



Clinical trial results:

A Phase I/II, observer-blind, randomised, placebo-controlled study to assess safety, immunogenicity and efficacy of GSK S. aureus candidate vaccine when administered to healthy adults (dose-escalation) and to adults 18 to 64 years of age with a recent S. aureus skin and soft tissue infection (SSTI).

Summary

EudraCT number	2021-006215-29
Trial protocol	PL
Global end of trial date	12 March 2024

Results information

Result version number	v2 (current)
This version publication date	10 September 2025
First version publication date	26 March 2025
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	208833
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	79 New Oxford Street, London, WC1A 1DG, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 June 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess safety and reactogenicity of investigational *S. aureus* vaccine
- To evaluate VE in the prevention of recurrent culture confirmed *S. aureus* SSTIs compared to placebo

Protection of trial subjects:

The participants were observed closely for at least 60 minutes following the administration of vaccine/placebo, with appropriate medical treatment readily available in case of anaphylaxis and syncope.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 June 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	Australia: 41
Country: Number of subjects enrolled	India: 63
Country: Number of subjects enrolled	New Zealand: 31
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	South Africa: 21
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 51
Worldwide total number of subjects	226
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	226
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In SLI and PoP, a total of 376 participants were screened, of which 149 were screening failures and 227 were enrolled. One of the enrolled participants was not included in the analysis population due to a protocol deviation.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject
Blinding implementation details:	
Observer-blind	

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)

Arm description:

Participants received 1 dose of the half dose formulation of the vaccine on Day 1.

Arm type	Experimental
Investigational medicinal product name	Sa-5Ag half dose nonadjuvanted
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose per participant

Arm title	Group 2 Dose-escalation Epoch: Full dose Non-Adj
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Arm description:

Participants received 1 dose of the full dose formulation of the vaccine on Day 1.

Arm type	Experimental
Investigational medicinal product name	Sa-5Ag full dose nonadjuvanted
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose per participant

Arm title	Group 3 Dose-escalation Epoch: Half dose Adj
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Arm description:

Participants received 1 dose of the half dose formulation of the vaccine with adjuvant on Day 1.

Arm type	Experimental
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Investigational medicinal product name	Sa-5Ag half dose adjuvanted
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 1 dose per participant	
Arm title	Group 4 Dose-escalation Epoch: Full dose Adj

Arm description:

Participants received 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.

Arm type	Experimental
Investigational medicinal product name	Sa-5Ag full dose adjuvanted
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 2 doses per participant	
Arm title	Dose-escalation Epoch: Placebo

Arm description:

Participants received matching placebo on Day 1 for Group 1, Group 2 and Group 3, and on Day 1 and Day 61 for Group 4 of the escalation epoch.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 1 dose per participant for Group 1, Group 2 and Group 3, and 2 doses per participant for Group 4	
Arm title	Proof of Principle (PoP): Full dose Adj

Arm description:

Participants were randomized to receive 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.

Arm type	Experimental
Investigational medicinal product name	Sa-5Ag full dose adjuvanted
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 2 doses per participant	
Arm title	PoP: Placebo

Arm description:

Participants were randomized to receive 2 doses of placebo on Day 1 and Day 61.

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

Dosage and administration details:

2 doses per participant

Number of subjects in period 1	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Migrated / Moved from the Study Area	-	-	-
Consent withdrawn by subject	-	-	-
Other	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Group 4 Dose-escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj
Started	6	8	105
Completed	6	8	80
Not completed	0	0	25
Migrated / Moved from the Study Area	-	-	1
Consent withdrawn by subject	-	-	20
Other	-	-	1
Lost to follow-up	-	-	3

Number of subjects in period 1	PoP: Placebo
Started	89
Completed	79
Not completed	10
Migrated / Moved from the Study Area	2
Consent withdrawn by subject	5
Other	1
Lost to follow-up	2

Baseline characteristics

Reporting groups

Reporting group title	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)
Reporting group description:	Participants received 1 dose of the half dose formulation of the vaccine on Day 1.
Reporting group title	Group 2 Dose-escalation Epoch: Full dose Non-Adj
Reporting group description:	Participants received 1 dose of the full dose formulation of the vaccine on Day 1.
Reporting group title	Group 3 Dose-escalation Epoch: Half dose Adj
Reporting group description:	Participants received 1 dose of the half dose formulation of the vaccine with adjuvant on Day 1.
Reporting group title	Group 4 Dose-escalation Epoch: Full dose Adj
Reporting group description:	Participants received 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.
Reporting group title	Dose-escalation Epoch: Placebo
Reporting group description:	Participants received matching placebo on Day 1 for Group 1, Group 2 and Group 3, and on Day 1 and Day 61 for Group 4 of the escalation epoch.
Reporting group title	Proof of Principle (PoP): Full dose Adj
Reporting group description:	Participants were randomized to receive 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.
Reporting group title	PoP: Placebo
Reporting group description:	Participants were randomized to receive 2 doses of placebo on Day 1 and Day 61.

Reporting group values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj
Number of subjects	6	6	6
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	6	6	6
>=65 years	0	0	0
Sex: Female, Male Units: Participants			
MALE	3	1	1
FEMALE	3	5	5
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	5	6	6
Not reported	0	0	0

Reporting group values	Group 4 Dose-escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj

Number of subjects	6	8	105
Age Categorical			
Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	6	8	105
>=65 years	0	0	0
Sex: Female, Male			
Units: Participants			
MALE	4	2	61
FEMALE	2	6	44
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	0	0	2
Not Hispanic or Latino	6	8	66
Not reported	0	0	37

Reporting group values	PoP: Placebo	Total	
Number of subjects	89	226	
Age Categorical			
Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	89	226	
>=65 years	0	0	
Sex: Female, Male			
Units: Participants			
MALE	55	127	
FEMALE	34	99	
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	2	5	
Not Hispanic or Latino	58	155	
Not reported	29	66	

End points

End points reporting groups

Reporting group title	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)
Reporting group description:	Participants received 1 dose of the half dose formulation of the vaccine on Day 1.
Reporting group title	Group 2 Dose-escalation Epoch: Full dose Non-Adj
Reporting group description:	Participants received 1 dose of the full dose formulation of the vaccine on Day 1.
Reporting group title	Group 3 Dose-escalation Epoch: Half dose Adj
Reporting group description:	Participants received 1 dose of the half dose formulation of the vaccine with adjuvant on Day 1.
Reporting group title	Group 4 Dose-escalation Epoch: Full dose Adj
Reporting group description:	Participants received 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.
Reporting group title	Dose-escalation Epoch: Placebo
Reporting group description:	Participants received matching placebo on Day 1 for Group 1, Group 2 and Group 3, and on Day 1 and Day 61 for Group 4 of the escalation epoch.
Reporting group title	Proof of Principle (PoP): Full dose Adj
Reporting group description:	Participants were randomized to receive 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.
Reporting group title	PoP: Placebo
Reporting group description:	Participants were randomized to receive 2 doses of placebo on Day 1 and Day 61.

Primary: Dose-escalation safety lead-in: Number of participants with any and grade 3 solicited administration site adverse events (AEs) after each vaccination

End point title	Dose-escalation safety lead-in: Number of participants with any and grade 3 solicited administration site adverse events (AEs) after each vaccination ^{[1][2]}
End point description:	<p>The solicited administration site AE(s) assessed are pain, redness and swelling. Any = any solicited administration site AE, regardless of intensity; Grade 3 Pain at injection site = Severe, significant pain at rest, that prevents normal everyday activities; Grade 3 redness/swelling = greater than (>)100 millimeter (mm) diameter.</p> <p>The analysis was performed on Solicited Safety Set (SSS) which included all subjects who received at least 1 dose of the study treatment (Exposed Set) who have solicited safety data. Analysis is presented for Dose-escalation safety lead-in participants. '99999' was entered as a placeholder value in those instances where there were 0 participants analyzed.</p>
End point type	Primary
End point timeframe:	Within 7 days post vaccination [day of administration and 6 subsequent days post-each vaccination; Vaccination 1 (V1) on Day 1 and Vaccination 2 (V2) on Day 61]
Notes:	<p>[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.</p> <p>Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.</p> <p>[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the</p>

baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj	Group 4 Dose-escalation Epoch: Full dose Adj
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Participants				
V1, Pain at injection site, Any (N=6;6;6;6;8)	2	3	5	5
V1, Pain at injection site, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Redness at injection site, Any (N=6;6;6;6;8)	0	1	0	2
V1, Redness at injection site, >100mm(N=6;6;6;6;8)	0	0	0	0
V1, Swelling at injection site, Any (N=6;6;6;6;8)	0	0	0	1
V1,Swelling at injection site, >100mm(N=6;6;6;6;8)	0	0	0	0
V2, Pain at injection site, Any (N=0;0;0;6;2)	99999	99999	99999	6
V2, Pain at injection site, Severe (N=0;0;0;6;2)	99999	99999	99999	0
V2, Redness at injection site, Any (N=0;0;0;6;2)	99999	99999	99999	3
V2, Redness at injection site, >100mm(N=0;0;0;6;2)	99999	99999	99999	0
V2, Swelling at injection site, Any (N=0;0;0;6;2)	99999	99999	99999	3
V2,Swelling at injection site, >100mm(N=0;0;0;6;2)	99999	99999	99999	0

End point values	Dose-escalation Epoch: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Participants				
V1, Pain at injection site, Any (N=6;6;6;6;8)	1			
V1, Pain at injection site, Severe (N=6;6;6;6;8)	0			
V1, Redness at injection site, Any (N=6;6;6;6;8)	0			
V1, Redness at injection site, >100mm(N=6;6;6;6;8)	0			
V1, Swelling at injection site, Any (N=6;6;6;6;8)	0			
V1,Swelling at injection site, >100mm(N=6;6;6;6;8)	0			
V2, Pain at injection site, Any (N=0;0;0;6;2)	0			

V2, Pain at injection site, Severe (N=0;0;0;6;2)	0			
V2, Redness at injection site, Any (N=0;0;0;6;2)	0			
V2, Redness at injection site, >100mm(N=0;0;0;6;2)	0			
V2, Swelling at injection site, Any (N=0;0;0;6;2)	0			
V2,Swelling at injection site, >100mm(N=0;0;0;6;2)	0			

Statistical analyses

No statistical analyses for this end point

Primary: PoP: Number of participants with any and grade 3 solicited administration site AEs after each vaccination

End point title	PoP: Number of participants with any and grade 3 solicited administration site AEs after each vaccination ^{[3][4]}
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End point description:

The solicited administration site AEs assessed are pain, redness and swelling. Any = any solicited administration site AE, regardless of intensity; Grade 3 Pain at injection site = Severe, significant pain at rest, that prevents normal everyday activities; Grade 3 redness/swelling = greater than (>)100 millimeter (mm) diameter.

The analysis was performed on Solicited Safety Set (SSS). Analysis is presented for PoP participants.

End point type	Primary
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End point timeframe:

Within 7 days post vaccination [day of administration and 6 subsequent days post-each vaccination; Vaccination 1 (V1) on Day 1 and Vaccination 2 (V2) on Day 61]

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[4] - 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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	88		
Units: Participants				
V1, Pain at injection site, Any (N=102;88)	56	11		
V1, Pain at injection site, Severe (N=102;88)	2	0		
V1, Redness at injection site, Any (N=102;88)	4	0		
V1, Redness at injection site, >100mm (N=102;88)	1	0		
V1, Swelling at injection site, Any (N=102;88)	7	1		
V1, Swelling at injection site, >100mm (N=102;88)	2	1		

V2, Pain at injection site, Any (N=66;47)	42	2		
V2, Pain at injection site, Severe (N=66;47)	3	0		
V2, Redness at injection site, Any (N=66;47)	10	0		
V2, Redness at injection site, >100mm (N=66;47)	4	0		
V2, Swelling at injection site, Any (N=66;47)	13	0		
V2, Swelling at injection site, >100mm (N=66;47)	3	0		

Statistical analyses

No statistical analyses for this end point

Primary: Dose-escalation safety lead-in: Number of participants with any and Grade 3 solicited systemic AEs after each vaccination

End point title	Dose-escalation safety lead-in: Number of participants with any and Grade 3 solicited systemic AEs after each vaccination ^[5] ^[6]
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End point description:

The solicited systemic AE(s) assessed are headache, fatigue, nausea, vomiting, diarrhea, abdominal pain, myalgia, shivering and fever. Any = any solicited systemic AE regardless of intensity; Grade 3 headache/fatigue/nausea/abdominal pain/myalgia/shivering = Severe: Prevents daily activity. Grade 3 vomiting = Severe: 6 or more times in 24 hours or requires intravenous hydration. Grade 3 diarrhea = Severe: 6 or more loose stools in 24 hours or requires intravenous hydration. Grade 3 fever = body temperature greater than (>) 40.0°C/104°F.

The analysis was performed on Solicited Safety Set (SSS). Analysis is presented for Dose-escalation safety lead-in participants. '99999' was entered as a placeholder value in those instances where there were 0 participants analyzed.

End point type	Primary
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End point timeframe:

Within 7 days post vaccination [day of administration and 6 subsequent days post-each vaccination; Vaccination 1 (V1) on Day 1 and Vaccination 2 (V2) on Day 61]

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj	Group 4 Dose-escalation Epoch: Full dose Adj
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Participants				
V1, Abdominal Pain, Any (N=6;6;6;6;8)	0	1	0	0
V1, Abdominal Pain, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Diarrhea, Any (N=6;6;6;6;8)	0	1	1	1

V1, Diarrhea, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Fatigue, Any (N=6;6;6;6;8)	1	2	3	3
V1, Fatigue, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Fever, Any (N=6;6;6;6;8)	0	0	0	0
V1, Fever (°C), > 40.0 (N=6;6;6;6;8)	0	0	0	0
V1, Headache, Any (N=6;6;6;6;8)	0	3	2	1
V1, Headache, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Myalgia, Any (N=6;6;6;6;8)	0	0	0	0
V1, Myalgia, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Nausea, Any (N=6;6;6;6;8)	0	1	2	0
V1, Nausea, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Shivering, Any (N=6;6;6;6;8)	0	0	0	0
V1, Shivering, Severe (N=6;6;6;6;8)	0	0	0	0
V1, Vomiting, Any (N=6;6;6;6;8)	0	0	0	0
V1, Vomiting, Severe (N=6;6;6;6;8)	0	0	0	0
V2, Abdominal Pain, Any (N=0;0;0;6;2)	99999	99999	99999	0
V2, Abdominal Pain, Severe (N=0;0;0;6;2)	99999	99999	99999	0
V2, Diarrhea, Any (N=0;0;0;6;2)	99999	99999	99999	0
V2, Diarrhea, Severe (N=0;0;0;6;2)	99999	99999	99999	0
V2, Fatigue, Any (N=0;0;0;6;2)	99999	99999	99999	5
V2, Fatigue, Severe (N=0;0;0;6;2)	99999	99999	99999	1
V2, Fever, Any (N=0;0;0;6;2)	99999	99999	99999	3
V2, Fever (°C), > 40.0 (N=0;0;0;6;2)	99999	99999	99999	0
V2, Headache, Any (N=0;0;0;6;2)	99999	99999	99999	3
V2, Headache, Severe (N=0;0;0;6;2)	99999	99999	99999	1
V2, Myalgia, Any (N=0;0;0;6;2)	99999	99999	99999	0
V2, Myalgia, Severe (N=0;0;0;6;2)	99999	99999	99999	0
V2, Nausea, Any (N=0;0;0;6;2)	99999	99999	99999	2
V2, Nausea, Severe (N=0;0;0;6;2)	99999	99999	99999	0
V2, Shivering, Any (N=0;0;0;6;2)	99999	99999	99999	0
V2, Shivering, Severe (N=0;0;0;6;2)	99999	99999	99999	0
V2, Vomiting, Any (N=0;0;0;6;2)	99999	99999	99999	0
V2, Vomiting, Severe (N=0;0;0;6;2)	99999	99999	99999	0

End point values	Dose-escalation Epoch: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Participants				
V1, Abdominal Pain, Any (N=6;6;6;6;8)	1			
V1, Abdominal Pain, Severe (N=6;6;6;6;8)	0			
V1, Diarrhea, Any (N=6;6;6;6;8)	0			
V1, Diarrhea, Severe (N=6;6;6;6;8)	0			
V1, Fatigue, Any (N=6;6;6;6;8)	2			
V1, Fatigue, Severe (N=6;6;6;6;8)	0			
V1, Fever, Any (N=6;6;6;6;8)	0			
V1, Fever (°C), > 40.0 (N=6;6;6;6;8)	0			

V1, Headache, Any (N=6;6;6;6;8)	4			
V1, Headache, Severe (N=6;6;6;6;8)	0			
V1, Myalgia, Any (N=6;6;6;6;8)	0			
V1, Myalgia, Severe (N=6;6;6;6;8)	0			
V1, Nausea, Any (N=6;6;6;6;8)	1			
V1, Nausea, Severe (N=6;6;6;6;8)	1			
V1, Shivering, Any (N=6;6;6;6;8)	0			
V1, Shivering, Severe (N=6;6;6;6;8)	0			
V1, Vomiting, Any (N=6;6;6;6;8)	0			
V1, Vomiting, Severe (N=6;6;6;6;8)	0			
V2, Abdominal Pain, Any (N=0;0;0;6;2)	0			
V2, Abdominal Pain, Severe (N=0;0;0;6;2)	0			
V2, Diarrhea, Any (N=0;0;0;6;2)	0			
V2, Diarrhea, Severe (N=0;0;0;6;2)	0			
V2, Fatigue, Any (N=0;0;0;6;2)	0			
V2, Fatigue, Severe (N=0;0;0;6;2)	0			
V2, Fever, Any (N=0;0;0;6;2)	0			
V2, Fever (°C), > 40.0 (N=0;0;0;6;2)	0			
V2, Headache, Any (N=0;0;0;6;2)	0			
V2, Headache, Severe (N=0;0;0;6;2)	0			
V2, Myalgia, Any (N=0;0;0;6;2)	0			
V2, Myalgia, Severe (N=0;0;0;6;2)	0			
V2, Nausea, Any (N=0;0;0;6;2)	0			
V2, Nausea, Severe (N=0;0;0;6;2)	0			
V2, Shivering, Any (N=0;0;0;6;2)	0			
V2, Shivering, Severe (N=0;0;0;6;2)	0			
V2, Vomiting, Any (N=0;0;0;6;2)	0			
V2, Vomiting, Severe (N=0;0;0;6;2)	0			

Statistical analyses

No statistical analyses for this end point

Primary: PoP: Number of participants with any and Grade 3 solicited systemic AEs after each vaccination

End point title	PoP: Number of participants with any and Grade 3 solicited systemic AEs after each vaccination ^{[7][8]}
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End point description:

The solicited systemic AE(s) assessed are headache, fatigue, nausea, vomiting, diarrhea, abdominal pain, myalgia, shivering and fever were assessed. Any = any solicited systemic AE regardless of intensity; Grade 3 headache/fatigue/nausea/abdominal pain/myalgia/shivering = Severe: Prevents daily activity. Grade 3 vomiting = Severe: 6 or more times in 24 hours or requires intravenous hydration. Grade 3 diarrhea = Severe: 6 or more loose stools in 24 hours or requires intravenous hydration. Grade 3 fever = body temperature greater than (>) 40.0°C/104°F. The analysis was performed on Solicited Safety Set (SSS). Analysis is presented for PoP participants.

End point type	Primary
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End point timeframe:

Within 7 days post vaccination [day of administration and 6 subsequent days post-each vaccination; Vaccination 1 (V1) on Day 1 and Vaccination 2 (V2) on Day 61]

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	88		
Units: Participants				
V1, Abdominal Pain, Any (N=102;88)	6	6		
V1, Abdominal Pain, Severe (N=102;88)	0	0		
V1, Diarrhea, Any (N=102;88)	11	4		
V1, Diarrhea, Severe (N=102;88)	0	0		
V1, Fatigue, Any (N=102;88)	34	21		
V1, Fatigue, Severe (N=102;88)	2	2		
V1, Fever, Any (N=102;88)	4	1		
V1, Fever (°C), > 40.0 (N=102;88)	0	0		
V1, Headache, Any (N=102;88)	28	26		
V1, Headache, Severe (N=102;88)	1	2		
V1, Myalgia, Any (N=102;88)	16	10		
V1, Myalgia, Severe (N=102;88)	1	0		
V1, Nausea, Any (N=102;88)	8	8		
V1, Nausea, Severe (N=102;88)	0	0		
V1, Shivering, Any (N=102;88)	8	5		
V1, Shivering, Severe (N=102;88)	0	0		
V1, Vomiting, Any (N=102;88)	2	1		
V1, Vomiting, Severe (N=102;88)	0	0		
V2, Abdominal Pain, Any (N=66;47)	4	0		
V2, Abdominal Pain, Severe (N=66;47)	0	0		
V2, Diarrhea, Any (N=66;47)	4	2		
V2, Diarrhea, Severe (N=66;47)	0	0		
V2, Fatigue, Any (N=66;47)	33	7		
V2, Fatigue, Severe (N=66;47)	3	1		
V2, Fever, Any (N=66;47)	4	1		
V2, Fever (°C), > 40.0 (N=66;47)	0	0		
V2, Headache, Any (N=66;47)	24	7		
V2, Headache, Severe (N=66;47)	3	0		
V2, Myalgia, Any (N=66;47)	15	2		
V2, Myalgia, Severe (N=66;47)	3	0		
V2, Nausea, Any (N=66;47)	11	4		
V2, Nausea, Severe (N=66;47)	1	0		
V2, Shivering, Any (N=66;47)	11	1		
V2, Shivering, Severe (N=66;47)	2	0		
V2, Vomiting, Any (N=66;47)	3	0		
V2, Vomiting, Severe (N=66;47)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Dose-escalation safety lead-in: Number of participants with unsolicited AEs (any, grade 3, related, related grade 3) after each vaccination

End point title	Dose-escalation safety lead-in: Number of participants with unsolicited AEs (any, grade 3, related, related grade 3) after each vaccination ^{[9][10]}
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End point description:

An unsolicited adverse event is defined as an adverse event that was not solicited using a Subject Diary and that was spontaneously communicated by a subject who has signed the informed consent. Any unsolicited AE, Grade 3 (G3) unsolicited AE, unsolicited AE causally related to the vaccination and G3 unsolicited AE causally related to the vaccination were assessed. A grade 3 AE is an AE that prevents normal, everyday activities.

The analysis was performed on the Unsolicited Safety Set (USS) which included all subjects who received at least 1 dose of the study treatment (Exposed Set) that report unsolicited AEs/report not having unsolicited AEs. '99999' was entered as a placeholder value in those instances where there were 0 participants analyzed.

End point type	Primary
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End point timeframe:

During 30 days after each vaccination [day of administration and 29 subsequent days post-each vaccination; Vaccination 1 (V1) on Day 1 and Vaccination 2 (V2) on Day 61]

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj	Group 4 Dose-escalation Epoch: Full dose Adj
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Participants				
V1,At least 1 unsolicited AE (N=6;6;6;6;8)	1	3	1	0
V1,At least 1 related unsolicited AE (N=6;6;6;6;8)	1	2	0	0
V1,At least 1 G3 unsolicited AE (N=6;6;6;6;8)	0	0	0	0
V1,At least 1 G3 related unsol. AE(N=6;6;6;6;8)	0	0	0	0
V2,At least 1 unsolicited AE (N=0;0;0;6;2)	99999	99999	99999	2

V2,At least 1 related unsolicited AE (N=0;0;0;6;2)	99999	99999	99999	2
V2,At least 1 G3 unsolicited AE (N=0;0;0;6;2)	99999	99999	99999	0
V2,At least 1 G3 related unsol. AE(N=0;0;0;6;2)	99999	99999	99999	0

End point values	Dose- escalation Epoch: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Participants				
V1,At least 1 unsolicited AE (N=6;6;6;6;8)	0			
V1,At least 1 related unsolicited AE (N=6;6;6;6;8)	0			
V1,At least 1 G3 unsolicited AE (N=6;6;6;6;8)	0			
V1,At least 1 G3 related unsol. AE(N=6;6;6;6;8)	0			
V2,At least 1 unsolicited AE (N=0;0;0;6;2)	0			
V2,At least 1 related unsolicited AE (N=0;0;0;6;2)	0			
V2,At least 1 G3 unsolicited AE (N=0;0;0;6;2)	0			
V2,At least 1 G3 related unsol. AE(N=0;0;0;6;2)	0			

Statistical analyses

No statistical analyses for this end point

Primary: PoP: Number of participants with unsolicited AEs (any, grade 3, related, related grade 3) after each vaccination

End point title	PoP: Number of participants with unsolicited AEs (any, grade 3, related, related grade 3) after each vaccination ^{[11][12]}
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End point description:

An unsolicited adverse event is defined as an adverse event that was not solicited using a Subject Diary and that was spontaneously communicated by a subject who has signed the informed consent. Any unsolicited AE, Grade 3 (G3) unsolicited AE, unsolicited AE causally related to the vaccination and G3 unsolicited AE causally related to the vaccination were assessed. A grade 3 AE is an AE that prevents normal, everyday activities.

The analysis was performed on USS.

End point type	Primary
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End point timeframe:

During 30 days after each vaccination [day of administration and 29 subsequent days post-each vaccination; Vaccination 1 (V1) on Day 1 and Vaccination 2 (V2) on Day 61]

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	89		
Units: Participants				
V1,At least 1 unsolicited AE (N=103;89)	32	26		
V1,At least 1 related unsolicited AE (N=103;89)	16	4		
V1,At least 1 G3 unsolicited AE (N=103;89)	0	1		
V1,At least 1 G3 related unsolicited AE (N=103;89)	0	0		
V2,At least 1 unsolicited AE (N=67;48)	23	7		
V2,At least 1 related unsolicited AE (N=67;48)	12	4		
V2,At least 1 G3 unsolicited AE (N=67;48)	1	1		
V2,At least 1 G3 related unsolicited AE (N=67;48)	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Dose-escalation safety lead-in: Number of participants with serious AEs (SAEs) up to 1 year post first vaccination

End point title	Dose-escalation safety lead-in: Number of participants with serious AEs (SAEs) up to 1 year post first vaccination ^{[13][14]}
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End point description:

A SAE is defined as any untoward medical occurrence that, at any dose: resulted in death, was life threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment. A grade 3 SAE is a SAE that prevents normal, everyday activities.

The analysis was performed on the Exposed Set (ES) that included all subjects who received at least 1 dose of the study treatment. The allocation in a group is done in function of the administered treatment.

End point type	Primary
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End point timeframe:

From Day 1 to Day 366

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj	Group 4 Dose-escalation Epoch: Full dose Adj
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Participants				
At least one SAE	0	0	0	0
At least one serious related AE	0	0	0	0
Any Grade 3 SAE	0	0	0	0

End point values	Dose-escalation Epoch: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Participants				
At least one SAE	0			
At least one serious related AE	0			
Any Grade 3 SAE	0			

Statistical analyses

No statistical analyses for this end point

Primary: PoP: Number of participants with SAEs

End point title	PoP: Number of participants with SAEs ^[15] ^[16]
End point description:	A SAE is defined as any untoward medical occurrence that, at any dose: resulted in death, was life threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment. A grade 3 SAE is a SAE that prevents normal, everyday activities. The analysis was performed on ES. The allocation in a group is done in function of the administered treatment.
End point type	Primary
End point timeframe:	From Day 1 to Day 426

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	89		
Units: Participants				
At least one SAE	5	5		
At least one serious related AE	0	0		
Any Grade 3 SAE	3	2		

Statistical analyses

No statistical analyses for this end point

Primary: Dose-escalation safety lead-in: Number of participants with SAEs up to 1 year post second vaccination

End point title	Dose-escalation safety lead-in: Number of participants with SAEs up to 1 year post second vaccination ^{[17][18]}
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End point description:

A SAE is defined as any untoward medical occurrence that, at any dose: resulted in death, was life threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment.

The analysis was performed on ES. Only participants that received a second vaccination on Day 61 were included in this analysis.

End point type	Primary
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End point timeframe:

From Day 61 to Day 426 (post vaccination at Day 61)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 4 Dose-escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Participants				
At least one SAE	0	0		
At least one serious related AE	0	0		
Any Grade 3 SAE	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Dose-escalation safety lead-in: Number of participants with potential immune-mediated diseases (pIMDs) up to 1 year post first vaccination

End point title	Dose-escalation safety lead-in: Number of participants with potential immune-mediated diseases (pIMDs) up to 1 year post first vaccination ^{[19][20]}
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End point description:

pIMDs are defined as a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

The analysis was performed on ES.

End point type	Primary
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End point timeframe:

From Day 1 to Day 366

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj	Group 4 Dose-escalation Epoch: Full dose Adj
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Participants	0	0	0	0

End point values	Dose-escalation Epoch: Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Dose-escalation safety lead-in: Number of participants with pIMDs up to 1 year post second vaccination

End point title	Dose-escalation safety lead-in: Number of participants with pIMDs up to 1 year post second vaccination ^{[21][22]}
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End point description:

pIMDs are defined as a subset of AEs that include autoimmune diseases and other inflammatory and/or

neurologic disorders of interest which may or may not have an autoimmune aetiology.
The analysis was performed on ES. Only participants that received a second vaccination on Day 61 were included in this analysis.

End point type	Primary
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End point timeframe:

From Day 61 to Day 426 (post vaccination at Day 61)

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 4 Dose-escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: PoP: Number of participants with potential immune-mediated diseases (pIMDs)

End point title	PoP: Number of participants with potential immune-mediated diseases (pIMDs) ^{[23][24]}
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End point description:

pIMDs are defined as a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

The analysis was performed on ES.

End point type	Primary
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End point timeframe:

From Day 1 to Day 426

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	89		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with maximum toxicity grade increase from baseline for haematological and biochemical laboratory parameters [On Day 8 compared to Baseline (Day 1)]

End point title	Number of participants with maximum toxicity grade increase from baseline for haematological and biochemical laboratory parameters [On Day 8 compared to Baseline (Day 1)] ^[25]
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End point description:

Biochemical parameters assessed: Creatinine, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT). Haematological parameters: Haemoglobin, white blood cells (WBC) decrease, WBC increase, Neutrophils decrease, Platelets decrease, Lymphocytes decrease, Eosinophils increase. Laboratory results defined as: <parameter>, <grade at baseline>, <grade at visit> (e.g. ALT, Grade 0, Grade 0). Grades: Grade 0 for non-missing values without derived grade; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life-Threatening per FDA Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (September 2007). Unknown = parameter value missing for the specified parameter. Analysis was performed on the Laboratory Safety Set, a subset of the Unsolicited Safety Set. Included participants had data at specified timepoints. '99999' used as placeholder for 0 participants analyzed.

End point type	Primary
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End point timeframe:

On Day 8 compared to Baseline (Day 1)

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj	Group 4 Dose-escalation Epoch: Full dose Adj
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	5	6
Units: Participants				
ALT, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	4	5
ALT, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	1	1
ALT, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
AST, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	5
AST, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999

AST, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	99999	1
Creatinine, Unknown, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
Creatinine, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
EOS Increase, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
EOS Increase, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
EOS Increase, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
Hb Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	5	4	6
Hb Decrease, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	0	0	1	0
Hb Decrease, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
Hb Decrease, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	1	99999	99999
LYM Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	4	6
LYM Decrease, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	1	99999
NEUT Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
NEUT Decrease, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	0	0	0	0
Plt Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
WBC Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
WBC Increase, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	6	5	4	6
WBC Increase, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	0	1	0	0
WBC Increase, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	1	99999

End point values	Dose- escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj	PoP: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	29	11	
Units: Participants				
ALT, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	26	11	
ALT, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	1	99999	
ALT, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	2	99999	
AST, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	28	11	
AST, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	99999	1	0	
AST, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	99999	

Creatinine, Unknown, Grade 0 (N=6;6;5;6;8;29;11)	99999	99999	1	
Creatinine, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	29	10	
EOS Increase, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	27	10	
EOS Increase, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	0	1	
EOS Increase, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	2	0	
Hb Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	20	10	
Hb Decrease, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	0	3	1	
Hb Decrease, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	99999	2	99999	
Hb Decrease, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	4	99999	
LYM Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	29	11	
LYM Decrease, Grade 1, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	99999	
NEUT Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	7	29	11	
NEUT Decrease, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	1	0	0	
Plt Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	29	11	
WBC Decrease, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	8	29	11	
WBC Increase, Grade 0, Grade 0 (N=6;6;5;6;8;29;11)	7	26	11	
WBC Increase, Grade 0, Grade 1 (N=6;6;5;6;8;29;11)	0	2	0	
WBC Increase, Grade 1, Grade 0 (N=6;6;5;6;8;29;11)	1	1	99999	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with maximum toxicity grade increase from baseline for haematological and biochemical laboratory parameters [On Day 68 compared to Baseline (Day 61)]

End point title	Number of participants with maximum toxicity grade increase from baseline for haematological and biochemical laboratory parameters [On Day 68 compared to Baseline (Day 61)] ^{[26][27]}
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End point description:

Biochemical parameters assessed: Creatinine, AST, ALT. Haematological parameters: Haemoglobin, WBC decrease, WBC increase, Neutrophils decrease, Platelets decrease, Lymphocytes decrease, Eosinophils increase. Laboratory results defined as: <parameter>, <grade at baseline>, <grade at visit> (e.g. ALT, Grade 0, Grade 0). Grades: Grade 0 for non-missing values without derived grade; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life-Threatening per FDA Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (September 2007). Unknown = parameter value missing for the specified parameter. Analysis was performed on the Laboratory Safety Set, a subset of the Unsolicited Safety Set. Included participants had data at specified timepoints. '99999' used as placeholder for 0 participants analyzed.

End point type	Primary
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End point timeframe:

On Day 68 compared to Baseline (Day 61)

Notes:

[26] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 4 Dose-escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj	PoP: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	2	28	11
Units: Participants				
ALT, Unknown, Grade 0 (N=6;2;28;11)	99999	99999	1	99999
ALT, Grade 0, Grade 0 (N=6;2;28;11)	6	2	26	11
ALT, Grade 1, Grade 1 (N=6;2;28;11)	99999	99999	1	99999
AST, Unknown, Grade 0 (N=6;2;28;11)	99999	99999	1	99999
AST, Grade 0, Grade 0 (N=6;2;28;11)	6	2	26	10
AST, Grade 0, Grade 1 (N=6;2;28;11)	99999	99999	1	0
AST, Grade 1, Grade 0 (N=6;2;28;11)	99999	99999	99999	1
Creatinine, Unknown, Grade 0 (N=6;2;28;11)	99999	99999	1	99999
Creatinine, Grade 0, Grade 0 (N=6;2;28;11)	6	2	27	11
EOS Increase, Unknown, Grade 0 (N=6;2;28;11)	1	99999	1	99999
EOS Increase, Grade 0, Grade 0 (N=6;2;28;11)	5	2	25	10
EOS Increase, Grade 0, Grade 1 (N=6;2;28;11)	99999	99999	1	0
EOS Increase, Grade 1, Grade 1 (N=6;2;28;11)	99999	99999	1	1
Hb Decrease, Unknown, Grade 0 (N=6;2;28;11)	1	99999	1	99999
Hb Decrease, Grade 0, Grade 0 (N=6;2;28;11)	5	2	21	9
Hb Decrease, Grade 0, Grade 1 (N=6;2;28;11)	99999	99999	2	0
Hb Decrease, Grade 1, Grade 0 (N=6;2;28;11)	99999	99999	2	0
Hb Decrease, Grade 1, Grade 1 (N=6;2;28;11)	99999	99999	1	2
Hb Decrease, Grade 1, Grade 2 (N=6;2;28;11)	99999	99999	1	0
LYM Decrease, Unknown, Grade 0 (N=6;2;28;11)	1	99999	1	0
LYM Decrease, Grade 0, Grade 0 (N=6;2;28;11)	5	2	26	11
LYM Decrease, Grade 0, Grade 1 (N=6;2;28;11)	99999	99999	1	0
NEUT Decrease, Unknown, Grade 0 (N=6;2;28;11)	1	99999	1	99999

NEUT Decrease, Grade 0, Grade 0 (N=6;2;28;11)	5	2	25	11
NEUT Decrease, Grade 1, Grade 0 (N=6;2;28;11)	99999	99999	1	99999
NEUT Decrease, Grade 1, Grade 1 (N=6;2;28;11)	99999	99999	1	99999
Plt Decrease, Unknown, Grade 0 (N=6;2;28;11)	1	99999	1	99999
Plt Decrease, Grade 0, Grade 0 (N=6;2;28;11)	5	2	27	11
WBC Decrease, Unknown, Grade 0 (N=6;2;28;11)	1	99999	1	99999
WBC Decrease, Grade 0, Grade 0 (N=6;2;28;11)	5	2	26	11
WBC Decrease, Grade 1, Grade 0 (N=6;2;28;11)	99999	99999	1	99999
WBC Increase, Unknown, Grade 0 (N=6;2;28;11)	1	99999	1	99999
WBC Increase, Grade 0, Grade 0 (N=6;2;28;11)	5	2	25	10
WBC Increase, Grade 0, Grade 1 (N=6;2;28;11)	99999	99999	1	1
WBC Increase, Grade 1, Grade 0 (N=6;2;28;11)	99999	99999	1	99999

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with haematological and biochemical laboratory change from baseline values [On Day 8]

End point title	Number of participants with haematological and biochemical laboratory change from baseline values [On Day 8] ^[28]
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End point description:

Biochemical parameters assessed: Creatinine, AST, ALT. Haematological parameters: Haemoglobin, WBC decrease, WBC increase, Neutrophils decrease, Platelets decrease, Lymphocytes decrease, Eosinophils increase. Laboratory results defined as: <parameter>, <any grade at baseline>, <grade at visit> (e.g. ALT, Any, Grade 0). Grades: Grade 0 for non-missing values without derived grade; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life-Threatening per FDA Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (September 2007). Unknown = parameter value missing for the specified parameter. Analysis was performed on the Laboratory Safety Set, a subset of the Unsolicited Safety Set. Included participants had data at specified timepoints. '99999' used as placeholder for 0 participants analyzed.

End point type	Primary
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End point timeframe:

On Day 8

Notes:

[28] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj	Group 4 Dose-escalation Epoch: Full dose Adj
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	5	6
Units: Participants				
ALT, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
ALT, Any, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
AST, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
AST, Any, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
Creatinine, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
EOS Increase, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
EOS Increase, Any, Grade 1 (N=6;6;5;6;8;29;11)	99999	99999	99999	99999
Hb Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	5	4	6
Hb Decrease, Any, Grade 1 (N=6;6;5;6;8;29;11)	0	1	1	0
LYM Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	4	6
LYM Decrease, Any, Grade 1 (N=6;6;5;6;8;29;11)	0	0	1	0
NEUT Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
NEUT Decrease, Any, Grade 1 (N=6;6;5;6;8;29;11)	0	0	0	0
Plt Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
WBC Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	6	5	6
WBC Increase, Any, Grade 0 (N=6;6;5;6;8;29;11)	6	5	5	6
WBC Increase, Any, Grade 1 (N=6;6;5;6;8;29;11)	0	1	0	0

End point values	Dose-escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj	PoP: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	29	11	
Units: Participants				
ALT, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	27	11	
ALT, Any, Grade 1 (N=6;6;5;6;8;29;11)	99999	2	0	
AST, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	28	11	
AST, Any, Grade 1 (N=6;6;5;6;8;29;11)	99999	1	0	
Creatinine, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	29	11	

EOS Increase, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	27	11	
EOS Increase, Any, Grade 1 (N=6;6;5;6;8;29;11)	99999	2	0	
Hb Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	22	10	
Hb Decrease, Any, Grade 1 (N=6;6;5;6;8;29;11)	0	7	1	
LYM Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	29	11	
LYM Decrease, Any, Grade 1 (N=6;6;5;6;8;29;11)	0	99999	99999	
NEUT Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	7	29	11	
NEUT Decrease, Any, Grade 1 (N=6;6;5;6;8;29;11)	1	99999	99999	
Plt Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	29	11	
WBC Decrease, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	29	11	
WBC Increase, Any, Grade 0 (N=6;6;5;6;8;29;11)	8	27	11	
WBC Increase, Any, Grade 1 (N=6;6;5;6;8;29;11)	0	2	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with haematological and biochemical laboratory change from baseline values [On Day 68]

End point title	Number of participants with haematological and biochemical laboratory change from baseline values [On Day 68] ^[29] ^[30]
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End point description:

Biochemical parameters assessed: Creatinine, AST, ALT. Haematological parameters: Haemoglobin, WBC decrease, WBC increase, Neutrophils decrease, Platelets decrease, Lymphocytes decrease, Eosinophils increase. Laboratory results defined as: <parameter>, <any grade at baseline>, <grade at visit> (e.g. ALT, Any, Grade 0). Grades: Grade 0 for non-missing values without derived grade; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life-Threatening per FDA Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (September 2007). Unknown = parameter value missing for the specified parameter. Analysis was performed on the Laboratory Safety Set, a subset of the Unsolicited Safety Set. Included participants had data at specified timepoints. '99999' used as placeholder for 0 participants analyzed.

End point type	Primary
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End point timeframe:

On Day 68

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[30] - 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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Group 4 Dose-escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj	PoP: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	2	28	11
Units: Participants				
ALT, Any, Grade 0 (N=6;2;28;11)	6	2	27	11
ALT, Any, Grade 1 (N=6;2;28;11)	99999	99999	1	0
AST, Any, Grade 0 (N=6;2;28;11)	6	2	27	11
AST, Any, Grade 1 (N=6;2;28;11)	99999	99999	1	0
Creatinine, Any, Grade 0 (N=6;2;28;11)	6	2	28	11
EOS Increase, Any, Grade 0 (N=6;2;28;11)	6	2	26	10
EOS Increase, Any, Grade 1 (N=6;2;28;11)	99999	99999	2	1
Hb Decrease, Any, Grade 0 (N=6;2;28;11)	6	2	24	9
Hb Decrease, Any, Grade 1 (N=6;2;28;11)	99999	99999	3	2
Hb Decrease, Any, Grade 2 (N=6;2;28;11)	99999	99999	1	0
LYM Decrease, Any, Grade 0 (N=6;2;28;11)	6	2	27	11
LYM Decrease, Any, Grade 1 (N=6;2;28;11)	99999	99999	1	0
NEUT Decrease, Any, Grade 0 (N=6;2;28;11)	6	2	27	11
NEUT Decrease, Any, Grade 1 (N=6;2;28;11)	99999	99999	1	0
Plt Decrease, Any, Grade 0 (N=6;2;28;11)	6	2	28	11
WBC Decrease, Any, Grade 0 (N=6;2;28;11)	6	2	28	11
WBC Increase, Any, Grade 0 (N=6;2;28;11)	6	2	27	10
WBC Increase, Any, Grade 1 (N=6;2;28;11)	99999	99999	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one culture confirmed case of recurrent Staphylococcus aureus (S. aureus) Skin and Soft Tissue Infection (SSTI) - Interim Analysis

End point title	Number of participants with at least one culture confirmed case of recurrent Staphylococcus aureus (S. aureus) Skin and Soft Tissue Infection (SSTI) - Interim Analysis ^[31]
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End point description:

An interim analysis was performed after 13 cases of recurrent SA-SSTI were reported following 14 days from the study intervention dose 2.

The analysis was performed on Interim analysis Proof of Principle (Pop) - modified Full Analysis Set (mFAS) which included all subjects who received full study treatment course to which they are randomised and have post-vaccination efficacy data.

End point type	Secondary
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End point timeframe:
From Day 75 to Day 426

Notes:

[31] - 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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	21		
Units: Participants	10	3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

One-sided Group Sequential Design with non-binding beta, yielding two CIs based on cumulative alpha (92.5%) and beta (80.5%) spending.

Comparison groups	Proof of Principle (PoP): Full dose Adj v PoP: Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority ^[32]
P-value	> 0.8042
Method	Logrank
Parameter estimate	Vaccine Efficacy (VE)
Point estimate	-74.76
Confidence interval	
level	Other: 92.5 %
sides	2-sided
lower limit	-680.61
upper limit	36.62

Notes:

[32] - Vaccine Efficacy (VE) is defined as 1 minus the hazard ratio times 100.

Secondary: Number of participants with at least one culture confirmed case of recurrent S. aureus SSTI - Final Analysis [From Day 75 to Day 426]

End point title	Number of participants with at least one culture confirmed case of recurrent S. aureus SSTI - Final Analysis [From Day 75 to Day 426] ^[33]
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End point description:

After encountering futility at the interim analysis, an EOS analysis was conducted when at least one culture-confirmed case of recurrent SA-SSTI was identified 14 days after the second dose of the vaccine. For the final analysis, all the data collected by End of Study (EoS; Last Participant Last Visit) were analyzed for descriptive purposes.

The analysis was performed on EoS analysis PoP mFAS.

End point type	Secondary
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End point timeframe:

From Day 75 to Day 426

Notes:

[33] - 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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	48		
Units: Participants	14	8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Proof of Principle (PoP): Full dose Adj v PoP: Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other ^[34]
Parameter estimate	Vaccine Efficacy (VE)
Point estimate	-38.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-245.77
upper limit	40.86

Notes:

[34] - Vaccine Efficacy (VE) is defined as 1 minus the hazard ratio times 100.

Secondary: Number of participants with at least one culture confirmed case of recurrent S. aureus SSTI - Final Analysis [From Day 15 to Day 426]

End point title	Number of participants with at least one culture confirmed case of recurrent S. aureus SSTI - Final Analysis [From Day 15 to Day 426] ^[35]
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End point description:

An EOS analysis was conducted when at least one culture-confirmed case of recurrent SA-SSTI was identified 14 days after the first dose of the vaccine. For the final analysis, all the data collected by End of Study (EoS; Last Participant Last Visit) were analyzed for descriptive purposes.

The analysis was performed on the EOS Pop: Full Analysis Set (FAS) which included all subjects who received at least 1 dose of the study treatment and have post-vaccination efficacy data.

End point type	Secondary
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End point timeframe:

From Day 15 to Day 426

Notes:

[35] - 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: This endpoint reports data only for the "dose-escalation epoch". Hence, the arms that correspond to only dose-escalation were included.

End point values	Proof of Principle (PoP): Full dose Adj	PoP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	89		
Units: Participants	18	10		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Proof of Principle (PoP): Full dose Adj v PoP: Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	other ^[36]
Parameter estimate	Vaccine Efficacy (VE)
Point estimate	-75.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-295.41
upper limit	17.46

Notes:

[36] - Vaccine Efficacy (VE) is defined as 1 minus the hazard ratio times 100.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: from Day (D) 1 to D7 and D61 to D67 [for Group 4 (G4) and PoP epoch]. Unsolicited AEs: from D1 to D30 and D61 to D90 (for G4 and PoP epoch). SAEs and pIMDs: from D1 to D366 (dose escalation), D61 to D426 (for G4), D1 to D426 for PoP epoch.

Adverse event reporting additional description:

Adverse events are reported on the Exposed Set, who received at least 1 dose of the study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	v22.1
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Dictionary version	22.1
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Reporting groups

Reporting group title	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)
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Reporting group description:

Participants received 1 dose of the half dose formulation of the vaccine on Day 1.

Reporting group title	Group 2 Dose-escalation Epoch: Full dose Non-Adj
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Reporting group description:

Participants received 1 dose of the full dose formulation of the vaccine on Day 1.

Reporting group title	Group 3 Dose-escalation Epoch: Half dose Adj
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Reporting group description:

Participants received 1 dose of the half dose formulation of the vaccine with adjuvant on Day 1.

Reporting group title	Group 4 Dose-escalation Epoch: Full dose Adj
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Reporting group description:

Participants received 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.

Reporting group title	Dose-escalation Epoch: Placebo
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Reporting group description:

Participants received matching placebo on Day 1 for Group 1, Group 2 and Group 3, and on Day 1 and Day 61 for Group 4 of the escalation epoch.

Reporting group title	Proof of Principle (PoP): Full dose Adj
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Reporting group description:

Participants were randomized to receive 2 doses of the full dose formulation of the vaccine with adjuvant on Day 1 and Day 61.

Reporting group title	PoP: Placebo
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Reporting group description:

Participants were randomized to receive 2 doses of placebo on Day 1 and Day 61.

Serious adverse events	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj
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			

Neoplasms benign, malignant and unspecified (incl cysts and polyps) Large intestine benign neoplasm 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 Concussion 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
Limb 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
Thermal burn 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 Transient ischaemic attack 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
Psychiatric disorders Suicidal ideation 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
Infections and infestations Cellulitis 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
Abscess limb			

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
Erysipelas			
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
Subcutaneous abscess			
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
Furuncle			
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	Group 4 Dose-escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	5 / 103 (4.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Large intestine benign neoplasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (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
Limb injury			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
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			
Transient ischaemic attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (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

Furuncle			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (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	PoP: Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 89 (5.62%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Large intestine benign neoplasm			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Limb injury			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thermal burn			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	0 / 89 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess limb			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Furuncle			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Group 1 Dose-escalation Epoch: Half dose Non-Adjuvant(Non-Adj)	Group 2 Dose-escalation Epoch: Full dose Non-Adj	Group 3 Dose-escalation Epoch: Half dose Adj
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	6 / 6 (100.00%)	5 / 6 (83.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Acrochordon subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions Chills subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 6 (33.33%) 2	3 / 6 (50.00%) 3
Feeling hot subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injection site induration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Injection site erythema subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Injection site macule subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injection site swelling			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injection site reaction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injection site rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	4 / 6 (66.67%) 4	5 / 6 (83.33%) 5
Injection site mass subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vaccination site erythema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Tonsillar hypertrophy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Insomnia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Investigations			
Haemoglobin decreased			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood creatinine increased			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Fall			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Limb injury			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Muscle rupture			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Muscle strain			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin laceration			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin graft failure			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Procedural pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders			
Migraine subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Lethargy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	3 / 6 (50.00%) 3	2 / 6 (33.33%) 2
Dizziness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood and lymphatic system disorders			
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Eye disorders			
Eye inflammation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders			

Angular cheilitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	2 / 6 (33.33%) 2
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1
Skin and subcutaneous tissue disorders Eczema			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis atopic			
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
Blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photodermatosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
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
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal impairment			
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			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fibromyalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
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
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
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
Candida infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear infection staphylococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye infection			
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	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Skin infection			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Staphylococcal skin infection			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Upper respiratory tract infection			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Viral infection			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vulvovaginal candidiasis			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders			
Vitamin B12 deficiency			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Type 2 diabetes mellitus			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dehydration			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0

Non-serious adverse events	Group 4 Dose- escalation Epoch: Full dose Adj	Dose-escalation Epoch: Placebo	Proof of Principle (PoP): Full dose Adj
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	5 / 8 (62.50%)	82 / 103 (79.61%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Vascular disorders			

Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	20 / 103 (19.42%)
occurrences (all)	0	0	22
Fatigue			
subjects affected / exposed	5 / 6 (83.33%)	2 / 8 (25.00%)	46 / 103 (44.66%)
occurrences (all)	8	2	70
Feeling hot			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	1	0	0
Injection site induration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	3 / 6 (50.00%)	0 / 8 (0.00%)	12 / 103 (11.65%)
occurrences (all)	6	0	16
Injection site macule			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 8 (0.00%)	12 / 103 (11.65%)
occurrences (all)	3	0	12
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	4 / 103 (3.88%)
occurrences (all)	0	0	4
Injection site swelling			
subjects affected / exposed	3 / 6 (50.00%)	0 / 8 (0.00%)	16 / 103 (15.53%)
occurrences (all)	5	0	23
Injection site reaction			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Injection site rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Injection site pain subjects affected / exposed occurrences (all)	6 / 6 (100.00%) 13	1 / 8 (12.50%) 1	65 / 103 (63.11%) 114
Injection site mass subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Vaccination site erythema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Respiratory, thoracic and mediastinal disorders Tonsillar hypertrophy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Dyspnoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	2 / 103 (1.94%) 2
Psychiatric disorders			

Anxiety disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Insomnia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Investigations			
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Injury, poisoning and procedural complications			
Arthropod sting subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Fall subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Limb injury subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Muscle rupture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Muscle strain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Skin laceration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Skin graft failure subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Procedural pain			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Nervous system disorders			
Migraine			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Lethargy			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	2 / 103 (1.94%) 2
Headache			
subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 4	4 / 8 (50.00%) 4	40 / 103 (38.83%) 58
Dizziness			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Sciatica			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Syncope			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	4 / 103 (3.88%) 4
Neutropenia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Eye disorders			
Eye inflammation			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Gastrointestinal disorders			
Angular cheilitis			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Abdominal pain upper			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	10 / 103 (9.71%)
occurrences (all)	0	1	12
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	5 / 103 (4.85%)
occurrences (all)	0	0	7
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	18 / 103 (17.48%)
occurrences (all)	2	1	23
Mouth ulceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	14 / 103 (13.59%)
occurrences (all)	1	0	17
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Dermatitis atopic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1

Dermatitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Blister subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Acne subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Photodermatosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Pain of skin subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Urticaria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	2 / 103 (1.94%) 2
Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Arthralgia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 103 (1.94%)
occurrences (all)	0	0	2
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Exostosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Fibromyalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Rotator cuff syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 103 (1.94%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	27 / 103 (26.21%)
occurrences (all)	2	0	32
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	4 / 103 (3.88%)
occurrences (all)	0	0	4
Candida infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Ear infection staphylococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0

Eye infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Otitis externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Furuncle			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 103 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 103 (0.97%)
occurrences (all)	0	0	1

Staphylococcal skin infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Viral infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0
Metabolism and nutrition disorders			
Vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 103 (0.97%) 1
Dehydration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 103 (0.00%) 0

Non-serious adverse events	PoP: Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	60 / 89 (67.42%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Acrochordon subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Vascular disorders			
Hot flush subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Hypertension subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		

General disorders and administration site conditions			
Chills			
subjects affected / exposed	6 / 89 (6.74%)		
occurrences (all)	6		
Fatigue			
subjects affected / exposed	24 / 89 (26.97%)		
occurrences (all)	29		
Feeling hot			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Injection site induration			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Injection site macule			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Injection site rash			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Injection site pain			

<p>subjects affected / exposed occurrences (all)</p> <p>Injection site mass subjects affected / exposed occurrences (all)</p> <p>Vaccination site erythema subjects affected / exposed occurrences (all)</p>	<p>13 / 89 (14.61%) 14</p> <p>0 / 89 (0.00%) 0</p> <p>0 / 89 (0.00%) 0</p>		
<p>Reproductive system and breast disorders</p> <p>Menstruation irregular subjects affected / exposed occurrences (all)</p>	<p>0 / 89 (0.00%) 0</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Tonsillar hypertrophy subjects affected / exposed occurrences (all)</p> <p>Rhinorrhoea subjects affected / exposed occurrences (all)</p> <p>Cough subjects affected / exposed occurrences (all)</p> <p>Dyspnoea subjects affected / exposed occurrences (all)</p> <p>Oropharyngeal pain subjects affected / exposed occurrences (all)</p>	<p>0 / 89 (0.00%) 0</p> <p>0 / 89 (0.00%) 0</p> <p>3 / 89 (3.37%) 4</p> <p>0 / 89 (0.00%) 0</p> <p>0 / 89 (0.00%) 0</p>		
<p>Psychiatric disorders</p> <p>Anxiety disorder subjects affected / exposed occurrences (all)</p> <p>Insomnia subjects affected / exposed occurrences (all)</p>	<p>0 / 89 (0.00%) 0</p> <p>1 / 89 (1.12%) 1</p>		
Investigations			

Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Injury, poisoning and procedural complications			
Arthropod sting subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Limb injury subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 2		
Muscle rupture subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Muscle strain subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Skin laceration subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Skin graft failure subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Procedural pain subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Nervous system disorders			
Migraine subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Lethargy			

subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	28 / 89 (31.46%) 37		
Dizziness subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Sciatica subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Syncope subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Eye disorders Eye inflammation subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Gastrointestinal disorders Angular cheilitis subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Abdominal pain subjects affected / exposed occurrences (all)	6 / 89 (6.74%) 6		
Abdominal discomfort			

subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	10 / 89 (11.24%)		
occurrences (all)	12		
Mouth ulceration			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	4 / 89 (4.49%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Dermatitis atopic			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Blister			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		

Acne			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Photodermatosis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Pain of skin			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Exostosis			

subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Fibromyalgia			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Rotator cuff syndrome			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	10 / 89 (11.24%)		
occurrences (all)	13		
Musculoskeletal discomfort			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Candida infection			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Ear infection staphylococcal			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Eye infection			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		

Otitis externa			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Laryngitis			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Impetigo			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Furuncle			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Pharyngitis streptococcal			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 89 (0.00%)		
occurrences (all)	0		
Staphylococcal skin infection			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		

Viral infection subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Metabolism and nutrition disorders			
Vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0		
Dehydration subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2020	The reason for this amendment was to make some minor corrections, remove the blood sample for cell mediated immunity (CMI) assessment at Visit 10 of proof of principle (PoP) phase to simplify study procedures, and to comply with selected recommendations from Center for Biologics Evaluation and Research (CBER). This protocol amendment 1 outlines also measures that may be applicable during special circumstances (e.g., COVID-19 pandemic), in order to protect participant's welfare and safety and promote data integrity.
09 April 2021	The main reasons for this protocol amendment have been to simplify the study procedures for the proof of principle (PoP) phase, including those related to the screening of subjects and to outline specific measures related to an emergency mass vaccination for an unforeseen public health threat (e.g.: a pandemic) that may be applicable during the subjects' participation in the study. Additionally, some minor corrections have been made as well.
16 June 2021	The sponsor is updating the clinical research phase of the study from Phase I to Phase I/II to account for the design of the study which, in its Proof of Principle epoch, aims to also generate evidence on the efficacy of the vaccine to prevent recurrences of Skin and Soft Tissue Infections due to Staphylococcus aureus in the target population.
30 November 2021	The aim of this protocol amendment is to facilitate the enrolment of subjects with S. aureus SSTIs for the PoP phase (Phase II) of the study, by extending the allowed upper age limit from 50 to 64 years, allowing enrolment of subjects with well-controlled type 2 diabetes mellitus and/or arterial hypertension, and extending the interval between S. aureus SSTI microbiological diagnosis and signature of the informed consent from 14 days to 30 days. In addition, correction of typographical error, minor edits for clarification, and the alignment of some sections to the current Company protocol template have also been made.
22 June 2022	The aim of this protocol amendment is to add that during study conduct a presentation of the placebo in a prefilled syringe (PFS) may be used. In addition, correction of typographical error, minor edits for clarification, and the alignment of some sections to the current Company protocol template have also been made.
06 October 2022	The aim of this protocol amendment is to ensure consistency across the different protocol sections related to the interim efficacy analysis, with reference to the possibility to continue the enrolment up to the planned number of events needed for the key efficacy endpoint evaluation (i.e. 27 events of recurrent S. aureus SSTI), and in case futility or efficacy criteria are met at the interim analysis based on 13 events of recurrent S. aureus SSTI. In addition, correction of typographical errors, and minor edits for clarification have been made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported