Clinical trial results:
A phase 2b, randomized, controlled, observer-blind, multi-center, non-inferiority immunogenicity and safety study of two formulations of GSK Biologicals' Meningococcal ACWY conjugate vaccine (GSK3536820A and Menveo) administered to healthy adults 18 to 40 years of age.

Summary

EudraCT number	2017-003692-61
Trial protocol	DE EE BE IT
Global end of trial date	22 September 2020

Results information

Result version number	v1 (current)
This version publication date	25 February 2021
First version publication date	25 February 2021

Trial information

Trial identification

Sponsor protocol code	205343

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GlaxoSmithKline, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 2089-904466, 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	27 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 January 2019
Global end of trial reached?	Yes
Global end of trial date	22 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate non-inferiority of the MenACWY liquid vaccine with approximately 30% Men A Free Saccharide (FS) to that of currently licensed MenACWY vaccine, as measured by the human serum bactericidal assay (hSBA) Geometric Mean Titers (GMTs) directed against N. meningitidis serogroup A at Day 29 after a single dose vaccination. Criterion to demonstrate non-inferiority: Non-inferiority will be concluded if the lower limit of the two-sided 95% confidence interval (CI) for the ratio of hSBA GMTs against serogroup A between the liquid formulation and the licensed formulation is greater than 0.5.

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes following the administration of the vaccine, with appropriate medical treatment readily available in case of anaphylaxis. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccine. Safety was monitored for 6 months after vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2018
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: 184
Country: Number of subjects enrolled	Belgium: 175
Country: Number of subjects enrolled	Canada: 285
Country: Number of subjects enrolled	Germany: 200
Country: Number of subjects enrolled	Italy: 152
Worldwide total number of subjects	996
EEA total number of subjects	527

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)	996
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrolment from 8 centers in Australia,2 in Belgium,10 in Canada,6 in Germany,4 in Italy.Planned age range in this study was 18-40 years.But 1 subject aged 44 years not meeting inclusion criteria was enrolled & vaccinated in GSK3536820A ACWY_Liq Group & therefore was considered for all analyses except per protocol set for immunogenicity analyses

Pre-assignment

Screening details:

Among 996 enrolled subjects,16 subjects did not receive any treatment and ICF documentation was not retrievable for 1 subject.

Pre-assignment period milestones

Number of subjects started	996
Number of subjects completed	979

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not receive any study treatment: 16
Reason: Number of subjects	ICF documentation not retrievable: 1

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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This was an observer blind study

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK3536820A ACWY_Liq Group

Arm description:

Healthy adults, 18 to 44 years of age, receiving at Day 1 a single dose of investigational MenACWY liquid vaccine (GSK3536820A) formulation with approximately 30% Men A FS.

Arm type	Experimental
Investigational medicinal product name	MenACWY liquid vaccine with approximately 30% MenA FS (GSK3536820A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose administered at Day 1, by intramuscular injection in the deltoid of the non-dominant arm

Arm title	ACWY Group

Arm description:

Healthy adults, 18 to 40 years of age, receiving at Day 1 a single dose of licensed GSK's MenACWY vaccine formulation (Menveo).

Arm type	Active comparator

Investigational medicinal product name	Licensed GSK MenACWY vaccine
Investigational medicinal product code	
Other name	Menveo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose administered at Day 1, by intramuscular injection in the deltoid of the non-dominant arm

Number of subjects in period 1[1]	GSK3536820A ACWY_Liq Group	ACWY Group
Started	490	489
Completed	486	484
Not completed	4	5
Consent withdrawn by subject	3	5
Lost to follow-up	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects reported in the baseline period are the number vaccinated and therefore differ from the worldwide enrolled number.

Baseline characteristics

Reporting groups	
Reporting group title	GSK3536820A ACWY_Liq Group
Reporting group description:	
Healthy adults, 18 to 44 years of age, receiving at Day 1 a single dose of investigational MenACWY liquid vaccine (GSK3536820A) formulation with approximately 30% Men A FS.	
Reporting group title	ACWY Group
Reporting group description:	
Healthy adults, 18 to 40 years of age, receiving at Day 1 a single dose of licensed GSK's MenACWY vaccine formulation (Menveo).	

Reporting group values	GSK3536820A ACWY_Liq Group	ACWY Group	Total
Number of subjects	490	489	979
Age categorical Units: Subjects			
Adults (18-64 years)	490	489	979
Age continuous Units: years			
arithmetic mean	31.7	31.9	
standard deviation	± 5.8	± 5.8	-
Sex: Female, Male Units: Participants			
Female	309	305	614
Male	181	184	365
Race/Ethnicity, Customized Units: Subjects			
American Indian Or Alaska Native	4	0	4
Asian	40	27	67
Black Or African American	4	8	12
Native Hawaiian Or Other Pacific Islander	2	2	4
Other	13	13	26
White	427	439	866

End points

End points reporting groups

Reporting group title	GSK3536820A ACWY_Liq Group
Reporting group description:	
Healthy adults, 18 to 44 years of age, receiving at Day 1 a single dose of investigational MenACWY liquid vaccine (GSK3536820A) formulation with approximately 30% Men A FS.	
Reporting group title	ACWY Group
Reporting group description:	
Healthy adults, 18 to 40 years of age, receiving at Day 1 a single dose of licensed GSK's MenACWY vaccine formulation (Menveo).	

Primary: Adjusted Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against N. meningitidis serogroup A for each vaccine group, and between-group ratios

End point title	Adjusted Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against N. meningitidis serogroup A for each vaccine group, and between-group ratios
End point description:	
hSBA titers against N.meningitidis serogroup A were calculated in terms of GMTs adjusted for pre-vaccination titer. Analysis was performed on the per protocol set for immunogenicity that includes subjects who received the vaccine, did not have any protocol deviation leading to exclusion, who were not excluded due to other reasons defined prior to unblinding or analysis and had available immuno data for any serogroup and time point considered.	
End point type	Primary
End point timeframe:	
At Day 29	

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	404		
Units: Titers				
geometric mean (confidence interval 95%)	185.16 (147.90 to 231.81)	211.33 (169.61 to 263.32)		

Statistical analyses

Statistical analysis title	hSBA GMT ratio for serogroup A at day 29
Statistical analysis description:	
To demonstrate non-inferiority of the investigational MenACWY liquid vaccine with approximately 30% Men A FS (GSK3536820A ACWY_Liq Group) to that of currently licensed MenACWY vaccine (ACWY Group), as measured by the adjusted human serum bactericidal assay (hSBA) Geometric Mean Titers (GMTs) directed against N. meningitidis serogroup A at Day 29 after a single dose vaccination	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	790

Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.2

Secondary: hSBA GMTs against each of the N.meningitidis serogroups A, C, W and Y for each vaccine group, and between-group ratios

End point title	hSBA GMTs against each of the N.meningitidis serogroups A, C, W and Y for each vaccine group, and between-group ratios

End point description:

hSBA titers were calculated in terms of GMTs, at Day 1 and Day 29, against each of the N. meningitidis serogroups A, C, W and Y. Analysis was performed on the per protocol set for immunogenicity that includes subjects who received the vaccine, did not have any protocol deviation leading to exclusion, who were not excluded due to other reasons defined prior to unblinding or analysis and had available immuno data for any serogroup and time point considered.

End point type	Secondary

End point timeframe:

At Day 1 and Day 29

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	459	467		
Units: Titers				
geometric mean (confidence interval 95%)				
Meningitis A, Day 1(N=446,446)	2.79 (2.52 to 3.10)	2.97 (2.68 to 3.29)		
Meningitis A, Day 29(N=386,404)	182.96 (145.11 to 230.68)	213.42 (170.11 to 267.77)		
Meningitis C, Day 1(N=459,467)	11.41 (9.81 to 13.27)	12.05 (10.38 to 14.00)		
Meningitis C, Day 29(N=437,441)	153.95 (115.03 to 206.04)	139.63 (104.56 to 186.47)		
Meningitis W, Day 1(N=455,457)	9.6 (8.05 to 11.45)	10.92 (9.16 to 13.02)		
Meningitis W, Day 29(N=445,443)	59.74 (47.67 to 74.86)	54.12 (43.17 to 67.86)		
Meningitis Y, Day 1(N=458,463)	4.14 (3.63 to 4.71)	4.75 (4.17 to 5.40)		
Meningitis Y, Day 29(N=452,455)	60.29 (48.67 to 74.68)	54.99 (44.44 to 68.06)		

Statistical analyses

Statistical analysis title	hSBA GMT ratio for serogroup C

Statistical analysis description:

To compare the immunogenicity of the investigational MenACWY liquid vaccine with approximately 30% Men A FS (GSK3536820A ACWY_Liq Group) and the currently licensed MenACWY vaccine (ACWY Group), as measured by the adjusted hSBA GMTs directed against N. meningitidis serogroup C at Day 29

Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	926
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.68

Statistical analysis title	hSBA GMT ratio for serogroup W

Statistical analysis description:

To compare the immunogenicity of the investigational MenACWY liquid vaccine with approximately 30% Men A FS (GSK3536820A ACWY_Liq Group) and the currently licensed MenACWY vaccine (ACWY Group), as measured by the adjusted hSBA GMTs directed against N. meningitidis serogroup W at Day 29

Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	926
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.58

Statistical analysis title	hSBA GMT ratio for serogroup Y

Statistical analysis description:

To compare the immunogenicity of the investigational MenACWY liquid vaccine with approximately 30% Men A FS (GSK3536820A ACWY_Liq Group) and the currently licensed MenACWY vaccine (ACWY Group), as measured by the adjusted hSBA GMTs directed against N. meningitidis serogroup Y at Day 29

Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	926
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.58

Secondary: Within-group Geometric Mean Ratios (GMRs) against each of the N.meningitidis serogroups A, C, W and Y

End point title	Within-group Geometric Mean Ratios (GMRs) against each of the N.meningitidis serogroups A, C, W and Y

End point description:

Within-group ratios of hSBA GMTs against each of the N.meningitidis serogroups A, C, W and Y at Day 29 compared to Day 1. Analysis was performed on the per protocol set for immunogenicity that includes subjects who received the vaccine, did not have any protocol deviation leading to exclusion, who were not excluded due to other reasons defined prior to unblinding or analysis and had available immuno data for any serogroup and time point considered.

End point type	Secondary

End point timeframe:

At Day 29

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	452	455		
Units: Ratio				
geometric mean (confidence interval 95%)				
Meningitis A(N=386,404)	65.24 (51.81 to 82.16)	73.01 (58.26 to 91.49)		
Meningitis C(N=437,441)	13.17 (10.30 to 16.84)	11.07 (8.68 to 14.13)		
Meningitis W(N=445,443)	6.1 (5.07 to 7.33)	4.8 (3.99 to 5.77)		
Meningitis Y(N=452,455)	14.64 (11.88 to 18.04)	11.48 (9.33 to 14.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with a ≥4 fold rise in hSBA antibody titers for each of the N.meningitidis serogroups A, C,W and Y for each vaccine group, and between-group differences

End point title	Percentages of subjects with a ≥4 fold rise in hSBA antibody titers for each of the N.meningitidis serogroups A, C,W and Y for each vaccine group, and between-group differences

End point description:

The percentages of subjects with a ≥ 4-fold rise in post-vaccination hSBA (at Day 29 compared to Day 1) and associated 2-sided 95% Clopper-Pearson CIs were computed by group and for each N. meningitidis serogroups A, C, W and Y. A 4-fold rise in the hSBA titers is defined as: for individuals, whose pre-vaccination titers are < the LOD (limit of detection), the post-vaccination titers must be ≥ 4-fold the LOD or ≥ the LLOQ (lower of limit of quantitation) whichever is greater; for individuals, whose pre-vaccination titers are ≥ the LOD and ≤ the LLOQ, the post-vaccination titers must be at least four times the LLOQ; for individuals whose pre-vaccination titers are > the LLOQ, the post-vaccination titers must be at least four times the pre-vaccination

End point type	Secondary

End point timeframe:

At Day 29

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	452	455		
Units: Percentages of subjects				
number (confidence interval 95%)				
Meningitis A(N=386,404)	79.8 (75.4 to 83.7)	83.7 (79.7 to 87.1)		
Meningitis C(N=437,441)	56.3 (51.5 to 61.0)	54.4 (49.6 to 59.1)		
Meningitis W(N=445,443)	44.7 (40.0 to 49.5)	40.2 (35.6 to 44.9)		
Meningitis Y(N=452,455)	63.3 (58.6 to 67.7)	58 (53.3 to 62.6)		

Statistical analyses

Statistical analysis title	Between-groups differences- Serogroup A

Statistical analysis description:

Between-group difference in percentage of subjects with a ≥ 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup A at Day 29.

Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	907
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects

Point estimate	-3.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	1.52

Statistical analysis title	Between-group differences- serogroup C
Statistical analysis description:	
Between-group difference in percentage of subjects with a ≥ 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup C at Day 29.	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	907
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	1.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	8.43

Statistical analysis title	Between-group differences- serogroup W
Statistical analysis description:	
Between-group difference in percentage of subjects with a ≥ 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup W at Day 29.	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	907
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	4.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.97
upper limit	11.01

Statistical analysis title	Between-group differences- serogroup Y
Statistical analysis description:	
Between-group difference in percentage of subjects with a ≥ 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup Y at Day 29.	

Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	907
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	5.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	11.57

Secondary: Percentages of subjects with hSBA titers ≥8 against each of the N. meningitidis serogroups A, C, W and Y for each vaccine group, and between-group differences

End point title	Percentages of subjects with hSBA titers ≥8 against each of the N. meningitidis serogroups A, C, W and Y for each vaccine group, and between-group differences

End point description:

For each vaccine group the percentage of subjects with hSBA titer ≥8, and its associated two-sided 95% Clopper-Pearson CIs were computed for each of the N. meningitidis serogroups A, C, W and Y. Analysis was performed on the per protocol set for immunogenicity that includes subjects who received the vaccine, did not have any protocol deviation leading to exclusion, who were not excluded due to other reasons defined prior to unblinding or analysis and had available immuno data for any serogroup and time point considered.

End point type	Secondary

End point timeframe:

At Day 1 and Day 29

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	460	467		
Units: Percentages of subjects				
number (confidence interval 95%)				
Meningitis A, Day 1(N=446,446)	8.7 (6.3 to 11.8)	11.2 (8.4 to 14.5)		
Meningitis A, Day 29(N=406, 428)	82.8 (78.7 to 86.3)	86.4 (82.8 to 89.5)		
Meningitis C, Day 1(N=459,467)	53.8 (49.1 to 58.4)	54.4 (49.7 to 59.0)		
Meningitis C, Day 29(N=443,446)	74.5 (70.2 to 78.5)	74.9 (70.6 to 78.8)		
Meningitis W, Day 1(N=455,457)	39.8 (35.3 to 44.4)	45.7 (41.1 to 50.4)		
Meningitis W, Day 29(N=454,457)	73.3 (69.0 to 77.4)	73.1 (68.8 to 77.1)		
Meningitis Y, Day 1(N=458,463)	22.7 (18.9 to 26.8)	25.5 (21.6 to 29.7)		

Meningitis Y, Day 29(N=460,463)	77.2 (73.1 to 80.9)	76 (71.9 to 79.8)		

Statistical analyses

Statistical analysis title	Between-group differences- Serogroup A, Day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup A at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-2.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.47
upper limit	1.49

Statistical analysis title	Between-group differences-Serogroup C, day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup C at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.99
upper limit	5.83

Statistical analysis title	Between-group differences-Serogroup W, day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup W at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group

Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-5.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.33
upper limit	0.47

Statistical analysis title	Between-group differences-Serogroup Y, day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup Y at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	2.76

Statistical analysis title	Between-group differences-Serogroup A, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup A at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-3.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.65
upper limit	1.21

Statistical analysis title	Between-group differences-Serogroup C, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup C at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.12
upper limit	5.33

Statistical analysis title	Between-group differences-Serogroup W, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup W at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.49
upper limit	6.02

Statistical analysis title	Between-group differences-Serogroup Y, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥8 for the N. meningitidis serogroup Y at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method

Parameter estimate	Difference in percentage of subjects
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.33
upper limit	6.62

Secondary: Percentages of subjects with hSBA titers ≥LLOQ against each of the N. meningitidis serogroups A, C, W and Y for each vaccine group, and between-group differences

End point title	Percentages of subjects with hSBA titers ≥LLOQ against each of the N. meningitidis serogroups A, C, W and Y for each vaccine group, and between-group differences

End point description:

For each vaccine group the percentage of subjects with hSBA titer ≥LLOQ, and its associated two-sided 95% Clopper-Pearson CIs were computed for each of the N. meningitidis serogroups A, C, W and Y. Analysis was performed on the per protocol set for immunogenicity that includes subjects who received the vaccine, did not have any protocol deviation leading to exclusion, who were not excluded due to other reasons defined prior to unblinding or analysis and had available immuno data for any serogroup and time point considered.

End point type	Secondary

End point timeframe:

At Day 1 and Day 29

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	460	467		
Units: Percentages of subjects				
number (confidence interval 95%)				
Meningitis A, Day 1(N=446,446)	10.5 (7.8 to 13.8)	13.5 (10.4 to 17.0)		
Meningitis A, Day 29(N=406,428)	82.8 (78.7 to 86.3)	86.7 (83.1 to 89.8)		
Meningitis C, Day 1(N=459,467)	61.2 (56.6 to 65.7)	62.3 (57.7 to 66.7)		
Meningitis C, Day 29(N=443,446)	76.5 (72.3 to 80.4)	76.5 (72.2 to 80.3)		
Meningitis W, Day 1(N=455,457)	41.3 (36.8 to 46.0)	47.3 (42.6 to 52.0)		
Meningitis W, Day 29(N=454,457)	73.3 (69.0 to 77.4)	73.5 (69.2 to 77.5)		
Meningitis Y, Day 1(N=458,463)	23.8 (20.0 to 28.0)	26.3 (22.4 to 30.6)		
Meningitis Y, Day 29(N=460, 463)	77.8 (73.7 to 81.5)	77.3 (73.2 to 81.1)		

Statistical analyses

Statistical analysis title	Between-group differences-Serogroup A, day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup A at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.24
upper limit	1.37

Statistical analysis title	Between-group differences-Serogroup C, day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup C at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.34
upper limit	5.16

Statistical analysis title	Between-group differences-Serogroup W, day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup W at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-5.95
Confidence interval	

level	95 %
sides	2-sided
lower limit	-12.35
upper limit	0.5

Statistical analysis title	Between-group differences-Serogroup Y, day 1
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup Y at Day 1	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.15
upper limit	3.06

Statistical analysis title	Between-group differences-Serogroup A, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup A at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-3.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.87
upper limit	0.96

Statistical analysis title	Between-group differences-Serogroup C, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup C at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927

Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.52
upper limit	5.65

Statistical analysis title	Between-group differences-Serogroup W, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup W at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.92
upper limit	5.57

Statistical analysis title	Between-group differences-Serogroup Y, day 29
Statistical analysis description:	
Between-group difference in percentages of subjects with hSBA titer ≥LLOQ for the N. meningitidis serogroup Y at Day 29	
Comparison groups	GSK3536820A ACWY_Liq Group v ACWY Group
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen and Nurminen score method
Parameter estimate	Difference in percentage of subjects
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.89
upper limit	5.9

Secondary: Number of subjects reported with solicited local and systemic AEs

End point title	Number of subjects reported with solicited local and systemic AEs

End point description:

Number of subjects with solicited local and systemic AEs during the 7-days period (including the day of vaccination) after the vaccination. Analysis was performed on the solicited safety set that includes all enrolled subjects who received a study vaccination and reported any solicited adverse events data for the defined period.

End point type	Secondary

End point timeframe:

From Day 1 (6 hours) to Day 7 after vaccination

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	489	487		
Units: Participants				
Erythema	28	28		
Induration	25	24		
Pain	200	182		
Arthralgia	43	46		
Chills	42	40		
Fatigue	159	159		
Fever (Temperature >= 38 C)	7	10		
Headache	158	165		
Loss of Appetite	31	40		
Myalgia	58	58		
Nausea	49	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with other indicators of reactogenicity

End point title	Number of subjects reported with other indicators of reactogenicity

End point description:

Number of subjects reporting other indicators of reactogenicity such as use of analgesics/antipyretics within 7 days after vaccination. Analysis was performed on the solicited safety set that includes all enrolled subjects who received a study vaccination and reported any indicators of reactogenicity data for the defined period.

End point type	Secondary

End point timeframe:

From Day 1 to Day 7 after vaccination

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	489	487		
Units: Participants				
Analgesic/Antipyretic Prevention, Yes	36	40		
Analgesic/Antipyretic Prevention, No	453	447		
Analgesic/Antipyretic Treatment, Yes	80	79		
Analgesic/Antipyretic Treatment, No	409	408		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with any unsolicited AEs within 29 days after vaccination

End point title	Number of subjects reported with any unsolicited AEs within 29 days after vaccination

End point description:

An AE is defined as any untoward medical occurrence in a subject or clinical investigation subject administered with a pharmaceutical product at any dose that does not necessarily have to have a causal relationship with this treatment. Analysis was performed on the unsolicited safety set that includes all enrolled subjects who received a study vaccination and reported unsolicited adverse events data for the defined period.

End point type	Secondary

End point timeframe:

From Day 1 to Day 29 after vaccination

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	489	489		
Units: Participants	117	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with AEs leading to withdrawal, medically attended AEs and serious adverse events (SAEs)

End point title	Number of subjects reported with AEs leading to withdrawal, medically attended AEs and serious adverse events (SAEs)

End point description:

Medically attended AEs are defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Any medically attended AE(s) is occurrence of any medically attended AE(s) regardless of

intensity grade or relation to vaccination. Serious adverse event is any congenital anomaly/birth defect in the offspring of a study subject or any untoward medical occurrence that results in death or life threatening or requires hospitalization or results in disability or incapacity. Analysis was performed on the unsolicited safety set that includes all enrolled subjects who received a study vaccination and reported any adverse events data in the defined period.

End point type	Secondary

End point timeframe:

From Day 1 to Day 181 (during the entire study period)

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	489	489		
Units: Participants				
Aes leading to withdrawal	0	0		
MAEs	79	84		
SAEs	6	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with any unsolicited adverse events (AEs) within 30 minutes after vaccination

End point title	Number of subjects reported with any unsolicited adverse events (AEs) within 30 minutes after vaccination

End point description:

An AE is defined as any untoward medical occurrence in a subject or clinical investigation subject administered with a pharmaceutical product at any dose that does not necessarily have to have a causal relationship with this treatment. Analysis was performed on the unsolicited safety set that includes all enrolled subjects who received a study vaccination and reported unsolicited adverse events data for the defined period.

End point type	Secondary

End point timeframe:

Within 30 minutes after vaccination at Day 1

End point values	GSK3536820A ACWY_Liq Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	489	489		
Units: Participants	5	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs were collected from Day 1 to Day 7 after vaccination and Unsolicited AEs from Day 1 to Day 29 after vaccination. SAEs were collected from Day 1 to Day 181 (during the entire study period)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	GSK3536820A ACWY_Liq Group

Reporting group description:

Healthy adults, 18 to 44 years of age, receiving at Day 1 a single dose of investigational MenACWY liquid vaccine (GSK3536820A) formulation with approximately 30% Men A FS.

Reporting group title	ACWY Group

Reporting group description:

Healthy adults, 18 to 40 years of age, receiving at Day 1 a single dose of licensed GSK's MenACWY vaccine formulation (Menveo).

Serious adverse events	GSK3536820A ACWY_Liq Group	ACWY Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 490 (1.22%)	9 / 489 (1.84%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine cancer			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hemiplegic migraine			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous incomplete			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Suicide attempt			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Dengue fever			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GSK3536820A ACWY_Liq Group	ACWY Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	336 / 490 (68.57%)	335 / 489 (68.51%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Benign breast neoplasm			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Administration site joint pain			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	160 / 490 (32.65%)	162 / 489 (33.13%)	
occurrences (all)	163	163	
Chills			
subjects affected / exposed	43 / 490 (8.78%)	40 / 489 (8.18%)	
occurrences (all)	44	40	
Feeling abnormal			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Feeling hot			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
Influenza like illness			
subjects affected / exposed	5 / 490 (1.02%)	2 / 489 (0.41%)	
occurrences (all)	5	2	
Injection site bruising			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
Injection site erythema			
subjects affected / exposed	30 / 490 (6.12%)	31 / 489 (6.34%)	
occurrences (all)	31	32	
Injection site haemorrhage			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Injection site induration			

subjects affected / exposed	26 / 490 (5.31%)	25 / 489 (5.11%)	
occurrences (all)	27	25	
Injection site joint pain			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Injection site oedema			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	200 / 490 (40.82%)	184 / 489 (37.63%)	
occurrences (all)	204	184	
Injection site pruritus			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Injection site rash			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Injection site swelling			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
Malaise			
subjects affected / exposed	2 / 490 (0.41%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Injection site warmth			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Mass			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	10 / 490 (2.04%)	10 / 489 (2.04%)	
occurrences (all)	11	10	
Vaccination site induration			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Vaccination site paraesthesia			

subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Disorientation			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	3 / 490 (0.61%)	0 / 489 (0.00%)	
occurrences (all)	4	0	
Panic attack			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 490 (0.41%)	1 / 489 (0.20%)	
occurrences (all)	2	1	
Menorrhagia			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Ovarian cyst			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			

subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	2 / 490 (0.41%)	1 / 489 (0.20%)	
occurrences (all)	2	1	
Post-traumatic pain			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	1 / 490 (0.20%)	2 / 489 (0.41%)	
occurrences (all)	1	2	
Skin laceration			
subjects affected / exposed	2 / 490 (0.41%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Bronchospasm			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	3 / 490 (0.61%)	1 / 489 (0.20%)	
occurrences (all)	3	1	
Dyspnoea			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	7 / 490 (1.43%)	2 / 489 (0.41%)	

occurrences (all)	7	2	
Rhinorrhoea			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 490 (0.20%)	3 / 489 (0.61%)	
occurrences (all)	1	4	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 490 (0.00%)	2 / 489 (0.41%)	
occurrences (all)	0	2	
Dizziness			
subjects affected / exposed	4 / 490 (0.82%)	1 / 489 (0.20%)	
occurrences (all)	4	1	
Dysgeusia			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	162 / 490 (33.06%)	171 / 489 (34.97%)	
occurrences (all)	167	183	
Loss of consciousness			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Migraine with aura			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Presyncope			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	

Eye disorders			
Eye pain			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			
subjects affected / exposed	2 / 490 (0.41%)	1 / 489 (0.20%)	
occurrences (all)	2	1	
Abdominal pain lower			
subjects affected / exposed	0 / 490 (0.00%)	2 / 489 (0.41%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	2 / 490 (0.41%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Dental caries			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 490 (0.41%)	2 / 489 (0.41%)	
occurrences (all)	2	2	
Dyspepsia			
subjects affected / exposed	2 / 490 (0.41%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Food poisoning			

subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Inguinal hernia			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	51 / 490 (10.41%)	51 / 489 (10.43%)	
occurrences (all)	52	52	
Stomatitis			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 490 (0.20%)	2 / 489 (0.41%)	
occurrences (all)	1	2	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Dermal cyst			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	

occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Rash pruritic			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Sensitive skin			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	43 / 490 (8.78%)	49 / 489 (10.02%)	
occurrences (all)	44	49	
Back pain			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
Bursitis			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Joint stiffness			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	59 / 490 (12.04%)	58 / 489 (11.86%)	
occurrences (all)	59	58	

Myosclerosis			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	2 / 490 (0.41%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
Rotator cuff syndrome			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Synovitis			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	31 / 490 (6.33%)	41 / 489 (8.38%)	
occurrences (all)	31	42	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 490 (0.20%)	2 / 489 (0.41%)	
occurrences (all)	1	2	
Candida infection			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
Cellulitis			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Cellulitis orbital			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	2 / 490 (0.41%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Diarrhoea infectious			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	

occurrences (all)	1	0	
Erysipelas			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	3 / 490 (0.61%)	0 / 489 (0.00%)	
occurrences (all)	3	0	
Gastroenteritis viral			
subjects affected / exposed	0 / 490 (0.00%)	2 / 489 (0.41%)	
occurrences (all)	0	2	
Gastrointestinal infection			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Infected cyst			
subjects affected / exposed	2 / 490 (0.41%)	0 / 489 (0.00%)	
occurrences (all)	2	0	
Influenza			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	2 / 490 (0.41%)	1 / 489 (0.20%)	
occurrences (all)	2	1	
Localised infection			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	11 / 490 (2.24%)	10 / 489 (2.04%)	
occurrences (all)	11	10	
Onychomycosis			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	

occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	2 / 490 (0.41%)	2 / 489 (0.41%)	
occurrences (all)	2	2	
Pneumonia			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Post procedural infection			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 490 (0.20%)	0 / 489 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 490 (0.20%)	6 / 489 (1.23%)	
occurrences (all)	1	6	
Sinusitis			
subjects affected / exposed	0 / 490 (0.00%)	4 / 489 (0.82%)	
occurrences (all)	0	4	
Streptococcal infection			
subjects affected / exposed	1 / 490 (0.20%)	1 / 489 (0.20%)	
occurrences (all)	1	1	
Tonsillitis			
subjects affected / exposed	2 / 490 (0.41%)	1 / 489 (0.20%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	10 / 490 (2.04%)	6 / 489 (1.23%)	
occurrences (all)	10	6	
Urinary tract infection			
subjects affected / exposed	0 / 490 (0.00%)	1 / 489 (0.20%)	
occurrences (all)	0	1	
Viral infection			
subjects affected / exposed	0 / 490 (0.00%)	2 / 489 (0.41%)	
occurrences (all)	0	2	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 490 (0.41%)	2 / 489 (0.41%)	

occurrences (all)	2	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 January 2018	-Two similar exclusion criteria combined into a single criterion -Clarification of immunogenicity endpoints that will be included in a sub group analysis -Editorial changes to the protocol
15 March 2018	Intensity scales for solicited AEs were updated to correct the intensity scores of some of the AEs solicited. Redness/ swelling changed to erythema/induration, in line with local AEs solicited.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported