Clinical trial results:
A Phase 1/2 randomized, observer-blinded, multi-country study to evaluate safety and immunogenicity of investigational adjuvanted human papillomavirus vaccine in females (16 to 26 years of age)

Summary

EudraCT number	2022-000090-15
Trial protocol	DE LT FR BG EE CZ PL
Global end of trial date	23 February 2024

Results information

Result version number	v1
This version publication date	28 December 2024
First version publication date	28 December 2024

Trial information

Trial identification

Sponsor protocol code	213749

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05496231
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, 44 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 44 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

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

Global end of trial reached?	Yes
Global end of trial date	23 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the safety and reactogenicity of GlaxoSmithKline Biologicals SA (GSK)’s investigational adjuvanted human papillomavirus (HPV) vaccine formulations.
• To evaluate the immune response to GSK’s investigational adjuvanted HPV vaccine formulations.

Protection of trial subjects:

All participants were observed for 60 minutes after vaccine administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible participants that had no contraindications to any components of the vaccines. Participants were followed-up for at least 28 days (for unsolicited AEs) and throughout the entire study period (for SAEs and pIMDs) after administration of each dose of the vaccine. Study safety monitoring was performed. Unblinding strategy in case of emergency safety situations was in place. Study stopping rules would have been applied in case of significant safety concerns.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 August 2022
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	Bulgaria: 8
Country: Number of subjects enrolled	Czechia: 74
Country: Number of subjects enrolled	Estonia: 364
Country: Number of subjects enrolled	France: 97
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Lithuania: 137
Country: Number of subjects enrolled	Poland: 169
Country: Number of subjects enrolled	United States: 199
Worldwide total number of subjects	1080
EEA total number of subjects	881

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	34
Adults (18-64 years)	1046
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was organized into 2 steps. Step 1 sentinel participants received the initial assigned dose prior to participants in Step 2 of the study, and sentinel participants had an additional blood sampling visit at Day 7 to assess for biochemical and hematological parameters.

Pre-assignment

Screening details:

A total of 1080 participants were enrolled into the study, of which 1079 participants received at least 1 dose of vaccine and were included in the Exposed Set.

Period 1

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

Blinding implementation details:

The study was conducted in an observer-blind manner.

Arms

Are arms mutually exclusive?	Yes
Arm title	HPV9 High Group

Arm description:

Participants received 3 doses of the high formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.

Arm type	Experimental
Investigational medicinal product name	HPV9-High formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the high formulation of HPV9 investigational adjuvanted vaccine were administered intramuscularly at Day 1, Month 2 and Month 6.

Arm title	HPV9 Med Group

Arm description:

Participants received 3 doses of the medium formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.

Arm type	Experimental
Investigational medicinal product name	HPV9-Medium formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the medium formulation of HPV9 investigational adjuvanted vaccine were administered intramuscularly at Day 1, Month 2 and Month 6.

Arm title	HPV9 Low Group

Arm description:

Participants received 3 doses of the low formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.

Arm type	Experimental
Investigational medicinal product name	HPV9-Low formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the low formulation of HPV9 investigational adjuvanted vaccine were administered intramuscularly at Day 1, Month 2 and Month 6.

Arm title	Gar9 Group

Arm description:

Participants received 3 doses of the marketed Human Papilloma Virus (HPV) vaccine (Gardasil 9) at Day 1, Month 2, and Month 6.

Arm type	Active comparator
Investigational medicinal product name	Gardasil 9
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the marketed HPV vaccine (Gardasil 9) were administered intramuscularly at Day 1, Month 2 and Month 6.

Number of subjects in period 1[1]	HPV9 High Group	HPV9 Med Group	HPV9 Low Group
Started	270	270	269
Completed	239	246	244
Not completed	31	24	25
Migrated/moved from the study area	3	5	3
Consent withdrawn by subject	5	5	4
Adverse event, non-fatal	1	1	-
Not specified	9	7	7
Lost to follow-up	13	6	11

Number of subjects in period 1[1]	Gar9 Group
Started	270
Completed	238
Not completed	32
Migrated/moved from the study area	3
Consent withdrawn by subject	11
Adverse event, non-fatal	4
Not specified	8
Lost to follow-up	6

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: A total of 1080 participants were enrolled into the study, of which 1079 participants received at least 1 dose of vaccine and were included in the Exposed Set.

Baseline characteristics

Reporting groups	
Reporting group title	HPV9 High Group
Reporting group description:	
Participants received 3 doses of the high formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.	
Reporting group title	HPV9 Med Group
Reporting group description:	
Participants received 3 doses of the medium formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.	
Reporting group title	HPV9 Low Group
Reporting group description:	
Participants received 3 doses of the low formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.	
Reporting group title	Gar9 Group
Reporting group description:	
Participants received 3 doses of the marketed Human Papilloma Virus (HPV) vaccine (Gardasil 9) at Day 1, Month 2, and Month 6.	

Reporting group values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group
Number of subjects	270	270	269
Age categorical Units: Participants			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years			
arithmetic mean	22.0	21.9	22.1
standard deviation	± 2.32	± 2.56	± 2.45
Sex: Female, Male Units: Participants			
Female	270	270	269
Male	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	25	25	27
Not Hispanic or Latino	245	245	242
Unknown or Not Reported	0	0	0

Reporting group values	Gar9 Group	Total	
Number of subjects	270	1079	

Age categorical Units: Participants			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years			
arithmetic mean	22.2		
standard deviation	± 2.25	-	
Sex: Female, Male Units: Participants			
Female	270	1079	
Male	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	26	103	
Not Hispanic or Latino	244	976	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	HPV9 High Group
Reporting group description:	
Participants received 3 doses of the high formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.	
Reporting group title	HPV9 Med Group
Reporting group description:	
Participants received 3 doses of the medium formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.	
Reporting group title	HPV9 Low Group
Reporting group description:	
Participants received 3 doses of the low formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.	
Reporting group title	Gar9 Group
Reporting group description:	
Participants received 3 doses of the marketed Human Papilloma Virus (HPV) vaccine (Gardasil 9) at Day 1, Month 2, and Month 6.	

Primary: Number of participants reporting Grade 3 solicited administration site events after vaccine Dose 1

End point title	Number of participants reporting Grade 3 solicited administration site events after vaccine Dose 1[1]
End point description:	
Assessed solicited administration site events included pain, redness and swelling at injection site. Grade 3 pain = significant pain at rest, which prevented normal everyday activities. Grade 3 redness/swelling = redness/swelling with a surface diameter greater than (>) 50 millimeters (mm). Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the electronic diary (eDiary) for solicited events completed after the administration of vaccine Dose 1 and for whom data were available during the specified period.	
End point type	Primary
End point timeframe:	
Within 7 days after vaccine Dose 1 (administered at Day 1)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants				
Grade 3 Pain (N=270;270;269;270)	11	12	6	2
Grade 3 Redness (N=270;270;269;270)	2	4	2	0
Grade 3 Swelling (N=270;270;269;270)	5	3	2	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 solicited administration site events after vaccine Dose 2

End point title	Number of participants reporting Grade 3 solicited administration site events after vaccine Dose 2[2]

End point description:

Assessed solicited administration site events included pain, redness and swelling at injection site. Grade 3 pain = significant pain at rest, which prevented normal everyday activities. Grade 3 redness/swelling = redness/swelling with a surface diameter >50 mm.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the eDiary for solicited events completed after the administration of vaccine Dose 2 and for whom data were available during the specified period.

End point type	Primary

End point timeframe:

Within 7 days after vaccine Dose 2 (administered at Month 2)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	257	261	258	260
Units: Participants				
Grade 3 Pain (N=257;261;258;260)	13	6	11	1
Grade 3 Redness (N=257;261;258;260)	4	0	2	1
Grade 3 Swelling (N=257;261;258;260)	5	3	2	3

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 solicited administration site events after vaccine Dose 3

End point title	Number of participants reporting Grade 3 solicited administration site events after vaccine Dose 3[3]

End point description:

Assessed solicited administration site events included pain, redness and swelling at injection site. Grade 3 pain = significant pain at rest, which prevented normal everyday activities. Grade 3 redness/swelling = redness/swelling with a surface diameter >50 mm.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the eDiary for solicited events completed after the administration of vaccine Dose 3 and for whom data were available during the specified period.

End point type	Primary

End point timeframe:

Within 7 days after vaccine Dose 3 (administered at Month 6)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	247	244	236
Units: Participants				
Grade 3 Pain (N=244;247;244;236)	9	3	6	1
Grade 3 Redness (N=244;247;244;236)	0	2	1	1
Grade 3 Swelling (N=244;247;244;236)	0	4	1	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 solicited systemic events after vaccine Dose 1

End point title	Number of participants reporting Grade 3 solicited systemic events after vaccine Dose 1[4]

End point description:

Assessed solicited systemic events included fever, headache, myalgia, arthralgia and fatigue. Grade 3 fever = body temperature >39.0 degrees Celsius (°C) or 102.2 Fahrenheit (°F). The preferred location for measuring temperature was the axilla. Grade 3 headache, myalgia, arthralgia and fatigue = symptoms that prevented normal, every day activities.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the eDiary for solicited events completed after the administration of vaccine Dose 1 and for whom data were available during the specified period.

End point type	Primary

End point timeframe:

Within 7 days after vaccine Dose 1 (administered at Day 1)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants				
Grade 3 Fever (N=270;270;269;270)	1	0	0	0
Grade 3 Headache (N=270;270;269;270)	11	3	6	3
Grade 3 Myalgia (N=270;270;269;270)	5	2	2	1
Grade 3 Arthralgia (N=270;270;269;270)	1	1	1	0
Grade 3 Fatigue (N=270;270;269;270)	12	9	7	5

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 solicited systemic events after vaccine Dose 2

End point title	Number of participants reporting Grade 3 solicited systemic events after vaccine Dose 2[5]

End point description:

Assessed solicited systemic events included fever, headache, myalgia, arthralgia and fatigue. Grade 3 fever = body temperature >39.0°C or 102.2°F. The preferred location for measuring temperature was the axilla. Grade 3 headache, myalgia, arthralgia and fatigue = symptoms that prevented normal, every day activity.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the eDiary for solicited events completed after the administration of vaccine Dose 2 and for whom data were available during the specified period.

End point type	Primary

End point timeframe:

Within 7 days after vaccine Dose 2 (administered at Month 2)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	257	261	258	260
Units: Participants				
Grade 3 Fever (N=257;261;258;260)	0	1	0	1
Grade 3 Headache (N=257;261;258;260)	7	7	8	5
Grade 3 Myalgia (N=257;261;258;260)	4	0	3	2
Grade 3 Arthralgia (N=257;261;258;260)	0	2	1	1
Grade 3 Fatigue (N=257;261;258;260)	12	11	12	11

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 solicited systemic events after vaccine Dose 3

End point title	Number of participants reporting Grade 3 solicited systemic events after vaccine Dose 3[6]

End point description:

Assessed solicited systemic events included fever, headache, myalgia, arthralgia and fatigue. Grade 3 fever = body temperature >39.0°C or 102.2°F. The preferred location for measuring temperature was the axilla. Grade 3 headache, myalgia, arthralgia and fatigue = symptoms that prevented normal, every day activity.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the eDiary for solicited events completed after the administration of vaccine Dose 3 and for whom data were available during the specified period.

End point type	Primary

End point timeframe:

Within 7 days after vaccine Dose 3 (administered at Month 6)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	247	244	236
Units: Participants				
Grade 3 Fever (N=244;247;244;236)	0	1	0	0
Grade 3 Headache (N=244;247;244;236)	10	4	9	7
Grade 3 Myalgia (N=244;247;244;236)	3	3	2	2
Grade 3 Arthralgia (N=244;247;244;236)	2	1	0	0
Grade 3 Fatigue (N=244;247;244;236)	15	8	11	6

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 unsolicited adverse events (AEs) after vaccine Dose 1

End point title	Number of participants reporting Grade 3 unsolicited adverse events (AEs) after vaccine Dose 1[7]

End point description:

An unsolicited AE is defined as an AE that was not included in the list of solicited events using an eDiary and that was spontaneously communicated by a participant/participant's parent(s)/legally acceptable representative(s) [LAR(s)] who has signed the informed consent. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited AE. Grade 3 unsolicited AEs = an AE which prevented normal, everyday activities.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine and for whom data were available for the specified period after the administration of vaccine Dose 1.

End point type	Primary

End point timeframe:

Within 28 days after vaccine Dose 1 (administered at Day 1)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants	0	1	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 unsolicited AEs after vaccine Dose 2

End point title	Number of participants reporting Grade 3 unsolicited AEs after vaccine Dose 2[8]

End point description:

An unsolicited AE is defined as an AE that was not included in the list of solicited events using an eDiary and that was spontaneously communicated by a participant/participant's parent(s)/LAR(s) who has signed the informed consent. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited AE. Grade 3 unsolicited AEs = an AE which prevented normal, everyday activities.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine and for whom data were available for the specified period after the administration of vaccine Dose 2.

End point type	Primary

End point timeframe:

Within 28 days after vaccine Dose 2 (administered at Month 2)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	257	261	258	260
Units: Participants	4	1	3	3

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting Grade 3 unsolicited AEs after vaccine Dose 3

End point title	Number of participants reporting Grade 3 unsolicited AEs after vaccine Dose 3[9]

End point description:

An unsolicited AE is defined as an AE that was not included in the list of solicited events using an eDiary and that was spontaneously communicated by a participant/ participant's parent(s)/LAR(s) who has signed the informed consent. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited AE. Grade 3 unsolicited AEs = an AE which prevented normal, everyday activities.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine and for whom data were available for the specified period after the administration of vaccine Dose 3.

End point type	Primary

End point timeframe:

Within 28 days after vaccine Dose 3 (administered at Month 6)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	244	247	244	236
Units: Participants	0	0	1	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting serious adverse events (SAEs)

End point title	Number of participants reporting serious adverse events

End point description:

An SAE is defined as any untoward medical occurrence that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity, was a congenital anomaly/birth defect in the offspring of a study participant, or resulted in abnormal pregnancy outcomes, or in other situations that were considered serious per medical or scientific judgment.
Analysis was performed on the Exposed Set, which included participants who received a study vaccine and for whom data were available for the specified period.

End point type	Primary

End point timeframe:

From first vaccination (Day 1) to study end (Month 12)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants	1	4	2	7

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants in Step 1 subset with clinically relevant biochemical abnormalities

End point title	Number of participants in Step 1 subset with clinically relevant biochemical abnormalities[11]

End point description:

As pre-specified in the protocol, the assessed biochemical parameters were blood urea nitrogen (BUN), alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Assessment of intensity: Grading of the biochemical parameters was based on the institutional normal reference ranges and derived from the standard Food and Drug Administration (FDA) Toxicity Grading Scale. Changes compared to normal reference ranges were graded as follows: Grade 0 = a non-missing parameter value for which grade could not be derived according to the grading scale and does not belong to Grade 1-4; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life-Threatening. Unknown = parameter value missing for the specified parameter.

Analysis was performed on the Step 1 subset from the Exposed Set, which included sentinel adult participants for whom blood samples were collected for the specified biochemical analyses at Day 7.

End point type	Primary

End point timeframe:

At Day 7

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: Participants				
BUN, Grade 0 (N=12;12;12;12)	11	12	11	11
BUN, Grade 1 (N=12;12;12;12)	0	0	0	0
BUN, Grade 2 (N=12;12;12;12)	0	0	0	0
BUN, Grade 3 (N=12;12;12;12)	0	0	0	0
BUN, Grade 4 (N=12;12;12;12)	0	0	0	0
BUN, Unknown (N=12;12;12;12)	1	0	1	1
AST, Grade 0 (N=12;12;12;12)	11	12	11	12
AST, Grade 1 (N=12;12;12;12)	0	0	0	0
AST, Grade 2 (N=12;12;12;12)	0	0	0	0
AST, Grade 3 (N=12;12;12;12)	0	0	0	0
AST, Grade 4 (N=12;12;12;12)	0	0	0	0
AST, Unknown (N=12;12;12;12)	1	0	1	0
ALT, Grade 0 (N=12;12;12;12)	11	12	11	12
ALT, Grade 1 (N=12;12;12;12)	0	0	0	0
ALT, Grade 2 (N=12;12;12;12)	0	0	0	0
ALT, Grade 3 (N=12;12;12;12)	0	0	0	0
ALT, Grade 4 (N=12;12;12;12)	0	0	0	0
ALT, Unknown (N=12;12;12;12)	1	0	1	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants in Step 1 subset with clinically relevant hematological abnormalities

End point title	Number of participants in Step 1 subset with clinically relevant hematological abnormalities[12]

End point description:

As pre-specified in the protocol, the assessed hematological parameters were hemoglobin, white blood cells (WBC) increase, WBC decrease, lymphocyte decrease, neutrophils decrease, eosinophils, and platelets decrease. Assessment of intensity: Grading of the biochemical parameters was based on the institutional normal reference ranges and derived from the standard FDA Toxicity Grading Scale. Changes compared to normal reference ranges were graded as follows: Grade 0 = a non-missing parameter value for which grade could not be derived according to the grading scale and does not belong to Grade 1-4; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially Life-Threatening; Unknown = parameter value missing for the specified parameter.
Analysis was performed on the Step 1 subset from the Exposed Set, which included sentinel adult participants for whom blood samples were collected for the specified hematological analyses at Day 7.

End point type	Primary

End point timeframe:

At Day 7

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: Participants				
Hemoglobin, Grade 0 (N=12;12;12;12)	8	10	9	8
Hemoglobin, Grade 1 (N=12;12;12;12)	3	1	2	4
Hemoglobin, Grade 2 (N=12;12;12;12)	0	0	0	0
Hemoglobin, Grade 3 (N=12;12;12;12)	0	1	0	0
Hemoglobin, Grade 4 (N=12;12;12;12)	0	0	0	0
Hemoglobin, Unknown (N=12;12;12;12)	1	0	1	0
WBC Increase, Grade 0 (N=12;12;12;12)	11	12	11	11
WBC Increase, Grade 1 (N=12;12;12;12)	0	0	0	1
WBC Increase, Grade 2 (N=12;12;12;12)	0	0	0	0
WBC Increase, Grade 3 (N=12;12;12;12)	0	0	0	0
WBC Increase, Grade 4 (N=12;12;12;12)	0	0	0	0
WBC Increase, Unknown (N=12;12;12;12)	1	0	1	0
WBC Decrease, Grade 0 (N=12;12;12;12)	11	11	10	11
WBC Decrease, Grade 1 (N=12;12;12;12)	0	1	1	1
WBC Decrease, Grade 2 (N=12;12;12;12)	0	0	0	0
WBC Decrease, Grade 3 (N=12;12;12;12)	0	0	0	0
WBC Decrease, Grade 4 (N=12;12;12;12)	0	0	0	0
WBC Decrease, Unknown (N=12;12;12;12)	1	0	1	0
Lymphocyte Decrease, Grade 0 (N=12;12;12;12)	11	12	11	12
Lymphocyte Decrease, Grade 1 (N=12;12;12;12)	0	0	0	0
Lymphocyte Decrease, Grade 2 (N=12;12;12;12)	0	0	0	0
Lymphocyte Decrease, Grade 3 (N=12;12;12;12)	0	0	0	0
Lymphocyte Decrease, Grade 4 (N=12;12;12;12)	0	0	0	0
Lymphocyte Decrease, Unknown (N=12;12;12;12)	1	0	1	0
Neutrophils Decrease, Grade 0 (N=12;12;12;12)	10	11	10	11

Neutrophils Decrease, Grade 1 (N=12;12;12;12)	1	0	1	1
Neutrophils Decrease, Grade 2 (N=12;12;12;12)	0	1	0	0
Neutrophils Decrease, Grade 3 (N=12;12;12;12)	0	0	0	0
Neutrophils Decrease, Grade 4 (N=12;12;12;12)	0	0	0	0
Neutrophils Decrease, Unknown (N=12;12;12;12)	1	0	1	0
Eosinophils, Grade 0 (N=12;12;12;12)	11	12	11	11
Eosinophils, Grade 1 (N=12;12;12;12)	0	0	0	1
Eosinophils, Grade 2 (N=12;12;12;12)	0	0	0	0
Eosinophils, Grade 3 (N=12;12;12;12)	0	0	0	0
Eosinophils, Grade 4 (N=12;12;12;12)	0	0	0	0
Eosinophils, Unknown (N=12;12;12;12)	1	0	1	0
Platelet Decrease, Grade 0 (N=12;12;12;12)	11	12	11	12
Platelet Decrease, Grade 1 (N=12;12;12;12)	0	0	0	0
Platelet Decrease, Grade 2 (N=12;12;12;12)	0	0	0	0
Platelet Decrease, Grade 3 (N=12;12;12;12)	0	0	0	0
Platelet Decrease, Grade 4 (N=12;12;12;12)	0	0	0	0
Platelet Decrease, Unknown (N=12;12;12;12)	1	0	1	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants in Step 1 subset with clinically relevant abnormalities in hemoglobin change from baseline levels

End point title	Number of participants in Step 1 subset with clinically relevant abnormalities in hemoglobin change from baseline levels[13]

End point description:

The number of participants with clinically relevant abnormalities in hemoglobin change from baseline levels is reported. Assessment of intensity:Grading of the biochemical parameters was based on the institutional normal reference ranges and derived from the standard FDA Toxicity Grading Scale. Changes compared to normal reference ranges were graded as follows: Grade 0=a non-missing parameter value for which grade could not be derived according to the grading scale and does not belong to Grade 1-4; Grade 1=Mild; Grade 2=Moderate; Grade 3=Severe; Grade 4=Potentially Life-Threatening; Unknown=parameter value missing for the specified parameter. Change from baseline=the difference between a participant's baseline (pre-intervention) parameter values and their follow-up (post-intervention) parameter values.
Analysis was performed on the Step 1 subset from the Exposed Set.

End point type	Primary

End point timeframe:

At Day 7 compared to baseline (Day 1)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: Participants				
Hemoglobin change, Grade 0 (N=12;12;12;12)	5	1	1	5
Hemoglobin change, Grade 1 (N=12;12;12;12)	5	11	8	6
Hemoglobin change, Grade 2 (N=12;12;12;12)	0	0	1	0
Hemoglobin change, Grade 3 (N=12;12;12;12)	0	0	0	0
Hemoglobin change, Grade 4 (N=12;12;12;12)	0	0	0	0
Hemoglobin change, Unknown (N=12;12;12;12)	2	0	2	1

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HPV immunoglobulin G (IgG) antibody concentrations

End point title	Anti-HPV immunoglobulin G (IgG) antibody concentrations[14]

End point description:

Anti-HPV IgG antibody concentrations were determined by electrochemiluminescence (ECL) assay and expressed as geometric mean concentrations (GMCs) in arbitrary units per milliliter (AU/mL). The assessed antigens were: HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 33, HPV 45, HPV 52 and HPV 58 type antigens.
Analysis was performed on Per Protocol Set (PPS) for immunogenicity, which included all participants from Exposed Set who met all eligibility criteria, followed the protocol for vaccine administration, adhered to vaccination schedule and blood sampling timings, and had post-vaccination immunogenicity results available for the specified analysis at the specified time point. The PPS excluded those participants with protocol deviations, interfering medications, or intercurrent medical conditions.

End point type	Primary

End point timeframe:

At Month 7 (one month after vaccine Dose 3 administration)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	211	201	206	203
Units: AU/mL				
geometric mean (confidence interval 95%)				
HPV 6 type antigen, (N=210;201;206;203)	124141.35 (110854.94 to 139020.20)	117881.81 (103701.90 to 134000.65)	119724.25 (105236.23 to 136206.84)	54710.66 (47259.35 to 63336.80)
HPV 11 type antigen, (N=211;201;205;203)	276225.68 (243524.62 to 313317.91)	250405.46 (217218.09 to 288663.30)	260309.15 (223319.56 to 303425.52)	187507.09 (162968.13 to 215740.99)

HPV 16 type antigen, (N=202;191;202;197)	297480.37 (254936.96 to 347123.34)	272728.60 (231905.67 to 320737.69)	294326.70 (252346.28 to 343290.99)	154844.90 (131166.44 to 182797.86)
HPV 18 type antigen, (N=211;200;205;203)	181939.71 (157766.95 to 209816.17)	172862.73 (148117.04 to 201742.65)	183180.47 (156207.11 to 214811.50)	86756.51 (73744.88 to 102063.92)
HPV 31 type antigen, (N=211;200;206;203)	241644.97 (215104.30 to 271460.37)	221590.60 (192869.71 to 254588.41)	230875.63 (202104.78 to 263742.19)	104667.37 (90853.53 to 120581.53)
HPV 33 type antigen, (N=208;200;198;198)	154537.14 (133354.03 to 179085.17)	146931.12 (125717.81 to 171723.90)	150919.88 (128301.37 to 177525.85)	96875.65 (84426.91 to 111159.96)
HPV 45 type antigen, (N=211;201;206;203)	170959.55 (149389.05 to 195644.64)	174740.31 (151200.15 to 201945.41)	174014.45 (150322.39 to 201440.58)	71768.92 (61224.65 to 84129.14)
HPV 52 type antigen, (N=211;200;206;201)	203994.24 (180491.88 to 230556.91)	196454.98 (172561.35 to 223657.02)	204005.75 (178367.04 to 233329.81)	103497.80 (90571.68 to 118268.69)
HPV 58 type antigen, (N=210;199;205;202)	193735.34 (167223.71 to 224450.13)	186513.90 (161169.95 to 215843.18)	190767.16 (162753.08 to 223603.20)	93456.26 (80147.35 to 108975.18)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting any solicited administration site events

End point title	Number of participants reporting any solicited administration site events

End point description:

Assessed solicited administration site events included pain, redness and swelling at injection site. Any = occurrence of the symptom regardless of intensity grade.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the eDiary for solicited events completed after the administration of each vaccine dose and for whom data were available during the specified period.

End point type	Secondary

End point timeframe:

Within 7 days after each vaccine dose (administered at Day 1, Month 2, and Month 6)

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants				
Any pain, post-dose 1, (N=270;270;269;270)	240	244	245	188
Any redness, post-dose 1, (N=270;270;269;270)	71	70	91	47
Any swelling, post-dose 1, (N=270;270;269;270)	61	54	66	21
Any pain, post-dose 2, (N=257;261;258;260)	208	221	218	185
Any redness, post-dose 2, (N=257;261;258;260)	79	83	69	46

Any swelling, post-dose 2, (N=257;261;258;260)	68	55	59	35
Any pain, post-dose 3, (N=244;247;244;236)	188	191	191	155
Any redness, post-dose 3, (N=244;247;244;236)	61	64	64	37
Any swelling, post-dose 3, (N=244;247;244;236)	59	52	58	24

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting any solicited systemic events

End point title	Number of participants reporting any solicited systemic events

End point description:

Assessed solicited systemic events included fever (defined as body temperature >=37.5°C/99.5°F), headache, myalgia, arthralgia and fatigue. The preferred location for measuring temperature was the axilla. Any = occurrence of the symptom regardless of intensity grade or relation to study vaccination. Analysis was performed on the Exposed Set, which included all participants who received a study vaccine, had the eDiary for solicited events completed after the administration of each vaccine dose and for whom data were available during the specified period.

End point type	Secondary

End point timeframe:

Within 7 days after each vaccine dose (administered at Day 1, Month 2, and Month 6)

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants				
Any fever, post-dose 1, (N=270;270;269;270)	15	12	10	13
Any headache, post-dose 1, (N=270;270;269;270)	137	113	131	127
Any myalgia, post-dose 1, (N=270;270;269;270)	87	105	92	75
Any arthralgia, post-dose 1, (N=270;270;269;270)	27	25	22	23
Any fatigue, post-dose 1, (N=270;270;269;270)	180	166	146	149
Any fever, post-dose 2, (N=257;261;258;260)	8	13	9	16
Any headache, post-dose 2, (N=257;261;258;260)	113	106	118	101
Any myalgia, post-dose 2, (N=257;261;258;260)	80	67	66	56
Any arthralgia, post-dose 2, (N=257;261;258;260)	25	19	21	20
Any fatigue, post-dose 2, (N=257;261;258;260)	152	132	124	127
Any fever, post-dose 3, (N=244;247;244;236)	13	11	11	8

Any headache, post-dose 3, (N=244;247;244;236)	106	81	84	85
Any myalgia, post-dose 3, (N=244;247;244;236)	61	59	54	45
Any arthralgia, post-dose 3, (N=244;247;244;236)	21	15	19	10
Any fatigue, post-dose 3, (N=244;247;244;236)	122	103	103	102

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting any unsolicited AEs

End point title	Number of participants reporting any unsolicited AEs

End point description:

An unsolicited AE is defined as an AE that was not included in the list of solicited events using an eDiary and that was spontaneously communicated by a participant/participant's parent(s)/LAR(s) who has signed the informed consent. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited AE. Any = occurrence of the symptom regardless of intensity grade or relation to study vaccination.
Analysis was performed on the Exposed Set, which included all participants who received a study vaccine and for whom data were available for the specified period after the administration of each vaccine dose.

End point type	Secondary

End point timeframe:

Within 28 days after each vaccine dose (administered at Day 1, Month 2, and Month 6)

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants				
Any unsolicited AEs,post-dose1,(N=270;270;269;270)	70	72	70	70
Any unsolicited AEs,post-dose2,(N=257;261;258;260)	51	38	58	55
Any unsolicited AEs,post-dose3,(N=244;247;244;236)	37	41	45	31

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting potential immune-mediated diseases (pIMDs)

End point title	Number of participants reporting potential immune-mediated diseases (pIMDs)

End point description:

pIMDs are defined as a subset of AEs of special interest (AESIs) that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune etiology.
Analysis was performed on the Exposed set, which included all participants who received a study vaccine and for whom data were available for the specified period.

End point type	Secondary

End point timeframe:

From first vaccination (Day 1) to study end (Month 12)

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants	0	0	2	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with outcomes of reported pregnancies

End point title	Number of participants with outcomes of reported pregnancies

End point description:

The participants with confirmed pregnancies were followed up to determine the outcomes of the reported pregnancies. Pregnancy outcomes were live infant, no apparent congenital anomaly (CA); elective termination, no apparent congenital anomaly (CA), and ectopic pregnancy.
Analysis was performed on the Exposed set, which included all participants who received a study vaccine, who reported any pregnancy and for whom data were available for the specified period.

End point type	Secondary

End point timeframe:

From Day 1 of pregnancy up to study end (Month 12)

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	0[15]	5
Units: Participants				
Live infant, no apparent CA (N=1;3;0;5)	1	2		2
Elective termination, no apparent CA (N=1;3;0;5)	0	1		2
Ectopic pregnancy (N=1;3;0;5)	0	0		1

Notes:

[15] - There were no participants with confirmed pregnancies in this group.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting pregnancies

End point title	Number of participants reporting pregnancies

End point description:

The number of participants who experienced pregnancy while participating in this study is reported. Analysis was performed on the Exposed Set, which included all participants who received a study vaccine and for whom data were available for the specified period.

End point type	Secondary

End point timeframe:

From Day 1 of pregnancy to study end (Month 12)

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	269	270
Units: Participants	1	3	0	5

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV IgG antibody concentrations

End point title	Anti-HPV IgG antibody concentrations

End point description:

Anti-HPV IgG antibody concentrations were determined by ECL assay and expressed as GMCs in AU/mL. The assessed antigens were: HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 33, HPV 45, HPV 52 and HPV 58 type antigens.
Analysis was performed on Per Protocol Set (PPS) for immunogenicity, which included all participants from Exposed Set who met all eligibility criteria, followed the protocol for vaccine administration, adhered to vaccination schedule and blood sampling timings, and had post-vaccination immunogenicity results available for the specified analysis at the specified time points. The PPS excluded those participants with protocol deviations, interfering medications, or intercurrent medical conditions.

End point type	Secondary

End point timeframe:

At Day 1, Month 2, Month 3, Month 6, Month 7 (Month 7 data was also reported in primary outcome measure 14, as pre-specified in protocol) and Month 12

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	265	261	264	261
Units: AU/mL				
geometric mean (confidence interval 95%)				

HPV 6 type antigen, Day 1, (N=264;261;263;261)	3621.58 (3245.94 to 4040.70)	3377.84 (3078.74 to 3705.98)	3124.40 (2891.32 to 3376.27)	2970.65 (2773.07 to 3182.30)
HPV 6 type antigen, Month 2,(N=235;235;234;235)	29701.14 (25289.04 to 34883.02)	29699.92 (25343.87 to 34804.68)	23870.12 (20301.64 to 28065.86)	10488.57 (8707.08 to 12634.56)
HPV 6 type antigen, Month 3,(N=223;232;231;229)	113669.75 (101762.75 to 126969.97)	106471.07 (95221.75 to 119049.37)	100258.49 (88766.41 to 113238.38)	63245.70 (55720.23 to 71787.54)
HPV 6 type antigen, Month 6,(N=225;222;220;212)	42722.37 (37809.13 to 48274.08)	38982.11 (34388.98 to 44188.73)	32792.55 (28876.62 to 37239.51)	18744.02 (15944.74 to 22034.74)
HPV 6 type antigen, Month 7,(N=210;201;206;203)	124141.35 (110854.94 to 139020.20)	117881.81 (103701.90 to 134000.65)	119724.25 (105236.23 to 136206.84)	54710.66 (47259.35 to 63336.80)
HPV 6 type antigen, Month 12,(N=198;200;197;196)	68118.04 (60118.11 to 77182.53)	65112.37 (56605.42 to 74897.80)	59776.32 (51986.07 to 68733.97)	26890.23 (22982.31 to 31462.65)
HPV 11 type antigen, Day 1,(N=265;261;263;261)	2217.95 (1860.09 to 2644.67)	2105.07 (1797.78 to 2464.89)	2013.18 (1725.27 to 2349.12)	1794.54 (1572.94 to 2047.37)
HPV 11 type antigen, Month 2, (N=236;235;230;234)	41618.25 (35124.62 to 49312.39)	37945.17 (32187.34 to 44732.98)	29437.94 (24557.93 to 35287.68)	38760.82 (32890.19 to 45679.30)
HPV 11 type antigen, Month 3, (N=224;232;230;229)	231064.29 (203232.17 to 262707.95)	212805.15 (185957.86 to 243528.46)	192296.18 (167234.40 to 221113.72)	220402.45 (196291.74 to 247474.71)
HPV 11 type antigen, Month 6, (N=226;222;219;212)	77600.50 (68286.55 to 88184.84)	67299.61 (58975.99 to 76798.00)	57076.00 (49315.68 to 66057.49)	68934.35 (59315.95 to 80112.44)
HPV 11 type antigen, Month 7, (N=211;201;205;203)	276225.68 (243524.62 to 313317.91)	250405.46 (217218.09 to 288663.30)	260309.15 (223319.56 to 303425.52)	187507.09 (162968.13 to 215740.99)
HPV 11 type antigen, Month 12, (N=210;209;205;205)	129019.87 (112127.85 to 148456.67)	120984.83 (103575.25 to 141320.73)	117640.77 (100745.01 to 137370.08)	87423.54 (75807.40 to 100819.64)
HPV 16 type antigen, Day 1, (N=258;253;260;254)	684.26 (518.08 to 903.75)	637.99 (490.56 to 829.73)	690.99 (530.87 to 899.40)	525.21 (416.24 to 662.71)
HPV 16 type antigen, Month 2, (N=231;227;230;229)	34918.40 (27711.11 to 44000.21)	31250.65 (24952.39 to 39138.66)	25605.94 (20018.80 to 32752.43)	17397.59 (13647.75 to 22177.73)
HPV 16 type antigen, Month 3,(N=219;224;227;223)	252250.95 (217434.89 to 292641.82)	217440.98 (184257.65 to 256600.37)	201303.15 (171349.89 to 236492.48)	158136.76 (134715.83 to 185629.53)
HPV 16 type antigen, Month 6, (N=219;214;217;208)	101518.07 (87448.85 to 117850.81)	83015.52 (71509.49 to 96372.89)	76558.80 (64740.19 to 90534.95)	56636.27 (47641.12 to 67329.80)
HPV 16 type antigen, Month 7, (N=202;191;202;197)	297480.37 (254936.96 to 347123.34)	272728.60 (231905.67 to 320737.69)	294326.70 (252346.28 to 343290.99)	154844.90 (131166.44 to 182797.86)
HPV 16 type antigen, Month 12,(N=205;202;203;201)	166953.66 (142318.06 to 195853.75)	149269.66 (125174.31 to 178003.24)	168097.78 (142244.20 to 198650.38)	85986.11 (73074.57 to 101178.98)
HPV 18 type antigen, Day 1, (N=265;260;263;260)	1246.54 (1036.67 to 1498.89)	1037.54 (885.47 to 1215.73)	1111.98 (948.66 to 1303.41)	952.51 (830.50 to 1092.44)
HPV 18 type antigen, Month 2, (N=236;233;231;233)	21700.85 (17733.79 to 26555.34)	18029.88 (14988.53 to 21688.36)	16571.70 (13555.92 to 20258.40)	11081.57 (9094.95 to 13502.12)
HPV 18 type antigen, Month 3, (N=224;231;230;229)	137838.37 (118980.92 to 159684.56)	127099.14 (108628.77 to 148710.05)	123342.91 (106423.50 to 142952.21)	79998.43 (68999.00 to 92751.33)

HPV 18 type antigen, Month 6, (N=226;221;219;212)	61676.34 (53576.84 to 71000.30)	51216.03 (44364.44 to 59125.78)	46904.59 (40385.36 to 54476.18)	26774.11 (22940.11 to 31248.90)
HPV 18 type antigen, Month 7,(N=211;200;205;203)	181939.71 (157766.95 to 209816.17)	172862.73 (148117.04 to 201742.65)	183180.47 (156207.11 to 214811.50)	86756.51 (73744.88 to 102063.92)
HPV 18 type antigen, Month 12, (N=210;208;205;205)	84949.48 (72424.07 to 99641.09)	77008.45 (64999.61 to 91235.95)	87334.91 (73919.46 to 103185.10)	36658.81 (31077.43 to 43242.59)
HPV 31 type antigen, Day 1, (N=265;260;264;261)	2748.41 (2441.79 to 3093.53)	2698.81 (2418.57 to 3011.52)	2595.69 (2371.22 to 2841.42)	2358.09 (2189.79 to 2539.33)
HPV 31 type antigen, Month 2,(N=236;234;234;234)	32102.49 (27409.98 to 37598.34)	31733.68 (27111.16 to 37144.34)	27652.57 (23288.94 to 32833.82)	12606.73 (10568.61 to 15037.90)
HPV 31 type antigen, Month 3, (N=224;231;231;229)	161264.11 (142962.02 to 181909.25)	146413.17 (128682.36 to 166587.07)	133818.05 (117762.32 to 152062.83)	89306.66 (79122.92 to 100801.13)
HPV 31 type antigen, Month 6, (N=226;221;220;212)	68516.79 (60395.61 to 77730.00)	61717.39 (54357.98 to 70073.18)	54672.61 (47682.67 to 62687.23)	32131.34 (27928.72 to 36966.36)
HPV 31 type antigen, Month 7, (N=211;200;206;203)	241644.97 (215104.30 to 271460.37)	221590.60 (192869.71 to 254588.41)	230875.63 (202104.78 to 263742.19)	104667.37 (90853.53 to 120581.53)
HPV 31 type antigen, Month 12, (N=205;207;204;204)	137744.87 (120414.00 to 157570.13)	132414.54 (113520.94 to 154452.65)	143396.41 (125201.11 to 164236.01)	55178.34 (47206.87 to 64495.90)
HPV 33 type antigen, Day 1, (N=264;258;260;259)	624.29 (528.02 to 738.12)	578.18 (489.56 to 682.84)	566.26 (487.33 to 657.97)	523.15 (456.49 to 599.54)
HPV 33 type antigen, Month 2,(N=235;231;230;233)	18225.37 (15231.33 to 21807.94)	16873.64 (14013.68 to 20317.26)	14523.05 (12060.26 to 17488.76)	12110.80 (10065.98 to 14571.01)
HPV 33 type antigen, Month 3, (N=220;223;224;223)	124361.59 (108348.67 to 142741.07)	113348.19 (96632.64 to 132955.20)	105284.68 (90915.50 to 121924.92)	87895.71 (76051.15 to 101585.00)
HPV 33 type antigen, Month 6, (N=215;212;201;204)	43736.52 (38187.42 to 50091.97)	41162.19 (35659.00 to 47514.67)	35892.14 (30909.82 to 41677.54)	30563.15 (26208.11 to 35641.88)
HPV 33 type antigen, Month 7, (N=208;200;198;198)	154537.14 (133354.03 to 179085.17)	146931.12 (125717.81 to 171723.90)	150919.88 (128301.37 to 177525.85)	96875.65 (84426.91 to 111159.96)
HPV 33 type antigen, Month 12, (N=209;207;202;203)	79450.21 (68289.18 to 92435.36)	75043.46 (63377.35 to 88857.01)	78826.94 (67275.95 to 92361.18)	46210.95 (40274.75 to 53022.09)
HPV 45 type antigen, Day 1, (N=265;261;264;261)	2431.92 (2233.39 to 2648.10)	2408.58 (2235.09 to 2595.54)	2315.53 (2182.69 to 2456.46)	2217.15 (2109.75 to 2330.02)
HPV 45 type antigen, Month 2, (N=236;235;234;234)	17122.75 (14408.88 to 20347.76)	17097.47 (14406.77 to 20290.70)	14345.03 (12174.35 to 16902.74)	6292.08 (5323.98 to 7436.22)
HPV 45 type antigen, Month 3, (N=224;232;231;229)	137598.43 (121615.96 to 155681.28)	127933.76 (111246.84 to 147123.69)	113479.94 (99528.64 to 129386.85)	55337.26 (48187.68 to 63547.61)
HPV 45 type antigen, Month 6, (N=226;222;220;212)	45691.56 (40155.51 to 51990.83)	41003.12 (35887.26 to 46848.26)	34796.86 (30257.59 to 40017.12)	16153.45 (13858.32 to 18828.69)
HPV 45 type antigen, Month 7, (N=211;201;206;203)	170959.55 (149389.05 to 195644.64)	174740.31 (151200.15 to 201945.41)	174014.45 (150322.39 to 201440.58)	71768.92 (61224.65 to 84129.14)
HPV 45 type antigen, Month 12, (N=210;209;206;205)	78692.83 (68331.72 to 90624.98)	80653.92 (68737.56 to 94636.11)	82021.92 (70210.67 to 95820.12)	29716.61 (25237.04 to 34991.31)

HPV 52 type antigen, Day 1, (N=265;260;264;260)	1641.65 (1464.30 to 1840.48)	1720.51 (1525.62 to 1940.31)	1611.71 (1461.90 to 1776.89)	1549.58 (1410.22 to 1702.72)
HPV 52 type antigen, Month 2,(N=236;233;234;234)	75187.13 (66352.61 to 85197.91)	83557.87 (73382.84 to 95143.74)	73047.67 (63982.97 to 83396.59)	25513.64 (21690.75 to 30010.30)
HPV 52 type antigen, Month 3,(N=224;231;231;228)	185490.54 (166270.48 to 206932.34)	176024.77 (153898.90 to 201331.66)	164122.51 (144482.99 to 186431.62)	95239.18 (84388.59 to 107484.91)
HPV 52 type antigen, Month 6, (N=226;221;220;211)	75353.61 (66851.68 to 84936.78)	77979.01 (68903.19 to 88250.29)	65136.98 (56955.32 to 74493.93)	32359.34 (28207.45 to 37122.36)
HPV 52 type antigen, Month 7, (N=211;200;206;201)	203994.24 (180491.88 to 230556.91)	196454.98 (172561.35 to 223657.02)	204005.75 (178367.04 to 233329.81)	103497.80 (90571.68 to 118268.69)
HPV 52 type antigen, Month 12, (N=207;208;206;203)	123724.49 (107358.59 to 142585.25)	131043.47 (113718.55 to 151007.84)	129678.87 (113220.94 to 148529.14)	54071.66 (46680.66 to 62632.89)
HPV 58 type antigen, Day 1, (N=265;261;263;261)	692.12 (578.03 to 828.72)	615.45 (518.19 to 730.95)	643.72 (548.71 to 755.18)	571.59 (492.66 to 663.17)
HPV 58 type antigen, Month 2, (N=236;235;233;235)	35027.13 (29855.93 to 41094.00)	33438.25 (28322.91 to 39477.45)	30732.28 (26045.95 to 36261.80)	13395.37 (11180.86 to 16048.50)
HPV 58 type antigen, Month 3, (N=224;232;230;229)	158592.29 (139984.81 to 179673.18)	144355.15 (124064.76 to 167963.98)	140028.57 (120462.67 to 162772.43)	79942.78 (69460.78 to 92006.58)
HPV 58 type antigen, Month 6, (N=226;221;219;212)	70466.12 (61803.06 to 80343.50)	66072.77 (57862.76 to 75447.68)	57807.95 (49486.07 to 67529.30)	33188.99 (28367.50 to 38829.98)
HPV 58 type antigen, Month 7, (N=210;199;205;202)	193735.34 (167223.71 to 224450.13)	186513.90 (161169.95 to 215843.18)	190767.16 (162753.08 to 223603.20)	93456.26 (80147.35 to 108975.18)
HPV 58 type antigen, Month 12, (N=202;205;203;204)	114626.18 (98236.18 to 133750.73)	110249.43 (93894.97 to 129452.48)	115765.42 (99881.91 to 134174.76)	51715.19 (44122.31 to 60614.71)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with seroconversion for anti-HPV IgG antibodies

End point title	Number of participants with seroconversion for anti-HPV IgG antibodies

End point description:

Seroconversion is defined as the appearance of antibodies [i.e., concentration greater than or equal to (>=) the lower limit of quantification (LLOQ) value] in the serum of participants seronegative [i.e, concentrations less than (<) the LLOQ value] before vaccination.
The assessed antigens were: HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 33, HPV 45, HPV 52 and HPV 58 type antigens.
The LLOQ values specific to each antigen are as follows: HPV 6 type: LLOQ = 5100 AU/mL; HPV 11 type: LLOQ = 2480 AU/mL; HPV 16 type: LLOQ = 404 AU/mL; HPV 18 type: LLOQ = 1234 AU/mL; HPV 31 type: LLOQ = 3849 AU/mL; HPV 33 type: LLOQ = 617 AU/mL; HPV 45 type: LLOQ = 4079 AU/mL; HPV 52 type: LLOQ = 2352 AU/mL and HPV 58 type: LLOQ = 660 AU/mL.
Analysis was performed on Per Protocol Set (PPS) for immunogenicity. The PPS excluded those participants with protocol deviations, interfering medications, or intercurrent medical conditions.

End point type	Secondary

End point timeframe:

At Month 2, Month 3, Month 6, Month 7 and Month 12

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	217	216	220	222
Units: Participants				
HPV 6 type antigen, Month 2, (N=199;200;209;219)	186	186	189	137
HPV 6 type antigen, Month 3,(N=190;201;207;213)	186	197	201	211
HPV 6 type antigen, Month 6, (N=190;193;198;198)	187	189	191	173
HPV 6 type antigen, Month 7, (N=181;177;184;191)	179	174	178	186
HPV 6 type antigen, Month 12, (N=168;174;178;184)	165	170	174	172
HPV 11 type antigen, Month 2, (N=200;196;195;211)	198	192	190	208
HPV 11 type antigen, Month 3, (N=194;195;196;207)	192	192	191	206
HPV 11 type antigen, Month 6, (N=191;187;188;190)	189	185	183	187
HPV 11 type antigen, Month 7, (N=184;174;174;184)	183	172	169	182
HPV 11 type antigen, Month 12, (N=179;177;174;185)	177	175	171	184
HPV 16 type antigen, Month 2, (N=170;164;171;178)	170	163	169	177
HPV 16 type antigen, Month 3, (N=166;164;172;173)	166	162	170	172
HPV 16 type antigen, Month 6, (N=161;155;166;164)	161	154	165	164
HPV 16 type antigen, Month 7, (N=156;145;152;157)	156	144	152	157
HPV 16 type antigen, Month 12, (N=155;148;152;160)	155	147	151	160
HPV 18 type antigen, Month 2, (N=190;192;188;197)	187	186	185	187
HPV 18 type antigen, Month 3, (N=185;192;188;193)	182	189	185	192
HPV 18 type antigen, Month 6,(N=182;184;181;179)	180	182	178	177
HPV 18 type antigen, Month 7, (N=175;170;167;172)	174	168	164	170
HPV 18 type antigen, Month 12,(N=172;176;166;174)	170	174	163	173
HPV 31 type antigen, Month 2, (N=203;197;196;208)	199	192	189	171
HPV 31 type antigen, Month 3, (N=196;196;196;203)	192	192	191	202
HPV 31 type antigen, Month 6, (N=195;188;189;187)	193	185	185	184
HPV 31 type antigen, Month 7, (N=187;173;174;180)	186	170	170	180
HPV 31 type antigen, Month 12, (N=180;178;173;179)	178	175	171	178
HPV 33 type antigen, Month 2, (N=170;173;171;181)	168	170	168	179

HPV 33 type antigen, Month 3, (N=161;169;169;173)	159	166	166	172
HPV 33 type antigen, Month 6, (N=155;160;155;159)	153	158	152	157
HPV 33 type antigen, Month 7, (N=155;159;151;157)	154	157	148	156
HPV 33 type antigen, Month 12, (N=155;161;153;161)	153	159	151	161
HPV 45 type antigen, Month 2, (N=217;216;220;222)	190	190	191	122
HPV 45 type antigen, Month 3, (N=206;213;218;217)	203	206	213	212
HPV 45 type antigen, Month 6, (N=207;203;208;200)	204	200	203	179
HPV 45 type antigen, Month 7, (N=194;188;194;192)	192	185	189	188
HPV 45 type antigen, Month 12, (N=194;193;194;194)	191	190	190	184
HPV 52 type antigen, Month 2, (N=205;200;200;201)	202	198	197	194
HPV 52 type antigen, Month 3, (N=198;200;199;196)	196	195	195	194
HPV 52 type antigen, Month 6, (N=197;191;190;185)	195	190	187	182
HPV 52 type antigen, Month 7, (N=188;177;177;175)	186	176	175	173
HPV 52 type antigen, Month 12, (N=183;181;177;177)	180	180	174	175
HPV 58 type antigen, Month 2, (N=182;183;173;186)	180	180	170	186
HPV 58 type antigen, Month 3, (N=175;184;174;181)	173	181	170	180
HPV 58 type antigen, Month 6, (N=174;176;167;169)	172	174	163	168
HPV 58 type antigen, Month 7, (N=166;164;155;162)	165	162	152	161
HPV 58 type antigen, Month 12, (N=158;166;153;165)	156	164	151	164

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV neutralizing titers

End point title	Anti-HPV neutralizing titers

End point description:

Anti-HPV neutralizing titers were determined by pseudovirion-based neutralization (PBNA) assay and expressed as geometric mean titers (GMTs). The assessed antigens were: HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 33, HPV 45, HPV 52 and HPV 58 type antigens.
Analysis was performed on Per Protocol Set (PPS) for immunogenicity, which included all participants from Exposed Set who met all eligibility criteria, followed the protocol for vaccine administration, adhered to vaccination schedule and blood sampling timings, and had post-vaccination immunogenicity results available for the specified analysis at the specified time points. The PPS excluded those participants with protocol deviations, interfering medications, or intercurrent medical conditions.

End point type	Secondary

End point timeframe:

At Day 1, Month 3 and Month 7

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	266	261	264	261
Units: Titers				
geometric mean (confidence interval 95%)				
HPV 6 type antigen, Day 1 (N=266;261;264;261)	328.72 (265.51 to 406.99)	280.37 (232.07 to 338.73)	242.72 (206.00 to 286.00)	230.40 (196.29 to 270.43)
HPV 6 type antigen, Month 3 (N=223;229;227;226)	45690.44 (39581.97 to 52741.61)	41126.63 (35026.80 to 48288.74)	39346.74 (33229.37 to 46590.30)	21637.85 (18354.48 to 25508.56)
HPV 6 type antigen, Month 7 (N=149;140;147;141)	82061.27 (70437.95 to 95602.62)	75228.75 (61603.93 to 91866.94)	71805.19 (57989.96 to 88911.69)	33651.69 (27317.93 to 41453.96)
HPV 11 type antigen, Day 1 (N=266;261;264;261)	225.65 (193.18 to 263.58)	210.97 (183.33 to 242.77)	204.12 (178.72 to 233.13)	189.59 (168.38 to 213.47)
HPV 11 type antigen, Month 3 (N=224;231;228;228)	13233.27 (11647.45 to 15035.00)	12081.23 (10600.08 to 13769.35)	10838.85 (9463.76 to 12413.73)	11547.59 (10251.71 to 13007.27)
HPV 11 type antigen, Month 7 (N=149;140;147;142)	17321.54 (14965.94 to 20047.91)	16793.17 (14214.38 to 19839.80)	16315.93 (13807.32 to 19280.31)	12607.96 (10724.69 to 14821.94)
HPV 16 type antigen, Day 1 (N=266;261;264;261)	361.27 (291.97 to 447.02)	325.48 (270.30 to 391.92)	356.83 (294.43 to 432.46)	277.19 (236.97 to 324.24)
HPV 16 type antigen, Month 3 (N=224;232;231;229)	35416.74 (29603.66 to 42371.29)	31018.79 (26065.77 to 36912.98)	29774.15 (24560.51 to 36094.53)	21870.13 (18225.32 to 26243.85)
HPV 16 type antigen, Month 7 (N=149;140;147;142)	83674.41 (68253.56 to 102579.36)	75779.10 (59852.62 to 95943.55)	81101.64 (64972.49 to 101234.78)	37820.19 (29988.35 to 47697.42)
HPV 18 type antigen, Day 1 (N=266;261;264;261)	73.24 (61.47 to 87.27)	63.14 (54.42 to 73.25)	64.18 (55.86 to 73.73)	57.05 (50.67 to 64.22)
HPV 18 type antigen, Month 3 (N=225;232;230;229)	3994.46 (3295.05 to 4842.33)	3610.97 (3001.43 to 4344.30)	3528.45 (2908.77 to 4280.15)	1705.98 (1394.09 to 2087.65)
HPV 18 type antigen, Month 7 (N=149;140;147;142)	9236.06 (7400.65 to 11526.67)	9539.94 (7507.03 to 12123.35)	9756.59 (7610.84 to 12507.29)	3518.33 (2745.04 to 4509.45)
HPV 31 type antigen, Day 1 (N=266;261;264;261)	86.49 (72.60 to 103.02)	85.98 (71.95 to 102.75)	86.03 (73.71 to 100.41)	76.01 (66.25 to 87.22)
HPV 31 type antigen, Month 3 (N=225;232;231;229)	22472.04 (19266.57 to 26210.81)	21241.61 (17729.34 to 25449.67)	18317.84 (15540.80 to 21591.12)	9156.79 (7772.33 to 10787.86)
HPV 31 type antigen, Month 7 (N=149;140;147;142)	69730.78 (56719.94 to 85726.14)	64413.46 (49797.87 to 83318.69)	59252.25 (46942.33 to 74790.26)	17581.92 (14014.44 to 22057.53)
HPV 33 type antigen, Day 1 (N=266;261;264;261)	207.88 (185.90 to 232.47)	216.99 (191.26 to 246.17)	200.17 (181.73 to 220.49)	186.32 (172.16 to 201.64)
HPV 33 type antigen, Month 3 (N=225;232;230;229)	17034.78 (14730.51 to 19699.52)	15199.08 (12954.60 to 17832.44)	12923.25 (10949.50 to 15252.79)	9132.50 (7752.49 to 10758.18)
HPV 33 type antigen, Month 7 (N=149;140;147;142)	33246.87 (27979.03 to 39506.53)	30752.43 (25717.48 to 36773.13)	27855.80 (22482.02 to 34514.06)	18696.71 (15656.33 to 22327.51)

HPV 45 type antigen, Day 1 (N=266;261;264;261)	55.65 (48.99 to 63.21)	61.43 (53.20 to 70.94)	53.80 (48.31 to 59.93)	49.89 (45.89 to 54.25)
HPV 45 type antigen, Month 3 (N=225;232;230;229)	13822.73 (11844.34 to 16131.59)	13197.57 (11085.72 to 15711.73)	11113.74 (9429.52 to 13098.77)	3488.90 (2963.94 to 4106.83)
HPV 45 type antigen, Month 7 (N=149;139;146;142)	25204.55 (20693.56 to 30698.90)	24537.36 (20030.78 to 30057.86)	22748.14 (18260.65 to 28338.42)	7853.20 (6210.60 to 9930.24)
HPV 52 type antigen, Day 1 (N=266;261;264;261)	78.63 (68.76 to 89.92)	85.37 (73.69 to 98.89)	75.58 (67.66 to 84.43)	72.37 (64.86 to 80.75)
HPV 52 type antigen, Month 3 (N=225;232;231;229)	18288.04 (16184.95 to 20664.41)	15548.20 (13427.71 to 18003.57)	14606.62 (12634.89 to 16886.04)	7903.98 (6883.36 to 9075.93)
HPV 52 type antigen, Month 7 (N=149;140;147;142)	21604.03 (18522.86 to 25197.74)	20617.17 (17543.87 to 24228.84)	20285.76 (17088.28 to 24081.54)	10904.65 (9006.10 to 13203.43)
HPV 58 type antigen, Day 1 (N=266;261;264;261)	87.31 (72.70 to 104.85)	87.15 (72.02 to 105.46)	82.06 (69.30 to 97.16)	73.81 (63.25 to 86.13)
HPV 58 type antigen, Month 3 (N=225;232;231;229)	31623.27 (27319.75 to 36604.69)	27936.10 (23519.92 to 33181.47)	27246.89 (22979.23 to 32307.15)	11650.18 (9904.82 to 13703.09)
HPV 58 type antigen, Month 7 (N=149;140;147;142)	51354.94 (42792.24 to 61631.03)	46896.70 (38584.84 to 56999.07)	46983.15 (37929.98 to 58197.15)	22245.13 (18114.56 to 27317.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV neutralizing titers in a subset of participants

End point title	Anti-HPV neutralizing titers in a subset of participants

End point description:

Anti-HPV neutralizing titers were determined by PBNA assay and expressed as GMTs. The assessed antigens were: HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 33, HPV 45, HPV 52 and HPV 58 type antigens.
Analysis was performed on a subset of participants from Per Protocol Set (PPS) for immunogenicity with post-vaccination immunogenicity results available for the specified analysis at the specified time point.

End point type	Secondary

End point timeframe:

At Month 2

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	91	89	88
Units: Titers				
geometric mean (confidence interval 95%)				
HPV 6 type antigen (N=84;82;82;80)	13438.35 (9145.74 to 19745.74)	11275.45 (7643.73 to 16632.69)	6658.75 (4614.67 to 9608.24)	3364.11 (2041.48 to 5543.64)
HPV 11 type antigen (N=92;91;89;88)	2592.37 (1870.39 to 3593.02)	2441.65 (1755.07 to 3396.81)	1531.82 (1119.26 to 2096.46)	2912.25 (2156.54 to 3932.76)

HPV 16 type antigen (N=92;91;89;88)	5888.86 (3547.05 to 9776.79)	4711.97 (2939.99 to 7551.96)	2947.73 (1742.01 to 4987.98)	2987.06 (1757.29 to 5077.45)
HPV 18 type antigen (N=92;91;89;88)	603.31 (365.97 to 994.56)	447.98 (286.20 to 701.20)	379.32 (237.94 to 604.69)	259.14 (161.99 to 414.56)
HPV 31 type antigen (N=92;91;89;88)	4005.68 (2737.23 to 5861.95)	3612.79 (2463.24 to 5298.82)	2193.35 (1620.34 to 2969.00)	1183.70 (775.15 to 1807.59)
HPV 33 type antigen (N=92;91;89;88)	1830.91 (1260.56 to 2659.31)	1782.19 (1234.63 to 2572.59)	1097.86 (810.20 to 1487.66)	1182.00 (818.69 to 1706.55)
HPV 45 type antigen (N=92;91;89;88)	1382.24 (973.72 to 1962.14)	1657.88 (1178.35 to 2332.56)	1119.04 (824.21 to 1519.32)	369.17 (267.20 to 510.05)
HPV 52 type antigen (N=92;91;89;88)	9664.68 (7775.37 to 12013.06)	9081.81 (7013.61 to 11759.89)	8379.90 (6544.29 to 10730.38)	4052.45 (3070.88 to 5347.77)
HPV 58 type antigen (N=92;91;89;88)	5169.27 (3769.39 to 7089.05)	5519.36 (3960.66 to 7691.47)	3848.83 (2823.14 to 5247.19)	1569.91 (1070.81 to 2301.63)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with seroconversion for anti-HPV neutralizing antibodies

End point title	Number of participants with seroconversion for anti-HPV neutralizing antibodies

End point description:

Seroconversion is defined as the appearance of antibodies (i.e., titer >=LLOQ value) in the serum of participants seronegative (i.e, titer <LLOQ value) before vaccination.
The assessed antigens were: HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 33, HPV 45, HPV 52 and HPV 58 type antigens.
The LLOQ values specific to each antigen are as follows: HPV 6 type: LLOQ = 269 titers; HPV 11 type: LLOQ = 279 titers; HPV 16 type: LLOQ = 339 titers; HPV 18 type: LLOQ = 84 titers; HPV 31 type: LLOQ = 96 titers; HPV 33 type: LLOQ = 323 titers; HPV 45 type: LLOQ = 76 titers; HPV 52 type: LLOQ = 104 titers and HPV 58 type: LLOQ = 95 titers.
Analysis was performed on Per Protocol Set (PPS) for immunogenicity. The PPS excluded those participants with protocol deviations, interfering medications, or intercurrent medical conditions.

End point type	Secondary

End point timeframe:

At Month 3 and Month 7

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	208	211	216	217
Units: Participants				
HPV 6 type antigen, Month 3 (N=173;182;186;194)	172	179	181	192
HPV 6 type antigen, Month 7 (N=112;111;120;120)	112	109	116	119

HPV 11 type antigen, Month 3 (N=199;200;203;208)	195	196	198	206
HPV 11 type antigen, Month 7 (N=132;121;132;129)	130	118	128	127
HPV 16 type antigen, Month 3 (N=189;188;191;199)	187	185	187	196
HPV 16 type antigen, Month 7 (N=125;111;115;123)	124	109	114	121
HPV 18 type antigen, Month 3 (N=195;204;198;203)	192	199	193	195
HPV 18 type antigen, Month 7 (N=131;122;123;123)	129	119	120	120
HPV 31 type antigen, Month 3 (N=190;188;187;192)	189	184	186	192
HPV 31 type antigen, Month 7 (N=120;109;116;118)	120	107	116	118
HPV 33 type antigen, Month 3 (N=208;211;216;217)	204	206	210	215
HPV 33 type antigen, Month 7 (N=139;123;140;132)	136	121	135	131
HPV 45 type antigen, Month 3 (N=187;188;192;188)	185	184	189	186
HPV 45 type antigen, Month 7 (N=124;113;122;117)	122	111	119	116
HPV 52 type antigen, Month 3 (N=188;191;193;194)	186	188	189	193
HPV 52 type antigen, Month 7 (N=121;112;119;118)	120	111	118	116
HPV 58 type antigen, Month 3 (N=195;192;195;195)	193	188	190	193
HPV 58 type antigen, Month 7 (N=128;116;121;118)	126	114	118	116

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between anti-HPV IgG antibody concentration and anti-HPV neutralizing antibody titers

End point title	Correlation between anti-HPV IgG antibody concentration and anti-HPV neutralizing antibody titers

End point description:

The Pearson coefficient of correlation between anti-HPV IgG antibody concentration and anti-HPV neutralizing antibody titers was calculated for each study group and for each antigen. The Pearson correlation was computed by the log10-transformation of specific antibody concentrations.
Analysis was performed on samples with both concentration and titer values collected from the participants included in the Per Protocol Set for analysis of immunogenicity, which were available for the specified analysis at the specified time points.
On each row, S represents the total number of samples analyzed, and N represents the total number of participants analyzed.

End point type	Secondary

End point timeframe:

At Day 1, Month 2, Month 3 and Month 7

End point values	HPV9 High Group	HPV9 Med Group	HPV9 Low Group	Gar9 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	266	263	265	265
Units: Correlation coefficient				
number (not applicable)				
HPV6,Day1(N=266;263;265;265.S=42;37;28;21)	0.850	0.818	0.756	0.830
HPV6,Month2(N=238;239;236;238.S=61;66;70;48)	0.824	0.851	0.766	0.786
HPV6,Month3(N=228;235;233;232.S=175;185;190;203)	0.813	0.790	0.789	0.867
HPV6,Month7(N=214;206;207;206.S=95;81;89;118)	0.820	0.810	0.786	0.892
HPV11,Day1(N=266;263;265;265.S=30;30;32;26)	0.907	0.921	0.951	0.932
HPV11,Month2(N=238;239;236;238.S=73;72;73;75)	0.840	0.831	0.807	0.820
HPV11,Month3(N=228;235;233;232.S=173;176;182;187)	0.806	0.808	0.820	0.856
HPV11,Month7(N=214;206;207;206.S=91;79;86;104)	0.659	0.839	0.787	0.820
HPV16,Day1(N=266;263;265;265.S=49;51;54;40)	0.934	0.927	0.918	0.951
HPV16,Month2(N=238;239;236;238.S=80;79;70;73)	0.965	0.951	0.880	0.958
HPV16,Month3(N=228;235;233;232.S=211;223;213;225)	0.871	0.862	0.827	0.904
HPV16,Month7(N=214;206;207;206.S=143;133;138;135)	0.866	0.893	0.894	0.894
HPV18,Day1(N=266;263;265;265.S=38;31;39;30)	0.903	0.863	0.896	0.920
HPV18,Month2(N=238;239;236;238.S=61;65;64;54)	0.885	0.885	0.811	0.866
HPV18,Month3(N=228;235;233;232.S=203;212;203;213)	0.881	0.880	0.860	0.884
HPV18,Month7(N=214;206;207;206.S=130;127;117;133)	0.899	0.871	0.881	0.905
HPV31,Day1(N=266;263;265;265.S=34;38;42;25)	0.751	0.811	0.708	0.344
HPV31,Month2(N=238;239;236;238.S=83;84;83;77)	0.768	0.820	0.824	0.745
HPV31,Month3(N=228;235;233;232.S=194;207;208;218)	0.800	0.800	0.798	0.845
HPV31,Month7(N=214;206;207;206.S=107;96;101;127)	0.814	0.824	0.806	0.842
HPV33,Day1(N=266;263;265;265.S=22;23;20;15)	0.664	0.843	0.831	0.886
HPV33,Month2(N=238;239;236;238.S=65;69;68;63)	0.794	0.790	0.672	0.711
HPV33,Month3(N=228;235;233;232.S=184;188;194;203)	0.811	0.767	0.783	0.859
HPV33,Month7(N=214;206;207;206.S=80;78;77;114)	0.649	0.807	0.789	0.768
HPV45,Day1(N=266;263;265;265.S=19;23;18;14)	0.721	0.885	0.692	0.557
HPV45,Month2(N=238;239;236;238.S=78;77;73;57)	0.834	0.859	0.740	0.805
HPV45,Month3(N=228;235;233;232.S=192;193;199;220)	0.846	0.863	0.799	0.882

HPV45,Month7(N=214;206;207;206.S=86;74;87;127)	0.869	0.870	0.737	0.882
HPV52,Day1(N=266;263;265;265.S=31;37;39;28)	0.809	0.790	0.847	0.804
HPV52,Month2(N=238;239;236;238.S=77;76;78;78)	0.748	0.832	0.606	0.767
HPV52,Month3(N=228;235;233;232.S=149;151;172;203)	0.797	0.821	0.754	0.861
HPV52,Month7(N=214;206;207;206.S=77;70;67;113)	0.777	0.834	0.829	0.831
HPV58,Day1(N=266;263;265;265.S=40;35;38;31)	0.632	0.816	0.791	0.831
HPV58,Month2(N=238;239;236;238.S=79;77;85;80)	0.666	0.733	0.666	0.803
HPV58,Month3(N=228;235;233;232.S=169;172;171;210)	0.831	0.721	0.789	0.852
HPV58,Month7(N=214;206;207;206.S=63;69;67;121)	0.851	0.860	0.825	0.851

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: during the 7-day follow-up period after any vaccination. Unsolicited AEs: during the 28-day follow-up period after any vaccination. All-cause mortality, SAEs and pIMDs: from first vaccination (Day 1) up to study end (Month 12).

Adverse event reporting additional description:

All events presented in the Serious Adverse Events and Non Serious Adverse Events modules are reported for the Exposed Set population during the specified time frames.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	HPV9 High Group

Reporting group description:

Participants received 3 doses of the high formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.

Reporting group title	Gar9 Group

Reporting group description:

Participants received 3 doses of the marketed Human Papilloma Virus (HPV) vaccine (Gardasil 9) at Day 1, Month 2, and Month 6.

Reporting group title	HPV9 Low Group

Reporting group description:

Participants received 3 doses of the low formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.

Reporting group title	HPV9 Med Group

Reporting group description:

Participants received 3 doses of the medium formulation of Human Papilloma Virus 9-valent (HPV9) investigational adjuvanted vaccine at Day 1, Month 2, and Month 6.

Serious adverse events	HPV9 High Group	Gar9 Group	HPV9 Low Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 270 (0.37%)	7 / 270 (2.59%)	2 / 269 (0.74%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (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
Joint injury			

subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Tibia fracture			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Surgical and medical procedures			
Gastric bypass			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (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
Nasal septal operation			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (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			
Ruptured ectopic pregnancy			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (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
Colitis ulcerative			

subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Personality disorder			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Affective disorder			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Appendiceal abscess			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (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
Chronic tonsillitis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bartholin's abscess			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	HPV9 Med Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 270 (1.48%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint injury			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Gastric bypass			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nasal septal operation			

subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Ruptured ectopic pregnancy			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Personality disorder			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Affective disorder			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendiceal abscess			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infectious mononucleosis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic tonsillitis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bartholin's abscess			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	HPV9 High Group	Gar9 Group	HPV9 Low Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	260 / 270 (96.30%)	254 / 270 (94.07%)	262 / 269 (97.40%)
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Haematoma			

subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	126 / 270 (46.67%)	89 / 270 (32.96%)	139 / 269 (51.67%)
occurrences (all)	211	130	224
Injection site pruritus			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	1
Administration site swelling			
subjects affected / exposed	113 / 270 (41.85%)	59 / 270 (21.85%)	106 / 269 (39.41%)
occurrences (all)	188	80	183
Asthenia			
subjects affected / exposed	2 / 270 (0.74%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	2	1	1
Axillary pain			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	2 / 269 (0.74%)
occurrences (all)	0	1	2
Chest pain			
subjects affected / exposed	2 / 270 (0.74%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	2	0	1
Chills			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	3
Fatigue			
subjects affected / exposed	213 / 270 (78.89%)	192 / 270 (71.11%)	192 / 269 (71.38%)
occurrences (all)	458	379	373
Induration			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	2	0
Influenza like illness			
subjects affected / exposed	2 / 270 (0.74%)	4 / 270 (1.48%)	0 / 269 (0.00%)
occurrences (all)	2	5	0
Injection site bruising			

subjects affected / exposed	1 / 270 (0.37%)	2 / 270 (0.74%)	0 / 269 (0.00%)
occurrences (all)	1	2	0
Injection site granuloma			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma			
subjects affected / exposed	1 / 270 (0.37%)	2 / 270 (0.74%)	0 / 269 (0.00%)
occurrences (all)	1	2	0
Injection site induration			
subjects affected / exposed	4 / 270 (1.48%)	3 / 270 (1.11%)	1 / 269 (0.37%)
occurrences (all)	5	5	1
Injection site mass			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	2 / 269 (0.74%)
occurrences (all)	0	1	2
Injection site nodule			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	2
Injection site pain			
subjects affected / exposed	2 / 270 (0.74%)	2 / 270 (0.74%)	0 / 269 (0.00%)
occurrences (all)	3	2	0
Administration site pain			
subjects affected / exposed	255 / 270 (94.44%)	235 / 270 (87.04%)	256 / 269 (95.17%)
occurrences (all)	636	528	654
Injection site reaction			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			

subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	34 / 270 (12.59%)	33 / 270 (12.22%)	25 / 269 (9.29%)
occurrences (all)	38	37	31
Swelling			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	1
Thirst			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Vaccination site bruising			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Vaccination site induration			
subjects affected / exposed	1 / 270 (0.37%)	2 / 270 (0.74%)	4 / 269 (1.49%)
occurrences (all)	1	4	4
Vaccination site nodule			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Vaccination site pain			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Vaccination site pruritus			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Vaccination site swelling			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	2 / 269 (0.74%)
occurrences (all)	0	0	2
General symptom	Additional description: Other symptoms/illnesses or reactions		
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			

Drug hypersensitivity			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	1	0
Seasonal allergy			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	13 / 270 (4.81%)	9 / 270 (3.33%)	11 / 269 (4.09%)
occurrences (all)	13	9	17
Menstruation delayed			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Uterine pain			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Vaginal discharge			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Menstruation irregular			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 270 (0.37%)	4 / 270 (1.48%)	3 / 269 (1.12%)
occurrences (all)	1	4	3
Rhinitis allergic			

subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	2 / 270 (0.74%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	2	1	1
Dyspnoea			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	1	0
Sinus pain			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 270 (0.37%)	2 / 270 (0.74%)	0 / 269 (0.00%)
occurrences (all)	1	2	0
Anxiety disorder			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Bipolar disorder			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0

Depression			
subjects affected / exposed	3 / 270 (1.11%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	3	0	1
Insomnia			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood prolactin increased			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Body temperature decreased			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Human papilloma virus test positive			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Platelet count increased			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Clavicle fracture			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	1
Foot fracture			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			

subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Joint injury			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Procedural headache			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 270 (0.00%)	2 / 270 (0.74%)	0 / 269 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 270 (1.11%)	4 / 270 (1.48%)	3 / 269 (1.12%)
occurrences (all)	3	4	3
Carpal tunnel syndrome			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Dizziness postural			

subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	1 / 270 (0.37%)	3 / 270 (1.11%)	5 / 269 (1.86%)
occurrences (all)	1	3	5
Multiple sclerosis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	1	0
Paraesthesia			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	2 / 269 (0.74%)
occurrences (all)	0	0	2
Presyncope			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	2	0	1
Syncope			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Tension headache			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	1	0
Thoracic radiculopathy			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	194 / 270 (71.85%)	179 / 270 (66.30%)	187 / 269 (69.52%)
occurrences (all)	384	337	354
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1

Lymphadenopathy			
subjects affected / exposed	3 / 270 (1.11%)	1 / 270 (0.37%)	3 / 269 (1.12%)
occurrences (all)	3	1	6
Lymphadenitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Lymph node pain			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	2 / 269 (0.74%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Ear inflammation			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	3 / 270 (1.11%)	3 / 270 (1.11%)	2 / 269 (0.74%)
occurrences (all)	3	4	2
Tinnitus			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Chalazion			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Eye inflammation			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Lacrimation increased			

subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	5 / 270 (1.85%)	1 / 270 (0.37%)	2 / 269 (0.74%)
occurrences (all)	5	1	4
Abdominal pain lower			
subjects affected / exposed	2 / 270 (0.74%)	1 / 270 (0.37%)	3 / 269 (1.12%)
occurrences (all)	2	1	3
Abdominal pain upper			
subjects affected / exposed	3 / 270 (1.11%)	3 / 270 (1.11%)	1 / 269 (0.37%)
occurrences (all)	3	3	1
Anal fissure			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	4 / 270 (1.48%)	5 / 270 (1.85%)	2 / 269 (0.74%)
occurrences (all)	4	5	2
Dry mouth			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	3 / 270 (1.11%)	1 / 270 (0.37%)	3 / 269 (1.12%)
occurrences (all)	3	1	3
Gastritis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Gastrointestinal pain			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	2 / 269 (0.74%)
occurrences (all)	0	0	2

Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	2 / 270 (0.74%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	12 / 270 (4.44%)	7 / 270 (2.59%)	15 / 269 (5.58%)
occurrences (all)	14	7	21
Odynophagia			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	3 / 270 (1.11%)	0 / 270 (0.00%)	2 / 269 (0.74%)
occurrences (all)	3	0	2
Abdominal pain			
subjects affected / exposed	5 / 270 (1.85%)	9 / 270 (3.33%)	5 / 269 (1.86%)
occurrences (all)	5	10	5
Skin and subcutaneous tissue disorders			
Rosacea			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Acne			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	0	1	1
Dermatitis allergic			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	0	1	1
Eczema			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Erythema			

subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	2	0
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Lipohypertrophy			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Macule			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Pityriasis rosea			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	2 / 270 (0.74%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	2	0	0
Psoriasis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	0	1	1
Rash erythematous			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Skin burning sensation			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Skin discolouration			

subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Polycystic ovarian syndrome			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	55 / 270 (20.37%)	45 / 270 (16.67%)	47 / 269 (17.47%)
occurrences (all)	75	56	65
Arthritis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	1 / 270 (0.37%)	5 / 270 (1.85%)	4 / 269 (1.49%)
occurrences (all)	1	5	4
Enthesopathy			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	137 / 270 (50.74%)	118 / 270 (43.70%)	126 / 269 (46.84%)
occurrences (all)	228	178	213
Pain in extremity			

subjects affected / exposed	1 / 270 (0.37%)	2 / 270 (0.74%)	1 / 269 (0.37%)
occurrences (all)	1	2	1
Pain in jaw			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Spinal pain			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Synovial cyst			
subjects affected / exposed	2 / 270 (0.74%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	2	0	0
Tendonitis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 270 (0.00%)	2 / 270 (0.74%)	0 / 269 (0.00%)
occurrences (all)	0	2	0
Bacterial vaginosis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	1
Infectious mononucleosis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Chlamydial infection			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Chronic sinusitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 270 (0.00%)	2 / 270 (0.74%)	0 / 269 (0.00%)
occurrences (all)	0	2	0
COVID-19			
subjects affected / exposed	6 / 270 (2.22%)	7 / 270 (2.59%)	2 / 269 (0.74%)
occurrences (all)	6	7	2

Cystitis			
subjects affected / exposed	1 / 270 (0.37%)	3 / 270 (1.11%)	1 / 269 (0.37%)
occurrences (all)	1	3	1
Enterovirus infection			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	2 / 269 (0.74%)
occurrences (all)	0	1	2
Fungal infection			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal viral infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	1
Genitourinary tract infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Helicobacter infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Herpes virus infection			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	0	1	1
Herpes zoster			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	0	1	1
Impetigo			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	4 / 270 (1.48%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	4	0	0

Influenza			
subjects affected / exposed	2 / 270 (0.74%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	2	0	1
Urinary tract infection			
subjects affected / exposed	0 / 270 (0.00%)	2 / 270 (0.74%)	1 / 269 (0.37%)
occurrences (all)	0	2	1
Lyme disease			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	10 / 270 (3.70%)	6 / 270 (2.22%)	10 / 269 (3.72%)
occurrences (all)	11	6	11
Oral herpes			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	1	1	3
Otitis externa			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	2 / 270 (0.74%)	1 / 270 (0.37%)	2 / 269 (0.74%)
occurrences (all)	2	1	2
Pharyngitis streptococcal			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Pulpitis dental			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Pyelonephritis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	1 / 269 (0.37%)
occurrences (all)	1	1	1
Respiratory tract infection viral			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	3

Rhinitis			
subjects affected / exposed	3 / 270 (1.11%)	5 / 270 (1.85%)	6 / 269 (2.23%)
occurrences (all)	3	5	6
Sinusitis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	1	0	1
Tracheitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	17 / 270 (6.30%)	15 / 270 (5.56%)	11 / 269 (4.09%)
occurrences (all)	17	16	15
Laryngitis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	1 / 270 (0.37%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	1	1	0
Viral infection			
subjects affected / exposed	3 / 270 (1.11%)	0 / 270 (0.00%)	1 / 269 (0.37%)
occurrences (all)	3	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 270 (0.37%)	2 / 270 (0.74%)	2 / 269 (0.74%)
occurrences (all)	2	2	2
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Vulvovaginitis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Folate deficiency			

subjects affected / exposed	0 / 270 (0.00%)	1 / 270 (0.37%)	0 / 269 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 270 (0.00%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	1 / 270 (0.37%)	0 / 270 (0.00%)	0 / 269 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	HPV9 Med Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	265 / 270 (98.15%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	131 / 270 (48.52%)		
occurrences (all)	217		
Injection site pruritus			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Administration site swelling			
subjects affected / exposed	99 / 270 (36.67%)		
occurrences (all)	161		
Asthenia			
subjects affected / exposed	2 / 270 (0.74%)		
occurrences (all)	2		
Axillary pain			

subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Chest pain				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Chills				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	205 / 270 (75.93%)			
occurrences (all)	402			
Induration				
subjects affected / exposed	3 / 270 (1.11%)			
occurrences (all)	4			
Influenza like illness				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Injection site bruising				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Injection site granuloma				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	2			
Injection site haematoma				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Injection site induration				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Injection site mass				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Injection site nodule				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Injection site pain				

subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Administration site pain				
subjects affected / exposed	262 / 270 (97.04%)			
occurrences (all)	656			
Injection site reaction				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Mucosal inflammation				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Pain				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Peripheral swelling				
subjects affected / exposed	2 / 270 (0.74%)			
occurrences (all)	2			
Pyrexia				
subjects affected / exposed	37 / 270 (13.70%)			
occurrences (all)	37			
Swelling				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Thirst				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Vaccination site bruising				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Vaccination site induration				
subjects affected / exposed	3 / 270 (1.11%)			
occurrences (all)	4			
Vaccination site nodule				

subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Vaccination site pain			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Vaccination site pruritus			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Vaccination site swelling			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	3 / 270 (1.11%)		
occurrences (all)	4		
General symptom	Additional description: Other symptoms/illnesses or reactions		
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Hypersensitivity			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Seasonal allergy			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	11 / 270 (4.07%)		
occurrences (all)	14		
Menstruation delayed			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	2		
Uterine pain			

subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Vaginal discharge			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Menstruation irregular			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	3 / 270 (1.11%)		
occurrences (all)	3		
Rhinitis allergic			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Dyspnoea exertional			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Dyspnoea			

subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Sinus pain			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Anxiety disorder			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Bipolar disorder			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	3 / 270 (1.11%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Investigations			
Blood prolactin increased			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Body temperature decreased			

subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Human papilloma virus test positive			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Platelet count increased			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Clavicle fracture			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Foot fracture			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Joint dislocation			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Joint injury			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Limb injury			

subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Procedural headache			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Carpal tunnel syndrome			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Dizziness postural			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Multiple sclerosis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Neuralgia			

subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Tension headache			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Thoracic radiculopathy			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	180 / 270 (66.67%)		
occurrences (all)	319		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	5 / 270 (1.85%)		
occurrences (all)	6		
Lymphadenitis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Lymph node pain			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear congestion			

subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Ear inflammation			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Chalazion			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Eye inflammation			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Lacrimation increased			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 270 (0.74%)		
occurrences (all)	2		
Abdominal pain lower			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Abdominal pain upper			

subjects affected / exposed	5 / 270 (1.85%)			
occurrences (all)	5			
Anal fissure				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	6 / 270 (2.22%)			
occurrences (all)	6			
Dry mouth				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Gastrointestinal pain				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Haemorrhoidal haemorrhage				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Haemorrhoids				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	5 / 270 (1.85%)			
occurrences (all)	5			
Odynophagia				

subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	3 / 270 (1.11%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Rosacea			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Acne			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			
subjects affected / exposed	2 / 270 (0.74%)		
occurrences (all)	2		
Eczema			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Haemorrhage subcutaneous			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Lipohypertrophy			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		

Macule subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Pityriasis rosea subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 1		
Psoriasis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	3 / 270 (1.11%) 3		
Rash erythematous subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 1		
Rash pruritic subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Skin burning sensation subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Skin discolouration subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 1		
Endocrine disorders Autoimmune thyroiditis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Polycystic ovarian syndrome			

subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	44 / 270 (16.30%)		
occurrences (all)	60		
Arthritis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	2 / 270 (0.74%)		
occurrences (all)	2		
Enthesopathy			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	133 / 270 (49.26%)		
occurrences (all)	231		
Pain in extremity			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Pain in jaw			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Spinal pain			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Synovial cyst			

subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Tendonitis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 270 (0.37%)		
occurrences (all)	1		
Bacterial vaginosis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Infectious mononucleosis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Chlamydial infection			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Chronic sinusitis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	5 / 270 (1.85%)		
occurrences (all)	5		
Cystitis			
subjects affected / exposed	9 / 270 (3.33%)		
occurrences (all)	9		
Enterovirus infection			
subjects affected / exposed	2 / 270 (0.74%)		
occurrences (all)	2		
Fungal infection			
subjects affected / exposed	0 / 270 (0.00%)		
occurrences (all)	0		

Gastroenteritis				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Gastrointestinal infection				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Gastrointestinal viral infection				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Genitourinary tract infection				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Helicobacter infection				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Herpes virus infection				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Impetigo				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Bronchitis				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	3 / 270 (1.11%)			
occurrences (all)	3			
Urinary tract infection				
subjects affected / exposed	1 / 270 (0.37%)			
occurrences (all)	1			
Lyme disease				
subjects affected / exposed	0 / 270 (0.00%)			
occurrences (all)	0			

Nasopharyngitis subjects affected / exposed occurrences (all)	5 / 270 (1.85%) 6			
Oral herpes subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0			
Otitis externa subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0			
Pharyngitis subjects affected / exposed occurrences (all)	2 / 270 (0.74%) 2			
Pharyngitis streptococcal subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 1			
Pulpitis dental subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 1			
Pyelonephritis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0			
Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 2			
Respiratory tract infection viral subjects affected / exposed occurrences (all)	4 / 270 (1.48%) 4			
Rhinitis subjects affected / exposed occurrences (all)	4 / 270 (1.48%) 4			
Sinusitis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0			
Tonsillitis subjects affected / exposed occurrences (all)	2 / 270 (0.74%) 2			

Tracheitis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	11 / 270 (4.07%) 11		
Laryngitis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Vaginal infection subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 1		
Viral infection subjects affected / exposed occurrences (all)	2 / 270 (0.74%) 2		
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Vulvovaginitis subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Metabolism and nutrition disorders Folate deficiency subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 270 (0.37%) 1		
Decreased appetite subjects affected / exposed occurrences (all)	0 / 270 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 June 2022	This is a country-specific amendment for Germany to clarify that only adults between and including 18 to 26 years of age would be included in the study in this country.
23 September 2022	The purpose of this amendment was to allow for additional iSRC review(s) in case of enrollment delay to mitigate the risk that the iSRC for all 48 Step 1 participants may occur after the allowed interval range for their second vaccination dose. Additionally, the country-specific amendment for Germany (Protocol Amendment 1/DEU-1) to clarify that only adults between and including 18 to 26 years of age would be included in the study in Germany was incorporated. Further updates (as summarized below) were made to clarify the study procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported