



Clinical trial results:

A phase 2b, randomized, controlled, observer-blind, multi-center study to evaluate safety and immunogenicity of different formulations of GSK Biologicals' Meningococcal ACWY conjugate vaccine (GSK3536820A and Menveo) administered to healthy adolescents and young adults 10 to 40 years of age.

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2017-003456-23 |
| Trial protocol | EE FI ES FR Outside EU/EEA |
| Global end of trial date | 22 October 2020 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 05 March 2021 |
| First version publication date | 05 March 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 207467 |
|-----------------------|--------|

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? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 10 December 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 July 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 October 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 product aged for approximately 24 months to that of MenACWY vaccine, as measured by hSBA GMTs directed against N. meningitidis serogroup A at Day 29 after a single dose vaccination. Criterion: Non-inferiority will be concluded if lower limit of the 2-sided 95% CI for ratio of hSBA GMTs against serogroup A between the MenACWY liquid vaccine aged for approximately 24 months and MenACWY vaccine is greater than 0.5.
- To demonstrate non-inferiority of the MenACWY liquid vaccine aged for approximately 30 months to that of MenACWY vaccine, as measured by hSBA GMTs directed against N. meningitidis serogroup A at Day 29 after a single dose vaccination. Criterion: Non-inferiority will be concluded if lower limit of the 2-sided 95% CI for ratio of hSBA GMTs against serogroup A between the MenACWY liquid vaccine aged for approximately 30 months and the MenACWY vaccine 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 have 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 | 30 August 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 | Brazil: 217 |
| Country: Number of subjects enrolled | Estonia: 176 |
| Country: Number of subjects enrolled | Finland: 202 |
| Country: Number of subjects enrolled | France: 155 |
| Country: Number of subjects enrolled | Mexico: 135 |
| Country: Number of subjects enrolled | Russian Federation: 267 |
| Country: Number of subjects enrolled | South Africa: 119 |
| Country: Number of subjects enrolled | Spain: 306 |
| Country: Number of subjects enrolled | Turkey: 130 |
| Worldwide total number of subjects | 1707 |
| EEA total number of subjects | 839 |

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) | 274 |
| Adolescents (12-17 years) | 417 |
| Adults (18-64 years) | 1016 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Enrollment was defined with 2 parallel groups per phase, in a 2-phase staggered design: both experimental groups subjects receiving respectively investigational vaccine aged for approximately 24 months in phase 1, and same vaccine aged for approximately 30 months in phase 2. Both comparator groups subjects receiving not aged licensed vaccine.

Pre-assignment

Screening details:

Out of the 1707 subjects enrolled in the study (inclusive of phase 1 and 2), only 1690 were exposed to the vaccination. Out of the 17 subjects excluded from study, 11 were not randomized, 5 were not administered any study treatment, 1 did not sign the informed consent form.

Pre-assignment period milestones

| | |
|------------------------------|------|
| Number of subjects started | 1707 |
| Number of subjects completed | 1690 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|-------------------------------------|
| Reason: Number of subjects | Not randomized: 11 |
| Reason: Number of subjects | Treatment not administered: 5 |
| Reason: Number of subjects | Informed consent form not signed: 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, Carer, Data analyst, Assessor |

Blinding implementation details:

This was an observer blind study

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | GSK3536820A ACWY_Liq24 Group |

Arm description:

Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 24 months, at Day 1 in the Study Phase1

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MenACWY liquid |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose administered on day 1 to all subjects in the experimental group

| | |
|------------------|--------------|
| Arm title | ACWY_1 Group |
|------------------|--------------|

Arm description:

Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase1.

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|--|
| Investigational medicinal product name | MenACWY |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose administered on day 1 to all subjects in the comparator group

| | |
|------------------|------------------------------|
| Arm title | GSK3536820A ACWY_Liq30 Group |
|------------------|------------------------------|

Arm description:

Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 30 months, at Day 1 in the Study Phase 2.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MenACWY liquid |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose administered on day 1 to all subjects in the experimental group

| | |
|------------------|--------------|
| Arm title | ACWY_2 Group |
|------------------|--------------|

Arm description:

Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase 2.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | MenACWY |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose administered on day 1 to all subjects in the comparator group

| Number of subjects in period 1^[1] | GSK3536820A ACWY_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group |
|---|------------------------------|--------------|------------------------------|
| Started | 420 | 424 | 427 |
| Completed | 419 | 424 | 423 |
| Not completed | 1 | 0 | 4 |
| Consent withdrawn by subject | - | - | 1 |
| Unknown reason | - | - | 2 |
| Lost to follow-up | 1 | - | 1 |

| Number of subjects in period 1^[1] | ACWY_2 Group |
|---|--------------|
| Started | 419 |
| Completed | 418 |
| Not completed | 1 |
| Consent withdrawn by subject | - |

| | |
|-------------------|---|
| Unknown reason | - |
| 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: Number of subjects reported in the baseline period are the actual number of subjects who were vaccinated, as compared to the number enrolled (started) in the study.

Baseline characteristics

Reporting groups

| | |
|------------------------------|---|
| Reporting group title | GSK3536820A ACWY_Liq24 Group |
| Reporting group description: | Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 24 months, at Day 1 in the Study Phase1 |
| Reporting group title | ACWY_1 Group |
| Reporting group description: | Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase1. |
| Reporting group title | GSK3536820A ACWY_Liq30 Group |
| Reporting group description: | Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 30 months, at Day 1 in the Study Phase 2. |
| Reporting group title | ACWY_2 Group |
| Reporting group description: | Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase 2. |

| Reporting group values | GSK3536820A ACWY_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group |
|------------------------|---------------------------------|--------------|---------------------------------|
| Number of subjects | 420 | 424 | 427 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|----------------------------------|-------|-------|-------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 22.5 | 22.2 | 22.3 |
| standard deviation | ± 9.4 | ± 9.6 | ± 9.8 |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 232 | 242 | 259 |
| Male | 188 | 182 | 168 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian Or Alaska Native | 0 | 1 | 1 |
| Asian | 4 | 4 | 2 |
| Black Or African American | 26 | 22 | 30 |
| Other | 58 | 54 | 83 |
| White | 332 | 343 | 311 |

| Reporting group values | ACWY_2 Group | Total | |
|------------------------|--------------|-------|--|
| Number of subjects | 419 | 1690 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|-----------------|------|--|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 22.0 | | |

| | | | |
|--------------------|-------|---|--|
| standard deviation | ± 9.3 | - | |
|--------------------|-------|---|--|

| | | | |
|----------------------------------|-----|------|--|
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 228 | 961 | |
| Male | 191 | 729 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| American Indian Or Alaska Native | 2 | 4 | |
| Asian | 3 | 13 | |
| Black Or African American | 26 | 104 | |
| Other | 84 | 279 | |
| White | 304 | 1290 | |

End points

End points reporting groups

| | |
|---|------------------------------|
| Reporting group title | GSK3536820A ACWY_Liq24 Group |
| Reporting group description: Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 24 months, at Day 1 in the Study Phase1 | |
| Reporting group title | ACWY_1 Group |
| Reporting group description: Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase1. | |
| Reporting group title | GSK3536820A ACWY_Liq30 Group |
| Reporting group description: Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 30 months, at Day 1 in the Study Phase 2. | |
| Reporting group title | ACWY_2 Group |
| Reporting group description: Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase 2. | |

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 are calculated in terms of GMTs adjusted for pre-vaccination titer. Analysis is 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|--|------------------------------|---------------------------|------------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 363 | 373 | 356 | 349 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | 386.66 (319.47 to 467.97) | 318.34 (264.14 to 383.67) | 387.06 (322.72 to 464.24) | 348.89 (290.09 to 419.61) |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Non-inferiority-MenACWYliq24 vs MenACWY |
| Statistical analysis description: | |
| To demonstrate non-inferiority of the MenACWY liquid vaccine aged for approximately 24 months to that of currently licensed MenACWY vaccine, as measured by the adjusted hSBA GMTs directed against N. meningitidis serogroup A at Day 29 after a single dose vaccination | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 736 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 1.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.94 |
| upper limit | 1.57 |

| | |
|--|---|
| Statistical analysis title | Non-inferiority-MenACWYliq30 vs MenACWY |
| Statistical analysis description: | |
| To demonstrate non-inferiority of the MenACWY liquid vaccine aged for approximately 30 months to that of currently licensed MenACWY vaccine, as measured by the adjusted hSBA GMTs directed against N. meningitidis serogroup A at Day 29 after a single dose vaccination. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.87 |
| upper limit | 1.42 |

| | |
|---|---|
| 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 serogroup A, C, W and Y. Analysis is 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|---|------------------------------------|------------------------------|------------------------------------|------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 394 | 398 | 395 | 392 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Meningitis A,Day 1(N=381,389,377,374) | 3.01 (2.69 to 3.36) | 2.91 (2.60 to 3.24) | 3.34 (2.94 to 3.79) | 3.16 (2.78 to 3.59) |
| Meningitis A,Day 29(N=363,373,356,349) | 388.53 (320.61 to 470.84) | 319.06 (264.39 to 385.03) | 394.16 (326.72 to 475.50) | 349 (288.45 to 422.27) |
| Meningitis C,Day 1(N=394,395,395,392) | 8.59 (7.40 to 9.98) | 7.06 (6.09 to 8.20) | 9.05 (7.77 to 10.53) | 8.7 (7.46 to 10.14) |
| Meningitis C,Day 29(N=385,377,376,377) | 143.69 (109.13 to 189.20) | 157.74 (119.39 to 208.42) | 244.44 (182.20 to 327.96) | 208.34 (154.96 to 280.11) |
| Meningitis W,Day 1(N=379,396,382,376) | 6.23 (5.17 to 7.50) | 5.8 (4.83 to 6.95) | 5.69 (4.75 to 6.82) | 5.74 (4.78 to 6.90) |
| Meningitis W,Day 29(N=372,388,374,366) | 62.73 (49.93 to 78.81) | 63.92 (51.11 to 79.94) | 80.51 (64.66 to 100.24) | 73.08 (58.45 to 91.36) |
| Meningitis Y,Day 1(N=390,398,391,385) | 4.39 (3.78 to 5.10) | 4.21 (3.63 to 4.89) | 4.14 (3.58 to 4.79) | 4.19 (3.62 to 4.86) |
| Meningitis Y,Day 29(N=379,390,386,377) | 116.42 (94.03 to 144.15) | 105.11 (85.17 to 129.71) | 112.95 (91.55 to 139.34) | 118.04 (95.27 to 146.25) |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Serogroup C-Day 29,ACWYliq24 versus ACWY |
| Statistical analysis description: | |
| Between-groups ratio of adjusted hSBA GMTs and its 95% CI, between vaccine groups GSK3536820A ACWY_Liq24 and ACWY_1, at Day 29 against serogroup C | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 1.19 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup W-Day 29,ACWYliq24 versus ACWY |
|-----------------------------------|--|

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|--|---|
| Statistical analysis description: | |
| Between-groups ratio of adjusted hSBA GMTs and its 95% CI, between vaccine groups GSK3536820A ACWY_Liq24 and ACWY_1, at Day 29 against serogroup W | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 0.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 1.24 |

| | |
|--|---|
| Statistical analysis title | Serogroup Y-Day 29,ACWYliq24 versus ACWY |
| Statistical analysis description: | |
| Between-groups ratio of adjusted hSBA GMTs and its 95% CI, between vaccine groups GSK3536820A ACWY_Liq24 and ACWY_1, at Day 29 against serogroup Y | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 1.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 1.44 |

| | |
|--|---|
| Statistical analysis title | Serogroup C-Day 29,ACWYLi30 versus ACWY |
| Statistical analysis description: | |
| Between-groups ratio of adjusted hSBA GMTs and its 95% CI, between vaccine groups GSK3536820A ACWY_Liq30 and ACWY_2, at Day 29 against serogroup C | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 1.14 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 1.64 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup W-Day 29,ACWYliq30 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-groups ratio of adjusted hSBA GMTs and its 95% CI, between vaccine groups GSK3536820A ACWY_Liq30 and ACWY_2, at Day 29 against serogroup W

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 1.45 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup Y-Day 29,ACWYliq30 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-groups ratio of adjusted hSBA GMTs and its 95% CI, between vaccine groups GSK3536820A ACWY_Liq30 and ACWY_2, at Day 29 against serogroup Y

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANCOVA |
| Parameter estimate | GMT ratio |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 1.26 |

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

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

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 is 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|--|------------------------------------|--------------------------|------------------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 385 | 390 | 386 | 377 |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Meningitis A(N=363,373,356,349) | 130.33 (105.49 to 161.02) | 108.39 (88.14 to 133.30) | 114.66 (93.75 to 140.22) | 106.79 (87.05 to 131.01) |
| Meningitis C(N=385,377,376,377) | 17.01 (13.00 to 22.25) | 21.68 (16.52 to 28.46) | 26.69 (20.22 to 35.22) | 23.85 (18.04 to 31.54) |
| Meningitis W(N=372,388,374,366) | 9.81 (7.84 to 12.27) | 10.77 (8.65 to 13.41) | 13.8 (11.08 to 17.19) | 12.48 (9.98 to 15.61) |
| Meningitis Y(N=379,390,386,377) | 26.53 (21.14 to 33.28) | 25.23 (20.18 to 31.54) | 27.18 (21.66 to 34.10) | 28.49 (22.60 to 35.92) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with ≥ 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 ≥ 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 are computed by group and 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 \geq the LLOQ (lower limit of quantitation) whichever is greater; - for individuals whose pre-vaccination titers are \geq the LOD and \leq 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 titer. Analysis is performed on the per protocol set for immunogenicity.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 29

| End point values | GSK3536820A ACWY_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|----------------------------------|------------------------------------|---------------------------|------------------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 385 | 390 | 386 | 377 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Meningitis A(N=363,373,356,349) | 92.29 (89.04 to 94.81) | 90.08 (86.59 to 92.92) | 91.57 (88.19 to 94.24) | 91.69 (88.28 to 94.36) |
| Meningitis C(N=385,377,376,377) | 62.34 (57.29 to 67.20) | 64.46 (59.39 to 69.29) | 72.61 (67.80 to 77.05) | 69.76 (64.85 to 74.36) |
| Meningitis W(N=372,388,374,366) | 59.41 (54.23 to 64.44) | 60.57 (55.51 to 65.46) | 66.58 (61.55 to 71.34) | 62.57 (57.39 to 67.54) |
| Meningitis Y(N=379,390,386,377) | 71.77 (66.95 to 76.25) | 73.33 (68.65 to 77.66) | 74.35 (69.69 to 78.64) | 77.19 (72.62 to 81.33) |

Statistical analyses

| Statistical analysis title | Serogroup A-ACWY Liq24 versus ACWY |
|---|---|
| Statistical analysis description: Between-group difference in percentage of subjects with a \geq 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup A at Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 775 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 2.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.94 |
| upper limit | 6.4 |

| Statistical analysis title | Serogroup C-ACWY Liq24 versus ACWY |
|---|---|
| Statistical analysis description: Between-group difference in percentage of subjects with a \geq 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup C at Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 775 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -2.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.94 |
| upper limit | 4.72 |

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Serogroup W-ACWY Liq24 versus ACWY |
|-----------------------------------|------------------------------------|

Statistical analysis description:

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

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 775 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -1.16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.11 |
| upper limit | 5.8 |

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Serogroup Y-ACWY Liq24 versus ACWY |
|-----------------------------------|------------------------------------|

Statistical analysis description:

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

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 775 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -1.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.88 |
| upper limit | 4.74 |

| | |
|---|---|
| Statistical analysis title | Serogroup A-ACWY Liq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentage of subjects with a \geq 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup A at Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 763 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.29 |
| upper limit | 4.07 |

| | |
|---|---|
| Statistical analysis title | Serogroup C-ACWY Liq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentage of subjects with a \geq 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup C at Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 763 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 2.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.63 |
| upper limit | 9.3 |

| | |
|---|---|
| Statistical analysis title | Serogroup W-ACWY Liq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentage of subjects with a \geq 4-fold rise in post-vaccination hSBA for N. meningitidis serogroup W at Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 763 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 4.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.89 |
| upper limit | 10.88 |

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | Serogroup Y-ACWY Liq30 versus ACWY |
|-----------------------------------|------------------------------------|

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_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 763 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -2.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.91 |
| upper limit | 3.26 |

Secondary: Percentages of subjects with hSBA antibody 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 antibody 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 are computed for each of the N. meningitidis serogroups A, C, W and Y. Analysis is 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|---|------------------------------------|---------------------------|------------------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 394 | 398 | 395 | 392 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Meningitis A,Day 1(N=381,389,377,374) | 12.07 (8.98 to 15.77) | 10.28 (7.45 to 13.74) | 13.53 (10.24 to 17.40) | 12.03 (8.91 to 15.77) |
| Meningitis A,Day 29(N=378,384,377,367) | 93.65 (90.70 to 95.89) | 92.19 (89.03 to 94.67) | 93.37 (90.37 to 95.66) | 94.01 (91.06 to 96.21) |
| Meningitis C,Day 1(N=394,395,395,392) | 48.48 (43.44 to 53.53) | 41.52 (36.61 to 46.55) | 50.63 (45.59 to 55.67) | 50.26 (45.19 to 55.31) |
| Meningitis C,Day 29(N=388,382,379,379) | 77.58 (73.10 to 81.63) | 78.01 (73.52 to 82.06) | 84.17 (80.10 to 87.70) | 82.85 (78.67 to 86.51) |
| Meningitis W,Day 1(N=379,396,382,376) | 31.66 (27.01 to 36.61) | 28.54 (24.14 to 33.26) | 28.8 (24.30 to 33.62) | 30.05 (25.46 to 34.96) |
| Meningitis W,Day 29(N=389,392,389,384) | 79.43 (75.07 to 83.34) | 80.87 (76.62 to 84.64) | 85.86 (82.00 to 89.17) | 81.77 (77.54 to 85.50) |
| Meningitis Y,Day 1(N=390,398,391,385) | 22.82 (18.75 to 27.31) | 21.86 (17.90 to 26.25) | 21.48 (17.51 to 25.89) | 22.34 (18.27 to 26.83) |
| Meningitis Y,Day 29(N=384,392,393,386) | 87.5 (83.77 to 90.64) | 85.46 (81.57 to 88.80) | 88.04 (84.42 to 91.08) | 87.56 (83.85 to 90.69) |

Statistical analyses

| Statistical analysis title | Serogroup A-Day1,ACWYliq24 versus ACWY |
|--|---|
| Statistical analysis description: | |
| Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup A on Day 1. | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.69 |
| upper limit | 6.32 |

| Statistical analysis title | Serogroup C-Day1,ACWYliq24 versus ACWY |
|--|---|
| Statistical analysis description: | |
| Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup C on Day 1. | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 6.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.01 |
| upper limit | 13.84 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup W-Day1,ACWYliq24 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup W on Day 1.

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 3.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.33 |
| upper limit | 9.58 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup Y-Day1,ACWYliq24 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup Y on Day 1.

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.86 |
| upper limit | 6.8 |

| | |
|--|---|
| Statistical analysis title | Serogroup A-Day29,ACWYliq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup A on Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.24 |
| upper limit | 5.22 |

| | |
|--|---|
| Statistical analysis title | Serogroup C-Day29,ACWYliq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup C on Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.32 |
| upper limit | 5.46 |

| | |
|--|---|
| Statistical analysis title | Serogroup W-Day29,ACWYliq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup W on Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -1.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.05 |
| upper limit | 4.18 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Serogroup Y-Day29,ACWYliq24 versus ACWY |
|-----------------------------------|---|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup Y on Day 29.

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 2.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.81 |
| upper limit | 6.9 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup A-Day1,ACWYliq30 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup A on Day 1.

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.32 |
| upper limit | 6.33 |

| | |
|---|---|
| Statistical analysis title | Serogroup C-Day1,ACWYliq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup C on Day 1. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 0.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.6 |
| upper limit | 7.35 |

| | |
|---|---|
| Statistical analysis title | Serogroup W-Day1,ACWYliq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup W on Day 1. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -1.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.75 |
| upper limit | 5.23 |

| | |
|---|---|
| Statistical analysis title | Serogroup Y-Day1,ACWYliq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup Y on Day 1. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.69 |
| upper limit | 4.98 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Serogroup A-Day29,ACWYliq30 versus ACWY |
|-----------------------------------|---|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup A on Day 29.

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.24 |
| upper limit | 2.96 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Serogroup C-Day29,ACWYliq30 versus ACWY |
|-----------------------------------|---|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup C on Day 29.

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.99 |
| upper limit | 6.64 |

| | |
|--|---|
| Statistical analysis title | Serogroup W-Day29,ACWYliq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 the N. meningitidis serogroup W on Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 4.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.11 |
| upper limit | 9.33 |

| | |
|--|---|
| Statistical analysis title | Serogroup Y-Day29,ACWYliq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer ≥ 8 for the N. meningitidis serogroup Y on Day 29. | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 0.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.16 |
| upper limit | 5.13 |

Secondary: Percentages of subjects with hSBA titers \geq 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 \geq 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 percentages of subjects with hSBA titer \geq LLOQ, and its associated two-sided 95% Clopper-Pearson CIs are computed for each of the N. meningitidis serogroups A, C, W and Y. Analysis is 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|---|------------------------------------|---------------------------|------------------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 394 | 398 | 395 | 392 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Meningitis A,Day 1(N=381,389,377,374) | 12.86 (9.67 to 16.64) | 11.57 (8.56 to 15.17) | 15.38 (11.89 to 19.43) | 13.64 (10.32 to 17.54) |
| Meningitis A,Day 29(N=378,384,377,367) | 93.92 (91.01 to 96.10) | 92.19 (89.03 to 94.67) | 93.37 (90.37 to 95.66) | 94.01 (91.06 to 96.21) |
| Meningitis C,Day 1(N=394,395,395,392) | 55.84 (50.78 to 60.81) | 48.61 (43.58 to 53.66) | 61.01 (56.01 to 65.85) | 57.14 (52.08 to 62.10) |
| Meningitis C,Day 29(N=388,382,379,379) | 79.38 (75.01 to 83.30) | 80.37 (76.02 to 84.23) | 84.7 (80.67 to 88.17) | 84.7 (80.67 to 88.17) |
| Meningitis W,Day 1(N=379,396,382,376) | 32.45 (27.76 to 37.42) | 28.54 (24.14 to 33.26) | 29.32 (24.80 to 34.16) | 30.05 (25.46 to 34.96) |
| Meningitis W,Day 29(N=389,392,389,384) | 79.43 (75.07 to 83.34) | 80.87 (76.62 to 84.64) | 85.86 (82.00 to 89.17) | 81.77 (77.54 to 85.50) |
| Meningitis Y,Day 1(N=390,398,391,385) | 24.36 (20.18 to 28.93) | 22.86 (18.83 to 27.31) | 21.74 (17.75 to 26.16) | 22.86 (18.76 to 27.38) |
| Meningitis Y,Day 29(N=384,392,393,386) | 88.28 (84.63 to 91.32) | 86.22 (82.41 to 89.48) | 88.3 (84.70 to 91.30) | 87.56 (83.85 to 90.69) |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Serogroup A-Day1,ACWY liq24 versus ACWY |
| Statistical analysis description: | |
| Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup A at Day 1 | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.37 |
| upper limit | 5.99 |

| | |
|---|---|
| Statistical analysis title | Serogroup C-Day1,ACWY liq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup C at Day 1 | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 7.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 14.13 |

| | |
|---|---|
| Statistical analysis title | Serogroup W-Day1,ACWY liq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup W at Day 1 | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| 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 | -2.57 |
| upper limit | 10.39 |

| | |
|---|---|
| Statistical analysis title | Serogroup Y-Day1,ACWY liq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup Y at Day 1 | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.44 |
| upper limit | 7.44 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup A-Day29,ACWY liq24 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup A at Day 29

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.94 |
| upper limit | 5.46 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup C-Day29,ACWY liq24 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup C at Day 29

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.66 |
| upper limit | 4.7 |

| | |
|--|---|
| Statistical analysis title | Serogroup W-Day29,ACWY liq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup W at Day 29 | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -1.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.05 |
| upper limit | 4.18 |

| | |
|--|---|
| Statistical analysis title | Serogroup Y-Day29,ACWY liq24 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup Y at Day 29 | |
| Comparison groups | GSK3536820A ACWY_Liq24 Group v ACWY_1 Group |
| Number of subjects included in analysis | 792 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 2.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.67 |
| upper limit | 6.8 |

| | |
|---|---|
| Statistical analysis title | Serogroup A-Day1,ACWY liq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup A at Day 1 | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 1.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.32 |
| upper limit | 6.83 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Serogroup C-Day1,ACWY liq30 versus ACWY |
|-----------------------------------|---|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup C at Day 1

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| 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 | -3 |
| upper limit | 10.71 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Serogroup W-Day1,ACWY liq30 versus ACWY |
|-----------------------------------|---|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup W at Day 1

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.24 |
| upper limit | 5.77 |

| | |
|---|---|
| Statistical analysis title | Serogroup Y-Day1,ACWY liq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup Y at Day 1 | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -1.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.99 |
| upper limit | 4.75 |

| | |
|--|---|
| Statistical analysis title | Serogroup A-Day29,ACWY liq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup A at Day 29 | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.24 |
| upper limit | 2.96 |

| | |
|--|---|
| Statistical analysis title | Serogroup C-Day29,ACWY liq30 versus ACWY |
| Statistical analysis description: Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup C at Day 29 | |
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.16 |
| upper limit | 5.16 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup W-Day29,ACWY liq30 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup W at Day 29

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 4.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.11 |
| upper limit | 9.33 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Serogroup Y-Day29,ACWY liq30 versus ACWY |
|-----------------------------------|--|

Statistical analysis description:

Between-group difference in percentages of subjects with hSBA titer \geq LLOQ for the N. meningitidis serogroup Y at Day 29

| | |
|---|---|
| Comparison groups | GSK3536820A ACWY_Liq30 Group v ACWY_2 Group |
| Number of subjects included in analysis | 787 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Miettinen and Nurminen score method |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 0.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.88 |
| upper limit | 5.37 |

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 unsolicited adverse event (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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|-----------------------------|------------------------------------|-----------------|------------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 420 | 424 | 427 | 419 |
| Units: Participants | 2 | 2 | 6 | 6 |

Statistical analyses

No statistical analyses for this end point

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:

Assessed solicited local AEs were erythema, induration and pain at injection site. Assessed solicited systemic AEs were Arthralgia, chills, fatigue, fever (body temperature $\geq 38.0^{\circ}\text{C}$), headache, loss of appetite, myalgia and nausea. Analysis was performed on the solicited safety set that includes all enrolled subjects who received a study vaccination and reported 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|---------------------------------|------------------------------------|-----------------|------------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 418 | 422 | 425 | 419 |
| Units: Participants | | | | |
| Arthralgia | 45 | 50 | 49 | 40 |
| Chills | 75 | 79 | 78 | 56 |
| Erythema | 48 | 51 | 58 | 40 |
| Fatigue | 174 | 175 | 149 | 147 |
| Fever (Temperature ≥ 38 C) | 15 | 18 | 15 | 12 |
| Headache | 164 | 151 | 169 | 157 |
| Induration | 50 | 51 | 54 | 39 |
| Loss of Appetite | 53 | 54 | 63 | 34 |
| Myalgia | 60 | 59 | 58 | 65 |
| Nausea | 54 | 48 | 42 | 46 |
| Pain | 189 | 181 | 202 | 192 |

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 any vaccination. Analysis was performed on the solicited safety set that includes all enrolled subjects who received a study vaccination and reported solicited adverse events 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|---------------------------------------|------------------------------------|-----------------|------------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 418 | 422 | 425 | 419 |
| Units: Participants | | | | |
| Analgesic/Antipyretic Prevention, No | 357 | 374 | 366 | 369 |
| Analgesic/Antipyretic Prevention, Yes | 61 | 48 | 59 | 50 |
| Analgesic/Antipyretic Treatment, No | 328 | 340 | 349 | 350 |
| Analgesic/Antipyretic Treatment, Yes | 90 | 82 | 76 | 69 |

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 unsolicited adverse event (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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|-----------------------------|------------------------------------|-----------------|------------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 420 | 424 | 427 | 419 |
| Units: Participants | 77 | 91 | 101 | 97 |

Statistical analyses

No statistical analyses for this end point

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

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

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 unsolicited adverse events data for 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_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group | ACWY_2 Group |
|-----------------------------|------------------------------------|-----------------|------------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 420 | 424 | 427 | 419 |
| Units: Participants | | | | |
| Leading to withdrawal | 0 | 0 | 0 | 0 |
| SAEs | 4 | 1 | 4 | 4 |
| MAEs | 88 | 69 | 81 | 77 |

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 | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------------------|
| Reporting group title | GSK3536820A ACWY_Liq24 Group |
|-----------------------|------------------------------|

Reporting group description:

Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 24 months, at Day 1 in the Study Phase1

| | |
|-----------------------|--------------|
| Reporting group title | ACWY_1 Group |
|-----------------------|--------------|

Reporting group description:

Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase1.

| | |
|-----------------------|------------------------------|
| Reporting group title | GSK3536820A ACWY_Liq30 Group |
|-----------------------|------------------------------|

Reporting group description:

Healthy subjects receiving a single dose of the investigational MenACWY liquid vaccine formulation aged for approximately 30 months, at Day 1 in the Study Phase 2.

| | |
|-----------------------|--------------|
| Reporting group title | ACWY_2 Group |
|-----------------------|--------------|

Reporting group description:

Healthy subjects receiving a single dose of the licensed GSK' MenACWY vaccine formulation (Menveo), not aged, at Day 1 in the Study Phase 2.

| Serious adverse events | GSK3536820A ACWY_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group |
|---|---------------------------------|-----------------|---------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 420 (0.95%) | 1 / 424 (0.24%) | 4 / 427 (0.94%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Post procedural haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue injury | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Phimosi | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (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 | | | |
| Tension headache | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Appendicitis noninfective | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Adnexa uteri pain | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (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 |
| Ovarian cyst ruptured | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (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 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|--|--|
| Serious adverse events | ACWY_2 Group | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 419 (0.95%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Post procedural haemorrhage | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Soft tissue injury | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Phimosis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Tension headache | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Appendicitis noninfective | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Adnexa uteri pain | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ovarian cyst ruptured | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | GSK3536820A ACWY_Liq24 Group | ACWY_1 Group | GSK3536820A ACWY_Liq30 Group |
|---|---------------------------------|--------------------|---------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 312 / 420 (74.29%) | 314 / 424 (74.06%) | 324 / 427 (75.88%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Administration site erythema | | | |

| | | | |
|--------------------------------|--------------------|--------------------|--------------------|
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Administration site induration | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Administration site pain | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Application site erythema | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Application site warmth | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 77 / 420 (18.33%) | 79 / 424 (18.63%) | 78 / 427 (18.27%) |
| occurrences (all) | 78 | 81 | 78 |
| Discomfort | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 175 / 420 (41.67%) | 175 / 424 (41.27%) | 150 / 427 (35.13%) |
| occurrences (all) | 175 | 179 | 157 |
| Induration | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 50 / 420 (11.90%) | 51 / 424 (12.03%) | 59 / 427 (13.82%) |
| occurrences (all) | 51 | 52 | 68 |
| Injection site haematoma | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site induration | | | |

| | | | |
|---------------------------------|--------------------|--------------------|--------------------|
| subjects affected / exposed | 52 / 420 (12.38%) | 51 / 424 (12.03%) | 54 / 427 (12.65%) |
| occurrences (all) | 53 | 51 | 62 |
| Injection site oedema | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 190 / 420 (45.24%) | 182 / 424 (42.92%) | 205 / 427 (48.01%) |
| occurrences (all) | 193 | 183 | 214 |
| Injection site pruritus | | | |
| subjects affected / exposed | 2 / 420 (0.48%) | 3 / 424 (0.71%) | 2 / 427 (0.47%) |
| occurrences (all) | 3 | 3 | 2 |
| Injection site rash | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site scab | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 1 | 0 | 1 |
| Oedema | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 2 / 427 (0.47%) |
| occurrences (all) | 0 | 0 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 20 / 420 (4.76%) | 19 / 424 (4.48%) | 19 / 427 (4.45%) |
| occurrences (all) | 21 | 20 | 19 |
| Vaccination site pain | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 1 | 1 |
| Vessel puncture site induration | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vessel puncture site pain | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Immune system disorders | | | |
| Allergy to arthropod sting subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Drug hypersensitivity subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 0 / 424 (0.00%) 0 | 1 / 427 (0.23%) 1 |
| Reproductive system and breast disorders | | | |
| Dysfunctional uterine bleeding subjects affected / exposed occurrences (all) | 1 / 420 (0.24%) 1 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |
| Dysmenorrhoea subjects affected / exposed occurrences (all) | 1 / 420 (0.24%) 1 | 0 / 424 (0.00%) 0 | 1 / 427 (0.23%) 1 |
| Endometriosis subjects affected / exposed occurrences (all) | 1 / 420 (0.24%) 1 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |
| Polycystic ovaries subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 2 / 420 (0.48%) 2 | 0 / 424 (0.00%) 0 | 2 / 427 (0.47%) 2 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 0 / 424 (0.00%) 0 | 1 / 427 (0.23%) 1 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |
| Nasal congestion | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 1 | 0 | 1 |
| Nasal obstruction | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 3 / 427 (0.70%) |
| occurrences (all) | 0 | 1 | 3 |
| Pharyngeal erythema | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 3 / 427 (0.70%) |
| occurrences (all) | 1 | 0 | 3 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Bulimia nervosa | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|----------------------------------|-----------------|-----------------|-----------------|
| Animal bite | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Fall | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hand fracture | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 1 / 427 (0.23%) |
| occurrences (all) | 2 | 1 | 1 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Generalised tonic-clonic seizure | | | |

| | | | |
|--------------------------------------|--------------------|--------------------|--------------------|
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Headache | | | |
| subjects affected / exposed | 168 / 420 (40.00%) | 155 / 424 (36.56%) | 178 / 427 (41.69%) |
| occurrences (all) | 177 | 164 | 200 |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 1 | 1 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 0 / 424 (0.00%) 0 | 1 / 427 (0.23%) 1 |
| Eye disorders | | | |
| Eye paraesthesia | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 420 (0.95%) | 4 / 424 (0.94%) | 4 / 427 (0.94%) |
| occurrences (all) | 4 | 4 | 4 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 420 (0.71%) | 0 / 424 (0.00%) | 6 / 427 (1.41%) |
| occurrences (all) | 4 | 0 | 6 |
| Enteritis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nausea | | | |

| | | | |
|--|-------------------|-------------------|-------------------|
| subjects affected / exposed | 54 / 420 (12.86%) | 48 / 424 (11.32%) | 43 / 427 (10.07%) |
| occurrences (all) | 56 | 49 | 45 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 2 / 427 (0.47%) |
| occurrences (all) | 0 | 1 | 2 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 1 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis atopic | | | |
| subjects affected / exposed | 2 / 420 (0.48%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hand dermatitis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|-------------------|-------------------|-------------------|
| Pruritus | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Hypertonic bladder | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 50 / 420 (11.90%) | 53 / 424 (12.50%) | 49 / 427 (11.48%) |
| occurrences (all) | 52 | 53 | 55 |
| Back pain | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 5 / 427 (1.17%) |
| occurrences (all) | 0 | 1 | 5 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 63 / 420 (15.00%) | 62 / 424 (14.62%) | 58 / 427 (13.58%) |
| occurrences (all) | 63 | 62 | 63 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Torticollis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| Abscess limb | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Abscess oral | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Balanitis candida | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 3 / 424 (0.71%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Enterobiasis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 1 / 427 (0.23%) |
| occurrences (all) | 1 | 1 | 1 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 1 | 0 | 1 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 2 / 424 (0.47%) | 3 / 427 (0.70%) |
| occurrences (all) | 1 | 2 | 3 |

| | | | |
|-----------------------------|-----------------|------------------|-----------------|
| Injection site cellulitis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 7 / 420 (1.67%) | 15 / 424 (3.54%) | 6 / 427 (1.41%) |
| occurrences (all) | 7 | 15 | 7 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 2 / 427 (0.47%) |
| occurrences (all) | 1 | 0 | 3 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 2 / 420 (0.48%) | 0 / 424 (0.00%) | 1 / 427 (0.23%) |
| occurrences (all) | 2 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 420 (0.24%) | 0 / 424 (0.00%) | 0 / 427 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 420 (0.00%) | 1 / 424 (0.24%) | 0 / 427 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Respiratory tract infection viral subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Rhinitis subjects affected / exposed occurrences (all) | 3 / 420 (0.71%) 3 | 4 / 424 (0.94%) 4 | 5 / 427 (1.17%) 5 |
| Sinusitis subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Tonsillitis subjects affected / exposed occurrences (all) | 2 / 420 (0.48%) 2 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |
| Tracheitis subjects affected / exposed occurrences (all) | 1 / 420 (0.24%) 1 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |
| Tracheobronchitis subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 8 / 420 (1.90%) 8 | 8 / 424 (1.89%) 8 | 7 / 427 (1.64%) 7 |
| Upper respiratory tract infection bacterial subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Urethritis subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 0 / 427 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 2 / 424 (0.47%) 2 | 1 / 427 (0.23%) 1 |
| Viral infection subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 1 / 424 (0.24%) 1 | 3 / 427 (0.70%) 3 |
| Vulvovaginal mycotic infection | | | |

| | | | |
|--|-------------------------|-------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 420 (0.00%) 0 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 54 / 420 (12.86%) 55 | 54 / 424 (12.74%) 56 | 63 / 427 (14.75%) 64 |
| Iron deficiency subjects affected / exposed occurrences (all) | 1 / 420 (0.24%) 1 | 0 / 424 (0.00%) 0 | 0 / 427 (0.00%) 0 |

| | | | |
|---|-------------------------|--|--|
| Non-serious adverse events | ACWY_2 Group | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 317 / 419 (75.66%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin papilloma subjects affected / exposed occurrences (all) | 1 / 419 (0.24%) 1 | | |
| General disorders and administration site conditions Administration site erythema subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Administration site induration subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Administration site pain subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Application site erythema subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Application site warmth subjects affected / exposed occurrences (all) | 1 / 419 (0.24%) 1 | | |
| Chills subjects affected / exposed occurrences (all) | 56 / 419 (13.37%) 57 | | |

| | | | |
|-----------------------------|--------------------|--|--|
| Discomfort | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Facial pain | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 147 / 419 (35.08%) | | |
| occurrences (all) | 150 | | |
| Induration | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 42 / 419 (10.02%) | | |
| occurrences (all) | 47 | | |
| Injection site haematoma | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Injection site induration | | | |
| subjects affected / exposed | 39 / 419 (9.31%) | | |
| occurrences (all) | 43 | | |
| Injection site oedema | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site pain | | | |
| subjects affected / exposed | 194 / 419 (46.30%) | | |
| occurrences (all) | 201 | | |
| Injection site pruritus | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Injection site rash | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site scab | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|------------------|--|--|
| Malaise | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Pain | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Pyrexia | | | |
| subjects affected / exposed | 14 / 419 (3.34%) | | |
| occurrences (all) | 14 | | |
| Vaccination site pain | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vessel puncture site induration | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Immune system disorders | | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |
| Dysfunctional uterine bleeding | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 4 / 419 (0.95%) | | |
| occurrences (all) | 4 | | |
| Endometriosis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Polycystic ovaries | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Cough | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 2 | | |
| Nasal obstruction | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Pharyngeal erythema | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis allergic | | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 419 (0.24%) 1 | | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Sneezing subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Psychiatric disorders Bulimia nervosa subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Irritability subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Injury, poisoning and procedural complications Animal bite subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Contusion subjects affected / exposed occurrences (all) | 1 / 419 (0.24%) 1 | | |
| Fall subjects affected / exposed occurrences (all) | 1 / 419 (0.24%) 1 | | |
| Hand fracture subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Joint dislocation subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Ligament sprain | | | |

| | | | |
|----------------------------------|--------------------|--|--|
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Limb injury | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 419 (0.95%) | | |
| occurrences (all) | 4 | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Headache | | | |
| subjects affected / exposed | 162 / 419 (38.66%) | | |
| occurrences (all) | 188 | | |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Presyncope | | | |

| | | | |
|--------------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Tremor | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Eye paraesthesia | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 6 / 419 (1.43%) | | |
| occurrences (all) | 7 | | |
| Abdominal pain lower | | | |

| | | | |
|--|-------------------|--|--|
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 419 (1.19%) | | |
| occurrences (all) | 5 | | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 46 / 419 (10.98%) | | |
| occurrences (all) | 46 | | |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Toothache | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermal cyst | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|------------------|--|--|
| Dermatitis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hand dermatitis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Hypertonic bladder | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 40 / 419 (9.55%) | | |
| occurrences (all) | 41 | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 419 (0.95%) | | |
| occurrences (all) | 4 | | |
| Muscle spasms | | | |

| | | | |
|-----------------------------|-------------------|--|--|
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 65 / 419 (15.51%) | | |
| occurrences (all) | 68 | | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Torticollis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abscess oral | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Balanitis candida | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Enterobiasis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Helicobacter infection | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hordeolum | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Influenza | | | |
| subjects affected / exposed | 3 / 419 (0.72%) | | |
| occurrences (all) | 3 | | |
| Injection site cellulitis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 419 (1.43%) | | |
| occurrences (all) | 6 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| Paronychia | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 419 (0.24%) | | |
| occurrences (all) | 1 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 7 / 419 (1.67%) | | |
| occurrences (all) | 7 | | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 419 (0.48%) | | |
| occurrences (all) | 2 | | |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tracheobronchitis | | | |
| subjects affected / exposed | 0 / 419 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|------------------------|--|--|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 4 / 419 (0.95%) 4 | | |
| Upper respiratory tract infection bacterial subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Urethritis subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 419 (0.48%) 2 | | |
| Viral infection subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |
| Vulvovaginal mycotic infection subjects affected / exposed occurrences (all) | 1 / 419 (0.24%) 1 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 34 / 419 (8.11%) 36 | | |
| Iron deficiency subjects affected / exposed occurrences (all) | 0 / 419 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 17 January 2018 | Two exclusion criteria were merged into one. Immunogenicity endpoints that were included in subgroup analysis were clarified. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported