
number (not applicable)	-14.24			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (weekly and monthly dosing): Relative change in prothrombin fragment 1 and 2

End point title	MAD part (weekly and monthly dosing): Relative change in prothrombin fragment 1 and 2[20]

End point description:

Relative change in prothrombin fragment 1 and 2 (measured in picomoles per liter (pmol/L)) from baseline (day 1) to week 12 is presented. The SAS included all subjects exposed to the trial product. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 12

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	8
Units: Percentage change in prothrombin				
number (not applicable)	26.08	93.99	323.65	606.41

End point values	MAD cohort 5			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage change in prothrombin				
number (not applicable)	310.25			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (weekly and monthly dosing): Relative change in platelets

End point title	MAD part (weekly and monthly dosing): Relative change in platelets[21]

End point description:

Relative change in platelets (measured in 10^9 per liter (10^9/L)) from baseline (day 1) to week 12 is presented. The SAS included all subjects exposed to the trial product. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (day 1) to week 12

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	8	8
Units: Percentage change in platelets				
number (not applicable)	2.01	-2.62	2.24	2.91

End point values	MAD cohort 5			

Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage change in platelets				
number (not applicable)	5.77			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part, PK session 2 (weekly dosing): Cmax, MD: the maximum concentration of Mim8 after multiple doses

End point title	MAD part, PK session 2 (weekly dosing): Cmax, MD: the maximum concentration of Mim8 after multiple doses[22]

End point description:

Maximum concentration of Mim8 after multiple doses from day 57 to day 64 is presented. The FAS included all subjects with at least one valid PK or PD assessment.

End point type	Secondary

End point timeframe:

From day 57 to day 64

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 5
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	8	10
Units: Micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)	1.025 (± 0.264)	3.077 (± 0.722)	9.328 (± 2.833)	18.369 (± 6.506)

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part, PK session 2 (weekly dosing): AUCτ, MD: the area under the Mim8 concentration-time curve in the dosing interval after multiple doses

End point title	MAD part, PK session 2 (weekly dosing): AUCτ, MD: the area under the Mim8 concentration-time curve in the dosing interval after multiple doses[23]

End point description:

Area under the Mim8 concentration-time curve in the dosing interval after multiple doses from day 57 to day 64 is presented. The FAS included all subjects with at least one valid PK or PD assessment.

End point type	Secondary

End point timeframe:

From day 57 to day 64

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 5
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	8	10
Units: Microgram*day per milliliter (µg*day/mL)				
arithmetic mean (standard deviation)	6.641 (± 1.431)	19.339 (± 3.822)	58.285 (± 17.772)	115.490 (± 38.824)

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part, PK session 2 (monthly dosing): Cmax, MD: the maximum concentration of Mim8 after multiple doses

End point title	MAD part, PK session 2 (monthly dosing): Cmax, MD: the maximum concentration of Mim8 after multiple doses[24]

End point description:

Maximum concentration of Mim8 after multiple doses from day 57 to day 85 is presented. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From day 57 to day 85

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	MAD cohort 4			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)	10.226 (± 2.118)			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (weekly dosing): Mean of maximum thrombin generation

(peak height)

End point title	MAD part (weekly dosing): Mean of maximum thrombin generation (peak height)[25]

End point description:

Mean of maximum thrombin generation (peak height) from day 57 to day 64 is presented. Thrombin peak height reflects the haemostatic potential as the maximum amount of thrombin produced during the thrombin generation assay. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From day 57 to day 64

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Multiple ascending dose (MAD) cohort 1	MAD cohort 2	MAD cohort 3	MAD cohort 5
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	7	10
Units: Nanometer (nM)				
arithmetic mean (standard deviation)	106.61 (± 23.50)	150.95 (± 33.18)	188.47 (± 26.51)	208.35 (± 25.23)

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part, PK session 2 (monthly dosing): AUCτ, MD: the area under the Mim8 concentration-time curve in the dosing interval after multiple doses

End point title	MAD part, PK session 2 (monthly dosing): AUCτ, MD: the area under the Mim8 concentration-time curve in the dosing interval after multiple doses[26]

End point description:

Area under the Mim8 concentration-time curve in the dosing interval after multiple doses from day 57 to day 85 is presented. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From day 57 to day 85

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	MAD cohort 4			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Microgram*day per milliliter (µg*day/mL)				
arithmetic mean (standard deviation)	230.934 (± 49.723)			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD part (monthly dosing): Mean of maximum thrombin generation (peak height)

End point title	MAD part (monthly dosing): Mean of maximum thrombin generation (peak height)[27]

End point description:

Mean of maximum thrombin generation (peak height) from day 57 to day 85 is presented. Thrombin peak height reflects the haemostatic potential as the maximum amount of thrombin produced during the thrombin generation assay. The FAS included all subjects with at least one valid PK or PD assessment. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From day 57 to day 85

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	MAD cohort 4			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Nanometer (nM)				
arithmetic mean (standard deviation)	204.22 (± 45.67)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension to the MAD part: Number of injection site reactions

End point title	Extension to the MAD part: Number of injection site reactions

End point description:

Number of injection site reactions from week 12 up to week 176 is presented. The SAS included all subjects exposed to the trial product.

End point type	Secondary

End point timeframe:

From week 12 up to week 176

End point values	MAD Extension Cohort 1	MAD Extension Cohort 2	MAD Extension Cohort 3	MAD Extension Cohort 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	13	11	8
Units: Events				
number (not applicable)	1	2	2	0

End point values	MAD Extension Cohort 5	MAD Extension Maintenance (QW)	MAD Extension Maintenance (QM)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	31	9	
Units: Events				
number (not applicable)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Extension to the MAD part: Occurrence of anti-Mim8 antibodies

End point title	Extension to the MAD part: Occurrence of anti-Mim8 antibodies

End point description:

Number of subjects with occurrence of anti-Mim8 antibodies from week 12 up to week 176 is presented. The SAS included all subjects exposed to the trial product.

End point type	Secondary

End point timeframe:

From week 12 up to week 176

End point values	MAD Extension Cohort 1	MAD Extension Cohort 2	MAD Extension Cohort 3	MAD Extension Cohort 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	13	11	8
Units: Subjects	0	0	0	0

End point values	MAD Extension Cohort 5	MAD Extension Maintenance (QW)	MAD Extension Maintenance (QM)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	31	9	

Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Single ascending dose (SAD): From time of dosing (Day 1) to Week 16
Multiple ascending dose (MAD): From time of first dosing (day 1) to week 12
Multiple ascending dose (MAD) extensíon: From Week 12 up to Week 176 (16 weeks after last dose)

Adverse event reporting additional description:

All presented AEs are treatment emergent. Treatment emergent adverse events (TEAEs) were defined as AEs occurring:
SAD part: after the first trial product administration and until week 16.
MAD part: after the first trial product administration and until 16 weeks after the last dose.
Exploratory biomarker cohort: from the first to last visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	MAD cohort 2

Reporting group description:

Subjects received 2.4/3.8 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.

Reporting group title	MAD cohort 1

Reporting group description:

Subjects received 1.0/1.2 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.

Reporting group title	MAD cohort 5

Reporting group description:

Subjects received 24.0/35.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.

Reporting group title	SAD cohort 1

Reporting group description:

Subjects received a single dose of 0.6 milligrams (mg) Mim8 (NNC0365-3769) subcutaneously.

Reporting group title	Emicizumab

Reporting group description:

Subjects received emicizumab in accordance with standard of care of the prescribed product.

Reporting group title	SAD cohort 3

Reporting group description:

Subjects received a single dose of 12 milligrams (mg) Mim8 subcutaneously.

Reporting group title	SAD cohort 4

Reporting group description:

Subjects received a single dose of 24 milligrams (mg) Mim8 subcutaneously.

Reporting group title	SAD cohort 5

Reporting group description:

Subjects received a single dose of 29 milligrams (mg) Mim8 subcutaneously.

Reporting group title	SAD cohort 6

Reporting group description:

Subjects received a single dose of 48 milligrams (mg) Mim8 subcutaneously.

Reporting group title	SAD placebo

Reporting group description:

Subjects received a single dose of placebo matched with Mim8 subcutaneously.

Reporting group title	MAD cohort 4

Reporting group description:

Subjects received 41.0/60.0 milligrams (mg) dose of Mim8 subcutaneously once monthly for 12-weeks.

Reporting group title	MAD cohort 3

Reporting group description:

Subjects received 11.0/15.0 milligrams (mg) dose of Mim8 subcutaneously once weekly for 12-weeks.

Reporting group title	SAD cohort 2

Reporting group description:

Subjects received a single dose of 3 milligrams (mg) Mim8 subcutaneously.

Serious adverse events	MAD cohort 2	MAD cohort 1	MAD cohort 5
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	1 / 10 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (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
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (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
Seizure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (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
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (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
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (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	SAD cohort 1	Emicizumab	SAD cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (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
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (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
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (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	SAD cohort 4	SAD cohort 5	SAD cohort 6
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Injury, poisoning and procedural complications			

Craniocerebral injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (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	SAD placebo	MAD cohort 4	MAD cohort 3
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	2 / 8 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SAD cohort 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MAD cohort 2	MAD cohort 1	MAD cohort 5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 9 (88.89%)	6 / 7 (85.71%)	10 / 10 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Microangiopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Artificial crown procedure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth restoration			

subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 9 (0.00%)	2 / 7 (28.57%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Injection site haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injection site induration			
subjects affected / exposed	1 / 9 (11.11%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Injection site pain			

subjects affected / exposed	1 / 9 (11.11%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Malaise			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Food allergy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dry throat			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nasal dryness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Antinuclear antibody positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Protein urine present			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Prothrombin fragment 1.2 increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Accidental overdose			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Arthropod bite			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Contusion			

subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Immunisation reaction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Incorrect route of product administration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Incorrect dose administered			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Skin laceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Spinal column injury			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tooth fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Venomous sting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 9 (22.22%)	1 / 7 (14.29%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharospasm			

subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Refraction disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erosive oesophagitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Faeces pale			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Haemorrhoids			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Intestinal mass			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oesophageal motility disorder			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Swollen tongue			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Non-alcoholic fatty liver			

subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal colic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ureterolithiasis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 7 (14.29%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Bone pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint noise			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Neck pain			

subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 9 (0.00%)	2 / 7 (28.57%)	4 / 10 (40.00%)
occurrences (all)	0	3	4
Folliculitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Helicobacter gastritis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Oral candidiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 7 (14.29%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 7 (14.29%)	1 / 10 (10.00%)
occurrences (all)	1	3	2
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperlipidaemia			

subjects affected / exposed	1 / 9 (11.11%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Iron deficiency			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 9 (0.00%)	0 / 7 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SAD cohort 1	Emicizumab	SAD cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	2 / 10 (20.00%)	3 / 6 (50.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Microangiopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Artificial crown procedure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth restoration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site induration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Food allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Panic attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Antinuclear antibody positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Protein urine present			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Prothrombin fragment 1.2 increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immunisation reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Incorrect route of product administration			

subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Incorrect dose administered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Spinal column injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Venomous sting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 10 (10.00%)	2 / 6 (33.33%)
occurrences (all)	0	3	2
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Refraction disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erosive oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faeces pale			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Intestinal mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			

subjects affected / exposed	1 / 6 (16.67%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oesophageal motility disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-alcoholic fatty liver			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ureterolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Joint noise			

subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 6 (16.67%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle twitching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 6 (50.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 6 (16.67%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 10 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SAD cohort 4	SAD cohort 5	SAD cohort 6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	3 / 6 (50.00%)	5 / 6 (83.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Microangiopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			

Artificial crown procedure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth restoration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site induration			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Food allergy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dry throat			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Antinuclear antibody positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Protein urine present			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Prothrombin fragment 1.2 increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immunisation reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Incorrect route of product administration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Incorrect dose administered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Road traffic accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Spinal column injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Venomous sting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	3
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Refraction disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Dental caries			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erosive oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faeces pale			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			

subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Intestinal mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oesophageal motility disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-alcoholic fatty liver			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ureterolithiasis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint noise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle tightness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	4 / 6 (66.67%)
occurrences (all)	1	1	4

Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SAD placebo	MAD cohort 4	MAD cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	7 / 8 (87.50%)	7 / 8 (87.50%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Microangiopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Artificial crown procedure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Tooth restoration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Chest discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injection site bruising			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injection site haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injection site induration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Food allergy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dry throat			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Rhinitis allergic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Panic attack			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Investigations			
Antinuclear antibody positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Heart rate increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Protein urine present			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Prothrombin fragment 1.2 increased			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Transaminases increased			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Accidental overdose			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Foot fracture			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Hand fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Immunisation reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	3
Incorrect route of product administration			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Incorrect dose administered			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Skin laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Spinal column injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Venomous sting			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	3 / 12 (25.00%)	2 / 8 (25.00%)	2 / 8 (25.00%)
occurrences (all)	4	2	2
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Refraction disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Strabismus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	3
Erosive oesophagitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Faeces pale			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Food poisoning			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Intestinal mass			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nausea			

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Oesophageal motility disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Non-alcoholic fatty liver			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	3
Dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rash erythematous			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Ureterolithiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	2 / 8 (25.00%)	3 / 8 (37.50%)
occurrences (all)	1	2	3
Bone pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Joint noise			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Muscle twitching			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Rhabdomyolysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 12 (0.00%)	3 / 8 (37.50%)	3 / 8 (37.50%)
occurrences (all)	0	3	3
Folliculitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Gingivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Helicobacter gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	4 / 12 (33.33%)	1 / 8 (12.50%)	2 / 8 (25.00%)
occurrences (all)	4	1	2
Oral candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Tooth infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	2 / 8 (25.00%)
occurrences (all)	0	1	4
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Viral infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Vitamin B12 deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Non-serious adverse events	SAD cohort 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Microangiopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			

Artificial crown procedure			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tooth restoration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Inflammation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site bruising			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site haematoma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site induration			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Food allergy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dry throat			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Epistaxis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Nasal dryness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Psychiatric disorders			
Irritability subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Panic attack subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Investigations			
Antinuclear antibody positive subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Heart rate increased			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Protein urine present			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Prothrombin fragment 1.2 increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Arthropod bite			

subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Contusion				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Fall				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Foot fracture				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Hand fracture				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Immunisation reaction				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Incorrect route of product administration				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Incorrect dose administered				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Joint injury				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Ligament sprain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Limb injury				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Muscle strain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Road traffic accident subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin laceration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Spinal column injury subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Tooth fracture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Venomous sting subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Nervous system disorders Disturbance in attention subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dizziness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		

Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Refraction disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Strabismus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Erosive oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Faeces pale			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Food poisoning			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flatulence			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hiatus hernia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperchlorhydria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Intestinal mass			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oesophageal motility disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Swollen tongue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Non-alcoholic fatty liver subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dermatitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Eczema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rash pruritic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rash erythematous subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Proteinuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Renal colic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Ureterolithiasis			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Joint noise			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Limb discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscle tightness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscle twitching			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neck pain			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhabdomyolysis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tendonitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Helicobacter gastritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

Oral candidiasis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Oral herpes subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rhinitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Tonsillitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Tooth abscess subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Tooth infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Viral infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Metabolism and nutrition disorders Hyperlipidaemia			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vitamin B12 deficiency			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 November 2019	A more conservative dose escalation than originally proposed was implemented in the SAD part of the trial and a population switching criterion was added. The SAD and MAD flowcharts were updated to reflect sampling timepoints for all PD markers and it was clarified that no formal statistical tests were to be performed. Minor changes to exclusion criteria and typographical corrections were made.
13 March 2020	Sentinel dosing was implemented in the MAD part of the trial to increase subject safety and a reduction of the washout period of prophylactic – or on demand – medicine was added. Genotyping was added as part of the screening procedure in the MAD part to reduce the number of screening failures. Subjects were invited to separately consent to genotyping. For subjects not consenting to genotyping the original exclusion criterion based on factor II activity or activated protein C resistance was applied. Three other exclusion criteria were clarified to give more guidance to the investigators. Randomisation was implemented for the MAD cohorts 3 and 4 to avoid selection bias issues.
10 June 2020	An extension to the MAD part of the trial was added, which would allow long-term safety assessment of Mim8 in male adults and adolescents with haemophilia A (HA) with or without factor VIII inhibitors. Coronavirus disease of 2019 (COVID-19) mitigation strategies were also included.
29 October 2020	The dose level for the MAD cohort 4 was changed. Subjects were randomised between MAD cohorts 3 and 4 representing regimens with once-weekly and once-monthly dosing, respectively. In order to randomise the subjects to similar expected average exposure levels in the two cohorts, the dose level for once-monthly dosing was increased to align with the corresponding dose level for once-weekly dosing. The rationale was to investigate the safety of Mim8 prophylaxis at a higher comparable dose level, yet still 10-fold below the no-observed-adverse-effect level (NOAEL), between once-weekly and once-monthly administration frequencies, in male adults and adolescents with HA with and without FVIII inhibitors.
07 May 2021	A 6th SAD cohort and a 5th MAD cohort (once-weekly dosing regimen) were added. The 6th SAD cohort was added to collect necessary data for dose proportionality analyses. The 5th MAD cohort was added to collect data from subjects who were exposed to a higher Mim8 dose, which was needed to determine the optimal Mim8 dosing scheme for different weight ranges in future trials. The predicted exposure level from this dose remained more than 3-fold below the NOAEL. Also, the protocol was amended to allow subjects to receive approved COVID-19 vaccines, to adjust the section for replacement of subjects (ensuring sufficient data for endpoint assessment), to define that data from a minimum of 5 subjects were needed for the trial safety group to evaluate safety and to decide on ascending to the next dose level, to adjust the section for interim reporting (ensuring that safety summaries and interim analyses could be prepared at relevant time points), and to make minor corrections throughout the protocol.
12 October 2021	A switch of subjects to a new trial product formulation (Mim8 formulation B) during the MAD extension was added and the interim reporting section was amended to accommodate this formulation switch. Also, the recommended activated prothrombin complex concentrate (aPCC) treatment of bleeding episodes was aligned with that of other future Mim8 trials.

28 April 2022	The duration of the MAD extension period of the trial has been extended with 56 weeks and total number of subject visits increased. Number of doses subjects will receive if completing the entire trial duration has been increased to 40 for once-monthly dosing and up to 160 for once-weekly dosing. The maximum amount of blood to be collected in the MAD extension period has been increased due to the additional visits. Discontinuation criterion for the MAD part has been updated to include major surgery and COVID-19.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported